INVESTIGATING SKILL ACQUISITION IN THE ABSENCE OF PHYSICAL PRACTICE: MOTOR IMAGERY-BASED SKILL ACQUISITION AND THE ROLE OF THE INFERIOR PARIETAL LOBULE

by

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TABLE OF CONTENTS

LIST OF TABLES v

LIST OF FIGURES vi

ABSTRACT vii

LIST OF ABBREVIATIONS USED viii

ACKNOWLEDGEMENTS ix

CHAPTER 1 INTRODUCTION 1

CHAPTER 2 BACKGROUND AND RATIONALE 4

2.1 MOTOR IMAGERY AS A FORM OF PRACTICE 4

2.2 MECHANISM FOR MI AS A MODALITY OF SKILL ACQUISITION 7

2.3 MOTOR IMAGERY AS A TOOL FOR NEUROREHABILITATION 11

2.4 CONFOUNDS IN THE MI LITERATURE 13

2.5 CHALLENGES ASSOCIATED WITH MI RESEARCH 15

2.6 ASSESSING MI PERFORMANCE USING IMPLICIT SEQUENCE LEARNING 18

2.7 PARIETAL CORTEX IN MI 19

2.8 TRANSCRANIAL MAGNETIC STIMULATION 21

2.7 THETA BURST STIMULATION 25

CHAPTER 3 RESEARCH OBJECTIVES AND HYPOTHESES 28

3.1 EXPERIMENT ONE: SKILL ACQUISITION VIA MI 29

3.2 EXPERIMENT TWO: PARIETAL INVOLVEMENT IN MI-BASED LEARNING 30

CHAPTER 4 EXPERIMENT ONE 32

4.1 INTRODUCTION 32

4.2 METHOD 36

4.2.1 PARTICIPANTS 36

4.2.2 EXPERIMENTAL TASK 36

4.2.3 EXPERIMENTAL PROCEDURE 38

4.2.4 DATA ANALYSIS 40

4.3 RESULTS 42

4.3.1 IMAGERY ABILITY 44

4.3.2 REACTION TIME 44

4.3.3 MI VS. PP-BASED TRAINING 45

4.4 DISCUSSION ... 47
4.4.1 MI-BASED SKILL ACQUISITION ... 47
4.4.2 MI VS. PP ... 48
4.4.3 TRANSFER EFFECTS ... 50
4.4.4 EXPLICIT LEARNING ... 51
4.4.5 EMG MONITORING ... 52
4.4.6 LIMITATIONS ... 53
4.5 CONCLUSIONS ... 54
4.6 SUMMARY TO CHAPTER 4 AND TRANSITION TO CHAPTER 5 ... 54
CHAPTER 5 EXPERIMENT TWO ... 56
5. 1 INTRODUCTION ... 56
5.2 METHOD ... 59
5.2.1 PARTICIPANTS ... 59
5.2.2 EXPERIMENTAL TASK ... 60
5.2.3 TRANSCRANIAL MAGNETIC STIMULATION ... 61
5.2.4 EXPERIMENTAL PROCEDURE ... 62
5.2.5 DATA ANALYSIS ... 64
5.3 RESULTS ... 66
5.3.1 REACTION TIME ... 66
5.3.2 GROUP COMPARISONS ... 68
5.4 DISCUSSION ... 69
5.4.1 IMPACT OF IPL DAMAGE TO MI ... 70
5.4.2 ROLE OF IPL TO MI ... 71
5.4.3 LIMITATIONS ... 73
5.5 CONCLUSION ... 75
CHAPTER 6 GENERAL DISCUSSION ... 76
6.1 THE NATURE OF MI-BASED SKILL ACQUISITION ... 77
6.2 MECHANISM FOR MI-BASED SKILL ACQUISITION ... 80
6.3 IMPLICATIONS FOR THE APPLICATION OF MI IN REHABILITATION ... 81
6.4 FUTURE DIRECTIONS ... 84
6.5 GENERAL LIMITATIONS ... 87

6.5.1 CHALLENGES ASSOCIATED WITH THE ISL PARADIGM 87
6.5.2 CHALLENGES ASSOCIATED WITH TMS 87
6.4 CONCLUSION 89
REFERENCES 91
APPENDIX I: EDINBURGH HANDEDNESS INVENTORY 103
APPENDIX II: MOTOR IMAGERY FAMILIARIZATION SCRIPT 105
APPENDIX III: TMS SCREENING FORM 106

LIST OF TABLES

Table 1. Group-averaged RT differences for Experiment Two 68

LIST OF FIGURES

Figure 1. Changes in activation during skill acquisition via PP.. 8
Figure 2. Brain activation of PP and MI 10
Figure 3. Differences in activation between PP and MI.. 14
Figure 4. Representative timeline of an MI-based learning paradigm 17
Figure 5. Depiction of the dorsal visual pathway 21
Figure 6. Induction of current in the brain via TMS 23
Figure 7. Representation of a motor evoked potential... 24
Figure 8. Theta burst stimulation protocols.. 26
Figure 9. Summary of participant inclusion/exclusion for Experiment One............ 43
Figure 10. Group-averaged test block results for Experiment One............................ 45
Figure 11. Effect sizes for MI vs PP groups for Experiment One 46
Figure 12. Timeline of the protocol employed in Experiment Two 63
Figure 13. Group-averaged test block results for Experiment Two........................... 67
Figure 14. RTs for random trials across groups for Experiment Two......................... 73
Figure 15. TMS group results excluding the non-responder (from Ex. 2)................ 74
Figure 16. PP group results for explicit vs implicit learnings (from Ex. 1) 79

ABSTRACT

Motor imagery (MI), the mental rehearsal of movement, is a useful adjunct to physical practice (PP) in numerous domains and shows promise for post-stroke rehabilitation. However, it is unknown if MI alone can produce robust learning without prior PP. To date, the impact of stroke-related brain damage on MI-based skill acquisition has yet to be addressed. The objective of the current work, addressed via two experiments, was to characterise MI-based skill acquisition with and without brain damage. Experiment One demonstrated that MI facilitated skill acquisition independent of PP. Experiment Two demonstrated that inhibition of a parietal region, commonly affected post-stroke, impaired MI-based learning. Therefore, this region is likely critical for MI performance and thus MI-based skill acquisition. Ultimately, these findings support the use of MI as a form of practice and inform on the application of MI in skill acquisition in both non-disabled individuals and those with neurological injury.

LIST OF ABBREVIATIONS USED

ARAT	Action Research Arm Test
cTBS	Continuous Theta Burst Stimulation
dRT	Reaction Time Difference
DLPFC	Dorsolateral Prefrontal Cortex
EEG	Electroencephalography
EMG	Electromyography
ERS/ERD	Event-related synchronization/desynchronization
FDI	First Dorsal Interosseus
fMRI	Functional Magnetic Resonance Imaging
IPL	Inferior Parietal Lobule
ISL	Implicit Sequence Learning
iTBS	Intermittent Theta Burst Stimulation
KVIQ	Kinaesthetic and Visual Imagery Questionnaire
MEG	Magnetoencephalography
MEP	Motor Evoked Potential
MI	Motor Imagery
PP	Physical Practice
PPC	Posterior Parietal Cortex
rTMS	Repetitive Transcranial Magnetic Stimulation
RT	Reaction Times
SMA	Supplementary Motor Area
TBS	Theta Burst Stimulation
TMS	Transcranial Magnetic Stimulation

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CHAPTER 1 INTRODUCTION

Motor learning is the process of acquiring or strengthening a skill via plastic changes in the brain that result from repetitive practice and the provision of feedback (Newell, 1991). While physical practice (PP) is recognized as the primary approach to motor learning, other forms of practice have been shown to facilitate skill acquisition. Motor imagery (MI), the mental rehearsal of a motor task, has been shown to be a useful adjunct to PP in numerous domains (Moran et al., 2012; Wulf, Shea, & Lewthwaite, 2010) and more recently has emerged as a potential tool to facilitate skill acquisition and the ensuing recovery following neurological injury such as stroke.

Relative to PP however, little research has been conducted examining the efficacy of MI alone as a modality of skill acquisition. Owing to the concealed nature of MI, a primary challenge to investigating motor skill acquisition using MI is the lack of a robust MI-based learning paradigm. Specifically, PP is typically performed prior to MI and behavioural changes attributed to MI-based practice are determined using physical test-retest paradigms. Further, many studies do not control for overt muscle activity during MI (Hétu et al., 2013). Thus, the impact of MI alone on skill acquisition is difficult, if not impossible, to isolate. Taken together, this evidence suggests we know little about the efficacy of MI, independent of PP, for skill acquisition.

Further, the basis for the effectiveness of MI as a modality for skill acquisition is that MI is thought to drive plasticity in the brain similar to that which results from

PP. Thus, in order to utilize MI as a tool for neurorehabilitation, it is critical to understand the impact that damage to these brain regions has on MI-based skill acquisition.

The lack of evidence related to MI-based skill acquisition coupled with our poor understanding of how brain damage impacts on MI motivated the present work, whose overall objective is to examine characteristics of skill acquisition occurring via MI with and without brain damage. Importantly, establishing that MI alone drives skill acquisition will provide support for its use as an adjunct to PP in facilitating the acquisition of motor skills in non-disabled individuals, and in domains in which PP is not always possible (e.g., in post-stroke rehabilitation). Furthermore, examining the impact of brain damage on learning that results following MI-based practice may reveal implications related to the use of MI for driving skill acquisition and thus recovery in post-stroke rehabilitation.

The overall research objective was addressed via two experiments. To address challenges associated with MI research as well as characterize MI-based learning, Experiment One utilized an implicit sequence learning paradigm that permitted the assessment of MI-based skill acquisition independent of PP. MI-based skill acquisition was further characterized relative to that resulting from PP of the same task. Results demonstrated that MI was as effective as PP in facilitating skill acquisition of an implicit motor skill without prior physical exposure. However, MI remained inferior to PP for skill acquisition as PP further resulted in generalized motor practice effects. Experiment One demonstrated skill acquisition resulting from MI-based practice alone, thus informing on the applications of MI as a form of practice.

Experiment Two utilized non-invasive brain stimulation to induce a virtual lesion prior to MI-based practice of the same task employed in Experiment One to identify the effect of altered activity of the left inferior parietal lobule (IPL) on MI-based skill acquisition. Following a virtual lesion to the left IPL, skill acquisition was impaired relative to those participants that did not receive stimulation or received placebo stimulation. Thus, Experiment Two demonstrated that the left IPL is critical to MI and damage to this area may limit the use of MI as a tool for skill acquisition in neurorehabilitation.

Collectively, the findings support the use of MI as a form of practice and inform on the applications of MI in skill acquisition in both non-disabled individuals and following neurological injury. The current work ultimately contributes to the literature related to the fundamental processes involved in skill acquisition via MI.

CHAPTER 2 BACKGROUND AND RATIONALE

2.1 MOTOR IMAGERY AS A FORM OF PRACTICE

Acquisition of a motor skill occurs through repetitive practice and the provision of feedback about task performance (Newell, 1991; Jeannerod, 1995; 2001). Repetitive practice drives changes in brain areas associated with motor planning and execution, establishing the neural network that underlies successful motor task performance (Newell, 1991). While physical practice (PP) is recognized as the 'gold standard' to drive brain plasticity and thus skill acquisition, motor imagery (MI) is a form of practice in which an individual mentally rehearses a motor task, facilitating skill acquisition in a manner similar to that of PP (Jeannerod, 1995; Johansson, 2011; Kraeutner, Gionfriddo, Barrdouille, & Boe, 2014; Sharma, Pomeroy, & Baron, 2006).

Motor imagery can take two forms, including first person or kinaesthetic imagery (i.e., imagining from "behind their own eyes"; Munzert & Zentgraf, 2009), or third person or visual imagery (i.e., imagining someone else performing the movement). Kinaesthetic imagery, in comparison with visual imagery, has been shown to facilitate greater improvements in motor performance. For instance, Féry and Morizot (2000) compared kinaesthetic imagery-based practice to visual imagery-based practice in novice tennis players. Performance of the tennis serve prior to and following the MI-based training was assessed based on speed and accuracy of the serve within specified course segments, and judgement of form via video-replay. The researchers demonstrated that kinaesthetic imagery led to greater improvements in performance (specifically for speed and form). Further, only kinaesthetic imagery has been demonstrated to facilitate excitability of the corticospinal pathway, as evidenced by neurophysiological assessment using cortical stimulation (Stinear, Byblow, Steyvers, Levin, & Swinnen, 2006). Collectively, this evidence has led to the notion that kinaesthetic MI is more effective than visual MI in facilitating basic motor skill learning in rehabilitation (Mulder, 2007).

Much of the rationale for the use of MI as an adjunct in facilitating skill acquisition is derived from its application in sport and music (Brown & Palmer, 2013; Driskell, Copper, & Moran, 1994; Jones & Stuth, 1997; Moran et al., 2012; Schuster et al., 2011; Wulf, Shea, & Lewthwaite, 2010). For instance, Smith, Wright, and Cantwell (2008) investigated performance gains associated with MI-based training and combined MI and PP-based training in experienced golfers. While the greatest performance gains after six weeks of training of a bunker shot resulted following combined MI and PP, MI-based training alone resulted in similar improvements in performance as the pure PP. Thus, MI was demonstrated to be an effective form of practice in golf. MI has also been shown to drive gains in strength (Lebon, Collet, & Guillot, 2010; Reiser, Büsch, & Munzert, 2011). A study conducted by Reiser et al. (2011) investigated training sessions involving combined MI and PP vs. the same number of sessions of PP alone in strength training using a maximal isometric contraction task consisting of four basic exercises. The researchers demonstrated that the combined MI and PP training protocol led to similar gain as the pure PP group, thus demonstrating that MI can be used to produce strength gains without the same level of muscle fatigue. Further, a study conducted by Lebon et al., (2010) compared strength gains of a leg press task following 12 sessions of combined PP and MI-based training to a control group who underwent PP and training of a neutral cognitive task. While both groups showed increased leg strength following the training sessions, leg strength was further enhanced in the MI group. Thus, support was provided for the efficacy of MI in facilitating strength gains and further applications of MI in limiting strength loss following injury. Indeed, many injured athletes have previously employed MI as a replacement to PP in order to aid the rehabilitation process (Jones & Stuth, 1997).

While MI has been shown to be most effective when paired with PP (Bovend'Eerdt, Dawes, Sackley, & Wade, 2012), performance gains from MI-based practice independent of PP have also been shown (Bovend'Eerdt et al., 2012; Jackson, Lafleur, Malouin, Richards, & Doyon, 2003; Malouin, Jackson, & Richards, 2013; Zhang et al., 2011). Jackson et al. (2003) conducted a study involving MI-based practice of a foot-tapping task, consisting of a sequence of ten dorsiflexions and plantarflexions in a specified order. Following five MI-based practice sessions of the sequence (for a total of 1500 repetitions), significant improvements in the skill were observed, as measured by response time of the sequence (Jackson et al., 2003). Similarly, Zhang et al. (2011) demonstrated significant improvements in behaviour of a finger-tapping task following 14 sessions of MI-based practice in comparison to a control group who received no training between the pre- and post-test. These results confirm that MI is better than no practice, and as indicated above, may therefore be of benefit in situations when PP is not possible (i.e., following injury).

2.2 MECHANISM FOR MI AS A MODALITY OF SKILL ACQUISITION

Similarly to PP, skill acquisition that results from MI is thought to occur from plastic changes in the brain that are driven by the repetitive mental practice (Jeannerod, 2001; Newell, 1991). It is well established that PP results in activation in core motor areas (i.e., primary motor cortices and premotor areas; Doyon & Benali, 2005) and fronto-parietal areas (Dayan & Cohen, 2011; Rushworth, Krams, & Passingham, 2001; Rushworth, Johansen-Berg, Göbel, & Devlin, 2003), all of which are associated with forming, executing, and updating the motor plan based on sensory feedback (Therrien & Bastian, 2015). Repetitive activation of these brain areas in turn drives synaptic plasticity, facilitating changes within the network as the skill becomes consolidated (Doyon & Benali, 2005). Specifically, motor learning that results from PP is generally associated with changes in activation in cerebellar and striatal circuits, dorsolateral prefrontal cortices (DLPFC; Figure 1) and functional connectivity between primary motor, supplementary motor, and premotor cortices (Dayan & Cohen, 2011; Hikosaka, Nakamura, Sakai, & Nakahara, 2002; Ungerleider, Doyon, & Karni, 2002).

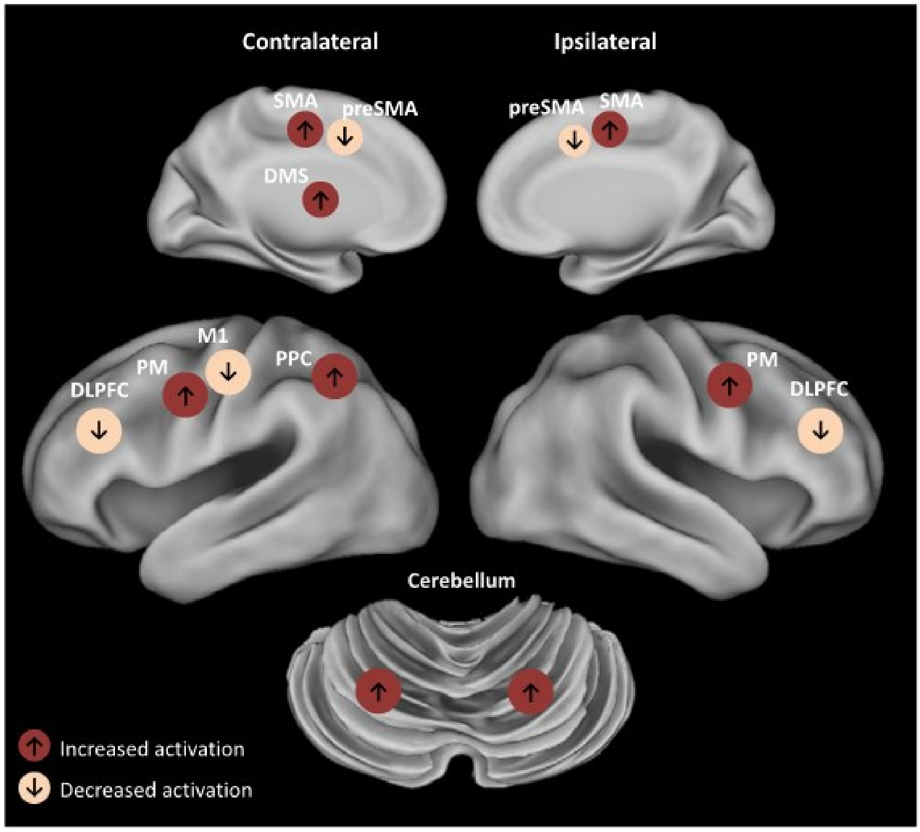

Figure 1. Changes in activation observed during within-session skill acquisition via PP, taken from Dayan and Cohen (2011). As learning occurs following repetitive PP, decreased activation within the dorsolateral prefrontal cortices (DLPFC) is observed, as well as increased activation within the supplementary motor area (SMA), posterior parietal regions (PPC), and the cerebellum.

For MI to be as effective as PP for skill acquisition, it follows that similar patterns of brain activity occur, with modulation of this activity paralleling that observed with PP. Indeed, similar patterns of brain activation have been observed between MI and PP (Hétu et al., 2013; Kraeutner et al., 2014). Neuroimaging investigations of MI, the majority of which have employed functional magnetic resonance imaging (fMRI), have determined that MI engages brain areas that largely overlap with PP, including the premotor, cingulate, and parietal cortices (Hanakawa, Dimyan, & Hallett, 2007; Lange, Roelofs, & Toni, 2008; Porro et al., 1996). Studies using electroencephaolography (EEG) and magnetoencephalography (MEG) have also been conducted, revealing more time-sensitive changes in brain activity associated with MI (Neuper et al., 2006; Burianová et al., 2013; Kraeutner et al., 2014; Pfurtscheller & Neuper, 1997). For example, EEG studies have shown similar activation over contralateral sensorimotor areas during MI, motor preparation, and PP, in tasks such as a simple cube manipulation involving finger and thumb movements (Neuper et al., 2006), simple dorsiflexions of the hands (Pfurtscheller & Neuper, 1997), and simple thumb movements performed in time with a metronome (Formaggio, Storti, Cerini, Fiaschi, & Manganotti, 2010). Burianová et al. (2013) employed both fMRI and MEG to investigate patterns of activity between PP and MI of a simple finger movement task. An overlap of activation was shown in premotor cortices, SMA, parietal cortices, and the cerebellum. Further, Kraeutner et al. (2014) employed MEG to investigate activation between PP and MI of a finger-tapping task to provide further evidence in support of similar patterns of activity observed during MI and PP (Figure 2).

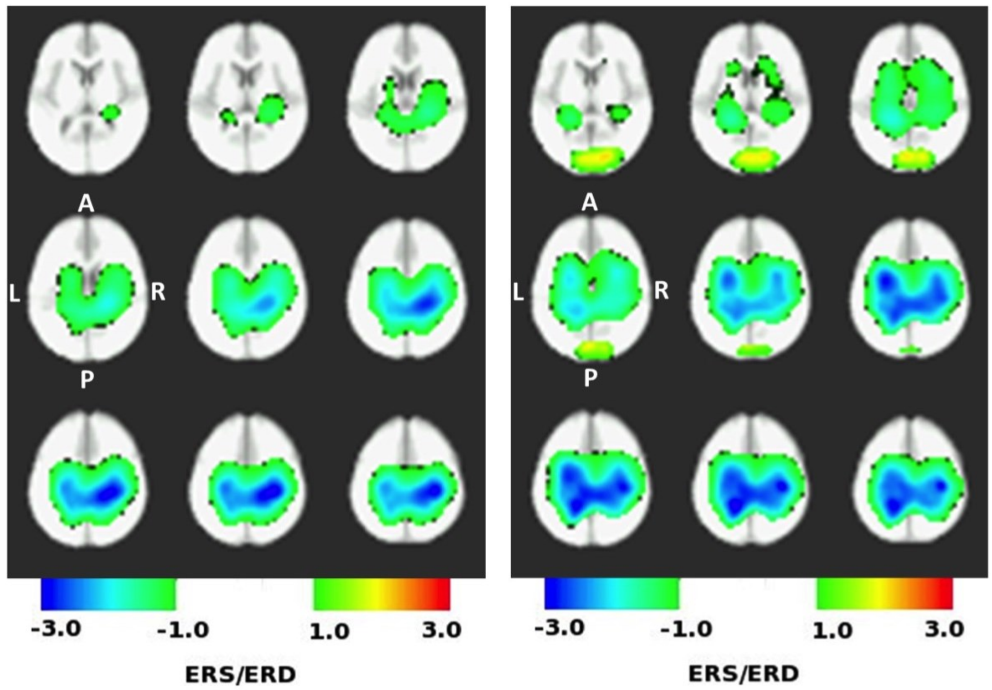

Figure 2. MEG-based group averaged source-level event-related synchronization/desynchronization (ERS/ERD; reflecting the power change of oscillatory activity in the beta band over time) of PP (left) and MI (right) overlaid on a template brain (taken from Kraeutner et al. 2014). Areas of significant activation ($p < 0.05$) were determined from 3d t-tests of task vs. rest blocks. Overlapping areas during MI and PP included contralateral primary motor and somatosensory cortices.
Note: 'Cool' colours are indicative of greater activity.

During acquisition of a novel skill, similar changes in activation patterns are observed between MI and PP (Lacourse, Orr, Cramer, & Cohen, 2005; Lafleur et al., 2002; Zhang et al., 2011). Lacourse et al. (2005) investigated activation patterns via fMRI before and after repeated sessions of MI and PP of a finger-sequence task. Activation patterns between MI and PP were shown to become more similar during post-test than at pre-test, including a shift in laterality associated with unilateral skill learning. The shift in laterality following repeated sessions of MI of a finger-sequence task was also shown in a MEG-based study conducted by (Boe et al., 2014).

Further, neural changes driven via MI or PP were investigated via positron emission tomography of a foot-tapping task consisting of a sequence of six dorsiflexions and plantarflexions in a specified order (Lafleur et al., 2002). Consistent with improved behavioural performance on the task following training, changes in activation resulting from MI and PP were observed within striatal, cerebellar, and orbitofrontal brain areas. Thus, the evident overlap in patterns of brain activity between the two forms of practice suggests that plastic changes in the brain are driven through repetitive mental practice akin to those driven via repetitive PP, thus serving as the basis for the efficacy of MI in skill acquisition.

2.3 MOTOR IMAGERY AS A TOOL FOR NEUROREHABILITATION

Due to the apparent similarities in activation between the two forms of practice, MI has been proposed and applied as an adjunct to PP in neurorehabilitation, primarily with the goal of promoting functional recovery post-stroke (Hovington & Brouwer, 2010; Johansson, 2011; McEwen, Huijbregts, Ryan, & Polatajko, 2009; Sharma, Baron, & Rowe, 2009; Sharma, Pomeroy, & Baron, 2006). Specifically, it is suggested that MI facilitates reorganization of the motor network post-stroke by promoting cortical plasticity in these regions (Johnson-Frey, 2004; Sharma et al., 2009). A study by Page, Szaflarski, Eliassen, Pan, and Cramer (2009) evaluated the effects of an MI-based intervention post-stroke using behavioural and imaging measures. It was shown that motor function improved as measured via the Action Research Arm Test (ARAT) and Fugl-Meyer assessment, which is a measure of post-stroke recovery based on five domains, including motor and sensory function, balance, joint pain, and range of motion (Gladstone, Danells, & Black, 2002), following the intervention. Further the resulting brain activation patterns were consistent with those observed following physical rehabilitation, thus demonstrating that MI drives cortical reorganization. Although few studies have investigated the effectiveness of MI post-stroke (Kho, Liu, & Chung, 2014; Zimmermann-Schlatter, Schuster, Puhan, Siekierka, & Steurer, 2008), it seems that MI is a useful adjunct to physical-based therapies (Faralli, Bigoni, Mauro, Rossi, & Carulli, 2013; Zimmermann-Schlatter et al., 2008). Notable improvements in recovery of gait post-stroke have been observed following imagery-based treatment compared to control treatment over four weeks (Dickstein et al., 2013). Similarly, Riccio, Iolascon, Barillari, Gimigliano, and Gimigliano (2010) examined the effects of combined imagery-based treatment with conventional rehabilitation protocols in comparison with the standard rehabilitation protocol of upper limb recovery post-stroke. Imagery-based treatment consisted of an additional 60 minutes of therapy following the conventional protocol, in which participants performed guided imagery of simple upper limb tasks. Employing imagery-based treatment in addition to standard rehabilitation resulted in significant clinical improvements in upper limb function as measured by an assessment consisting of 12 upper limb motor tasks varying in complexity, and the upper limb subset of the Motricity Index (Gor-García-Fogeda et al., 2014; Riccio et al., 2010).

The support for the use in MI in neurorehabilitation is conflicting in the literature however, as research has also demonstrated limited efficacy of MI in neurorehabilitation (Barclay-Goddard, Stevenson, Poluha, & Thalman, 2011). Liu, Chan, Lee, and Hui-Chan (2004) showed that while three weeks of mental training led to improved performance of novel and practiced tasks in comparison to a control group, no clinical improvement of motor function was observed based on the Fugl-Meyer Assessment. Further, a study by (Ietswaart et al., 2011) utilized the ARAT to assess improvements in function following twelve 45 minute supervised and eight unsupervised MI sessions of simple upper limb movements in comparison with a placebo intervention and a 'normal-care' control group. At a five-week follow-up, similar improvements in ARAT scores were observed following both 'normal-care' and MI training. Thus, it was suggested that MI may have no clinical benefit above and beyond therapies already implemented for post-stroke rehabilitation (Barclay-Goddard et al., 2011; Ietswaart et al., 2011). Importantly however, lesion location and size was not controlled for in these studies and it is thus possible that the stroke-related damage impacted upon MI performance, contributing to the limited efficacy of MI for skill acquisition post-stroke. Further, many studies did not assess MI ability or alternatively include an objective measure of MI performance. Therefore, while many factors may have contributed to the conflicting results, it is critical to understand how stroke-related brain damage may impact upon the effectiveness of MI as a modality for skill acquisition.

2.4 CONFOUNDS IN THE MI LITERATURE

While a clear overlap in activation patterns exists between MI and PP, providing a basis for the effectiveness of MI as a modality of skill acquisition, it is suggested that MI relies on a more widespread neural network in comparison with PP (Figure 3; Burianova et al., 2013; Hétu et al., 2013; Kraeutner et al., 2014). Activation differences are observed in brain areas involved in visuospatial processing during MI (e.g., left IPL, parahippocampus, right superior temporal gyrus and superior frontal gyrus; Burianová et al., 2013) and heavier involvement of ipsilateral brain areas, specifically within the parietal cortices, have been observed during MI in comparison with PP (Hétu et al., 2013; Kraeutner et al., 2014). In addition, it is suggested that differences in these activation patterns may be further influenced by imagery ability (Kraeutner et al., 2014). Lastly, it is speculated that the increased activation in parietal regions is attributable to this region playing a critical role in MI (more so than PP) due to its role in attentional and visuospatial processes (Rushworth et al., 2001, 2003; Kraeutner et al., 2014).

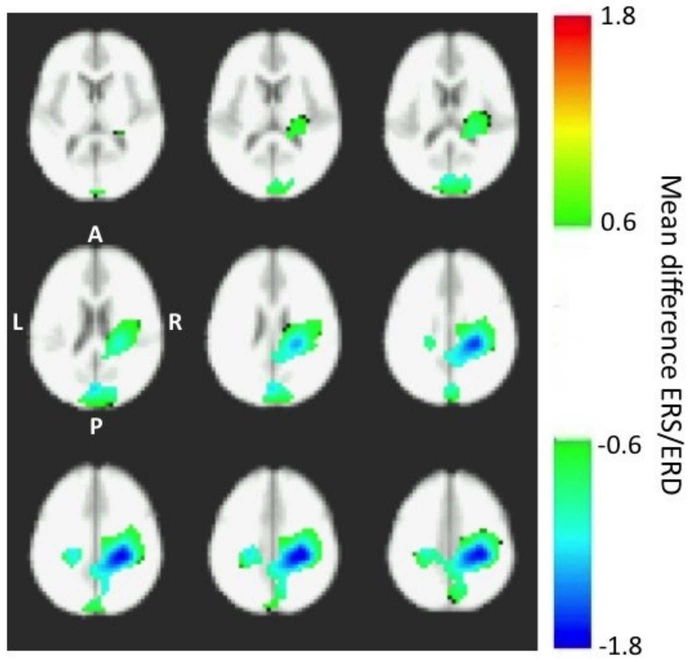

Figure 3. MEG-based group averaged source-level activity comparison of PP and MI overlaid on a template brain (taken from Kraeutner et al., 2014). Significant differences in activation ($p < 0.05$) were determined from 3d t-tests of PP vs. MI blocks and included differences in contralateral primary motor and somatosensory cortices, indicating that activity during PP was lateralized to the contralateral hemisphere while activity during MI was more bilateral. *Note: 'Cool' colours are indicative of greater activity.*

2.5 CHALLENGES ASSOCIATED WITH MI RESEARCH

Although MI has been demonstrated in numerous domains as a useful adjunct to PP, a primary challenge to MI research is the lack of a robust paradigm to measure gains in performance (e.g., skill acquisition) resulting from MI-based training. As mentioned above, many tasks employed in the MI literature do not include an objective measure of performance (e.g., a behavioural measure) that is quantifiable in nature. Specifically, MI performance is assessed using subjective self-report such as the Kinaesthetic and Visual Imagery Questionnaire (Malouin et al., 2007) or mental chronometry (Malouin, Richards, Durand, & Doyon, 2008). Questionnaires such as the KVIQ are designed to assess the vividness and clarity of the imagined images, with an impairment of MI demonstrated by scores associated with weak or blurry mental pictures. While these questionnaires are demonstrated to have high reliability, the validity of these scales has been criticized (Collet, Guillot, Lebon, MacIntyre, & Moran, 2011), as there is no way to confirm the perspective in which each person performs MI and there is no representative baseline associated with the questionnaires with which to anchor responses. Mental chronometry is suggested to provide a more quantifiable measure of MI performance, as performance is assessed based on timing between real and imagined movements. It has been demonstrated that equal time is required to perform real and imagined movements (Guillot & Collet, 2005), and thus a latency of the imagined movement relative to the real movement suggests an impairment of MI. For instance, an investigation of mental chronometry in MI demonstrated equivalent timings between performance and imagination of a walking task (Papaxanthis, Pozzo, Skoura, & Schieppati, 2002). Participants physically performed a 6m walk at their own pace and imagination of the same task, yielding equivalent mean performance durations. However, the authors noted that the MI condition resulted in increased variability, which they explained by the lack of sensory feedback associated with MI (Papaxanthis et al., 2002). Similarly, Papaxanthis, Pozza, Skoura, and Schippati (2002b) had participants perform and imagine simple arm movements with and without added weight. It was demonstrated that both performed and imagined movements lasted for similar durations, and that these durations were similarly influenced by the added mass (i.e., the added weight caused a latency in the performed movement, which was also observed during imagination of the movement; Papaxanthis et al., 2002b).

As mental chronometry still relies on self-reported outcomes however, it is difficult to control for any external influences that may influence the reported timings. Many factors including task complexity, environmental influences such as completing the task during competition, and the focus point of the movement (i.e., whether the person doing the imagery is focusing on a specific component of the movement or the movement as a whole, further influenced by the nature of instructions given) have been shown to result in under or over-estimations of the duration of the task (Guillot & Collet, 2005). Due to the number of factors that may influence these self-reported outcomes, it is difficult to interpret their relation to MI-based learning (McInnes et al., under review). Thus, it is critical to be able to assess MI-based learning via objective measures, independent of self-report techniques.

Owing to the concealed nature of MI however, it is difficult to employ a paradigm that allows for performance outcomes to be captured independent of any PP. Specifically, behavioural changes resulting from MI-based practice are typically determined by calculating differences between values derived via physical execution before and after the MI-based practice (Figure 4). Bookending the MI-based practice with physical practice in this manner prevents isolating the impact of MI alone on skill acquisition. Although previous studies have stated that MI can facilitate acquisition of a novel skill (Jackson et al., 2003; Wohldmann et al., 2007), the resulting skill acquisition may be influenced by the prior physical exposure (Kraeutner et al., 2014).

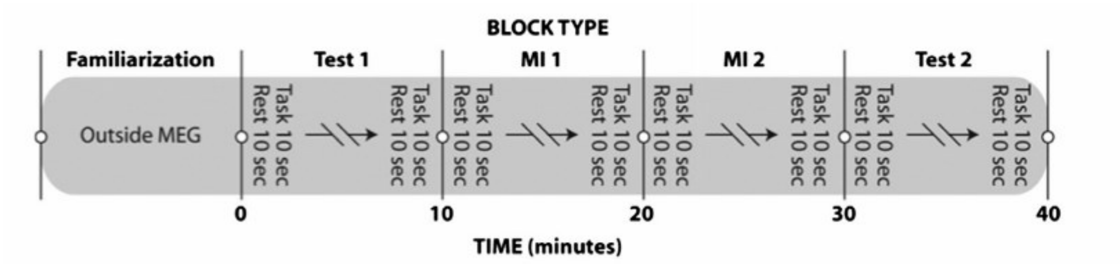

Figure 4. Representative timeline of an MI-based learning paradigm (from Boe et al., 2014). Participants first undergo a task familiarization block, and then switch between rest and task throughout the study. The MI blocks (MI 1 and 2) are bookended by physical test blocks (Test 1 and 2) in order to measure behavioural changes driven by MI.

Further, behavioural changes resulting from MI may also be driven in part due to actual movement, as the majority of studies examining MI do not control for overt muscle activity during the imagined movements (Hétu et al., 2013). A meta-analysis conducted by Hétu et al. (2013) reported that only two of 75 studies utilized electromyography (EMG) in addition to visual monitoring to control for muscle activity. As such, it is likely that changes in brain activation patterns and concomitant learning occurring following MI-based practice are in part driven by actual movement undetected by visual monitoring (Kraeutner et al., 2014). Previous work investigating brain activation associated with MI demonstrated that different activation maps were generated when trials with and without muscle activity were included (Kraeutner et al., 2014). Collectively, this evidence suggests that we know very little about the efficacy of MI independent of PP for skill acquisition. Understanding the efficacy of MI for skill acquisition in the absence of PP is critical to employing MI as a modality for motor learning in disciplines wherein PP is not possible. Further, without a robust method to investigate the effect of 'pure MI' on skill acquisition, the effectiveness of MI as a tool for neurorehabilitation cannot be fully understood.

2.6 ASSESSING MI PERFORMANCE USING IMPLICIT SEQUENCE LEARNING

While the challenge of isolating 'pure MI' driven effects has not yet been addressed in the literature, one approach that may provide a solution to eliminating any effect of prior PP is the use of an implicit sequence learning (ISL) task (Nissen & Bullemer, 1987). The use of ISL is well established in the literature for exploring mechanisms underlying motor sequence learning. Typically, ISL paradigms involve motor practice of a seemingly random motor sequence. Embedded within this seemingly random sequence is a repeated (implicit) sequence that the individual learns in spite of not retaining explicit knowledge of having learned it, as demonstrated by a difference in reaction time (RT) to the sequence types during a follow-up test block (Goschke & Bolte, 2012). Thus, no pre-test is necessary, as learning is not evaluated based on a pre-/post-test comparison in performance.

While the use of ISL in PP-based studies is widespread, its use in MI-based work is limited. A previous study that employed an MI-based ISL task was conducted to assess the effectiveness of MI in improving typing ability (Wohldmann et al., 2007). While MI was shown to improve and maintain improvements of typing ability, participants still underwent a familiarization block consisting of generalized typing practice, which may have influenced the resulting learning. Thus, it remains unknown whether MI can facilitate skill acquisition in the absence of physical practice. However, employing an ISL task may allow for changes driven by MI to be quantified and measured independent of PP.

2.7 PARIETAL CORTEX IN MI

Having a paradigm that captures learning independent of PP is critical to establishing that MI is an effective modality of skill acquisition in the absence of PP, and expanding the evidence for its use in neurorehabilitation. However, as mentioned above, the impact of stroke-related brain damage on the effectiveness of MI remains unknown. Of particular interest is the parietal cortex, which is often damaged following stroke, as it is thought to be a critical brain region underlying MI performance (Hétu et al., 2013). Indeed, the parietal cortex has been shown to have increased involvement in MI relative to PP, with the left parietal cortex active during MI regardless of the hand (left or right) being imagined (Burianová et al., 2013).

The basis for increased parietal cortex activation during MI is its purported involvement in processes related to motor attention, shown to be critical for movement selection and planning (Binkofski & Buxbaum, 2013; Rushworth et al., 2001, 2003), and thus its inclusion as part of the dorsal visual pathway. The dorsal visual pathway involves information transfer from the primary visual cortex to the posterior parietal cortex and is responsible for the integration of visuospatial information (Figure 5; Binkofski & Buxbaum, 2013; Kandel, Schwartz, & Jessell, 2000; Rizzolatti & Matelli, 2003; Rushworth et al., 2001). Given the seemingly heavier reliance of MI on visuospatial processes relative to PP, the involvement of the parietal cortex in the dorsal visual pathway thus further supports its role in MI. Buch et al. (2012), studying stroke-related lesions, sought to assess structural and functional morphology relating to imagery of a grasping task. Performance was assessed based on changes in power that corresponded to sensorimotor activity (i.e., changes in activity observed from a cluster of sensors located over sensorimotor areas within 9-12 and 20-24Hz, previously demonstrated to correspond to movement preparation, MI, and actual execution of movement) during the task, using a visual feedback paradigm. Connectivity between premotor and posterior parietal regions was related to modulation of the sensorimotor rhythms during task performance. This finding indicates that parietal cortex integrity may be correlated with MI ability (Buch et al., 2012). Findings from lesion-based studies further support this notion, including a study that showed impairments in generating movement representations via MI following lesions to parietal regions, as evidenced by increased time to imagine vs. execute finger movements (Sirigu et al., 1996). Due to the limited number of cases typically included in these lesion studies, as well as the variability in lesion location and size (Rorden & Karnath, 2004), findings from studies examining MI ability in patients with damage to the parietal cortex are difficult to interpret. Thus, it remains unknown what impact damage to the parietal cortex has on one's ability to perform MI, and in-turn to utilize it as an intervention to promote skill acquisition post-stroke.

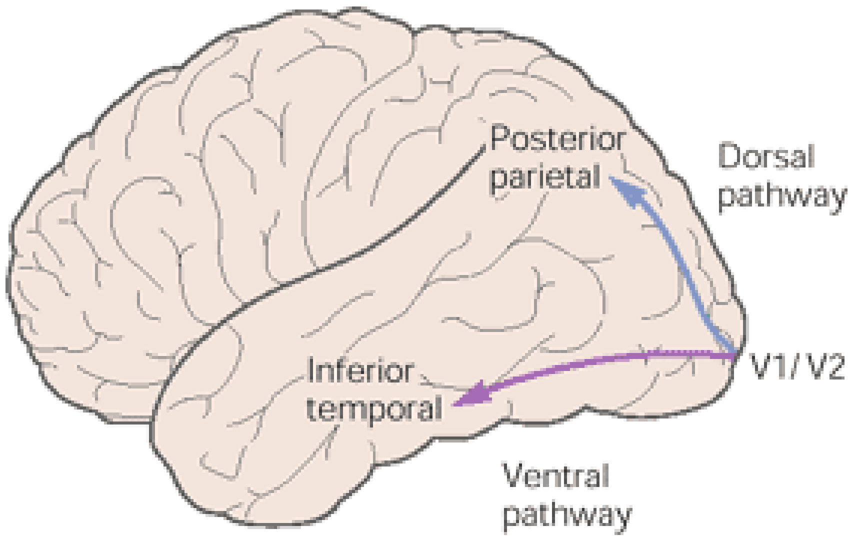

Figure 5. Depiction of the dorsal visual pathway, indicated in blue (taken from Kandel et al., 2000). Parietal areas, including the inferior and superior parietal lobule, are implicated in the guidance of actions and visuomotor integration.

2.8 TRANSCRANIAL MAGNETIC STIMULATION

Ideally, lesion location and size would be controlled for to examine the role of parietal regions in MI-based learning, as assessed through a robust and objective outcome measure. While extremely difficult to control for variability associated with patient populations, a technique called repetitive transcranial magnetic stimulation (rTMS) permits the creation of transient virtual lesions in non-disabled individuals (Miyawaki, Shinozaki, & Okada, 2012). TMS is a non-invasive and painless procedure that has been used in a growing number of laboratories worldwide after its development in 1985. TMS is a widely used technique that alters cortical excitability in humans for both experimental and clinical purposes via application of a series of brief magnetic pulses applied on the outside of the head over cortical regions of the brain. Based on the properties of electromagnetic induction, a rapidly changing magnetic field is generated when a high-voltage current is passed through a coil. When this coil is held in close proximity to any electrically conducting medium, such as the brain, this time-varying magnetic field induces an electrical current in a direction opposite to the original current in the coil (Figure 6; Hallett, 2000; Bolognini & Ro, 2010). A placebo treatment known as sham TMS can also be used to control for potential placebo effects. Sham TMS is conducted using either a coil that mimics the noise and vibration of a true magnetic coil, but generates an attenuated magnetic field, or by using the true magnetic coil over the vertex of the head, or angled away from the target region, at a pre-determined percentage of stimulator output. The sham TMS appears genuine, both to the operator of the TMS (when using a sham coil) and to the patient, thus enabling double blind procedures (Lisanby et al., 2001; Malcolm et al., 2007).

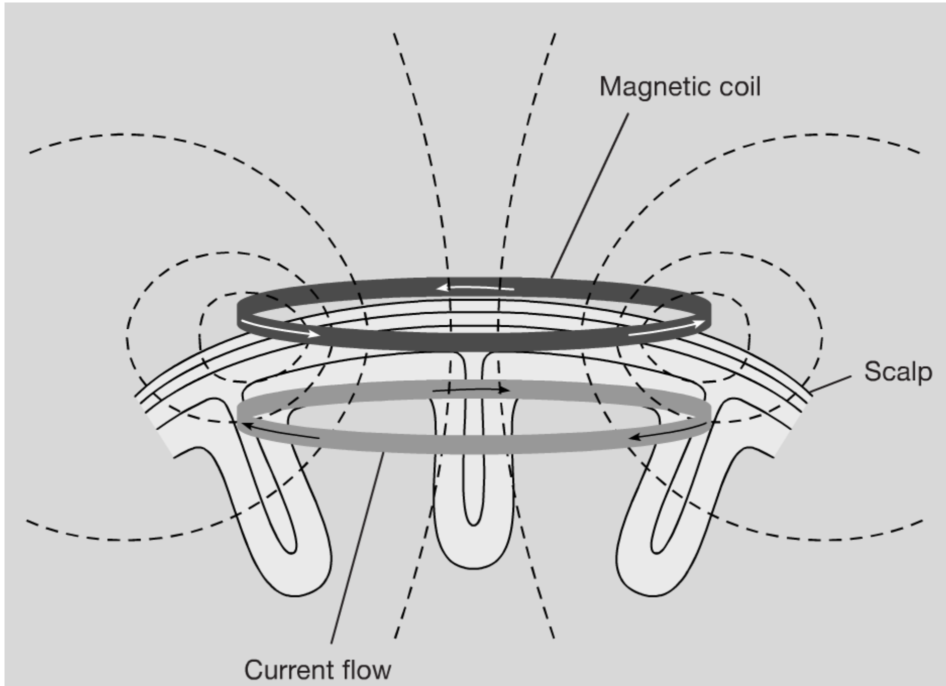

Figure 6. Induction of current in the brain via TMS, as illustrated in Hallet (2000). Current is passed through the TMS coil (indicated by the solid black ellipse), held over the scalp, to induce a magnetic field perpendicular to the coil. In turn, an electrical field is induced perpendicular to the magnetic field (indicated by the dashed lines) and current is induced into the brain (indicated by the grey ellipse). Different coil types can be used to induce more focal or deeper stimulation. For instance, figure-eight coils produce a more focal pattern of stimulation that penetrates at a depth of 1.5-2.5cm, while H-coils deliver stimulation at a depth of 6cm.

Cortical excitability via TMS is measured by recording motor evoked potentials (MEPs) from relevant muscles following stimulation of the region corresponding to the target muscle within the motor cortex (Figure 7). Generally, stimulus intensity used for rTMS (or other TMS paradigms including paired-pulse procedures) is expressed as a percentage of resting motor threshold (RMT), defined as the lowest stimulator output that produces MEPs greater than 50 μV in amplitude (peak-to-peak) over the corresponding muscle (typically the first dorsal interosseus; FDI) for five out of ten trials (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005; Pascual-Leone, Valls-Solé, Wassermann, & Hallett, 1994; Rossini & Rossi, 1998).

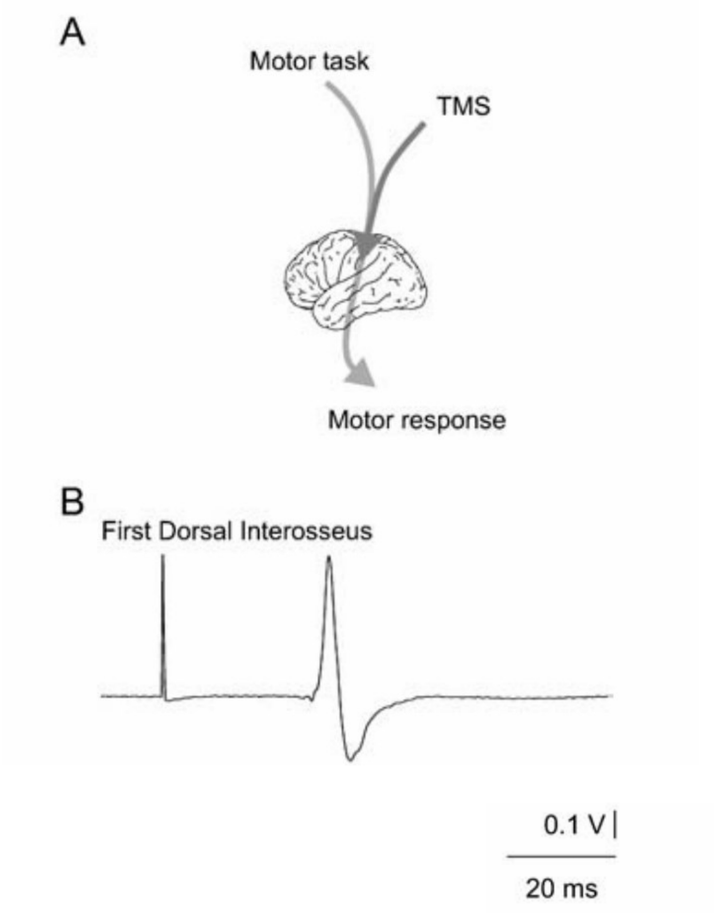

Figure 7. Representation of a motor evoked potential (MEP), taken from Petersen, Pyndt, and Nielsen (2003). When TMS is applied over primary motor cortex (A) a MEP is produced and recorded by surface electromyography over the relevant muscle (B; in this instance the first dorsal interosseus). Resting motor threshold is then determined by measuring the lowest stimulator output required to elicit an MEP ≥ 50 μV on five out of ten trials.

TMS can be applied according to a number of different protocols including one stimulus at a time, termed single-pulse TMS, or in trains, termed rTMS. Single-pulse TMS can be used, for example, for mapping motor cortical outputs, studying central motor conduction time, and tracking cortical excitability over a duration of time.

rTMS can be used to transiently facilitate (excite) via high frequency protocols (i.e., ≥ 10 Hz), or disrupt (inhibit) via low frequency protocols (i.e., ≤ 5 Hz), neural activity (Rossi, Hallett, Rossini, & Pascual-Leone, 2009).

2.7 THETA BURST STIMULATION

Theta Burst Stimulation (TBS) is a form of rTMS in which magnetic pulses are applied in bursts of three, 50Hz pulses, delivered at intervals of 200ms, which can result in increased cortical excitability, through intermittent TBS (iTBS), or cortical inhibition, through continuous TBS (cTBS; Figure 8; Huang et al., 2005). For the purposes of investigating the contribution of a specific brain region to a behavioural outcome, cTBS thus represents an ideal protocol.

In cTBS, the bursts of three pulses are applied at a frequency of 5Hz for approximately 40 seconds (200 bursts for a total of 600 pulses). Typically, the stimulator intensity is set at 90% of RMT, although variations of the power settings have been employed (Huang et al., 2005). cTBS has been used in an increasing number of laboratories since 2004 as this protocol uses fewer pulses and a much shorter duration of stimulation than typical low-frequency rTMS paradigms (Oberman et al., 2011). cTBS is both more convenient for participants and the potential for discomfort due to unnecessary strain on the muscles of the head and neck from continuous stimulation of the head for an extended period of time is minimized (Huang & Rothwell, 2010). Specifically, one session of cTBS lasts only 40 seconds, compared to a typical 20-minute session using rTMS performed at low frequency. Further, while typical rTMS effects last for approximately 20 minutes, the effects of cTBS have been found to last for approximately 40 minutes (Huang et al., 2005).

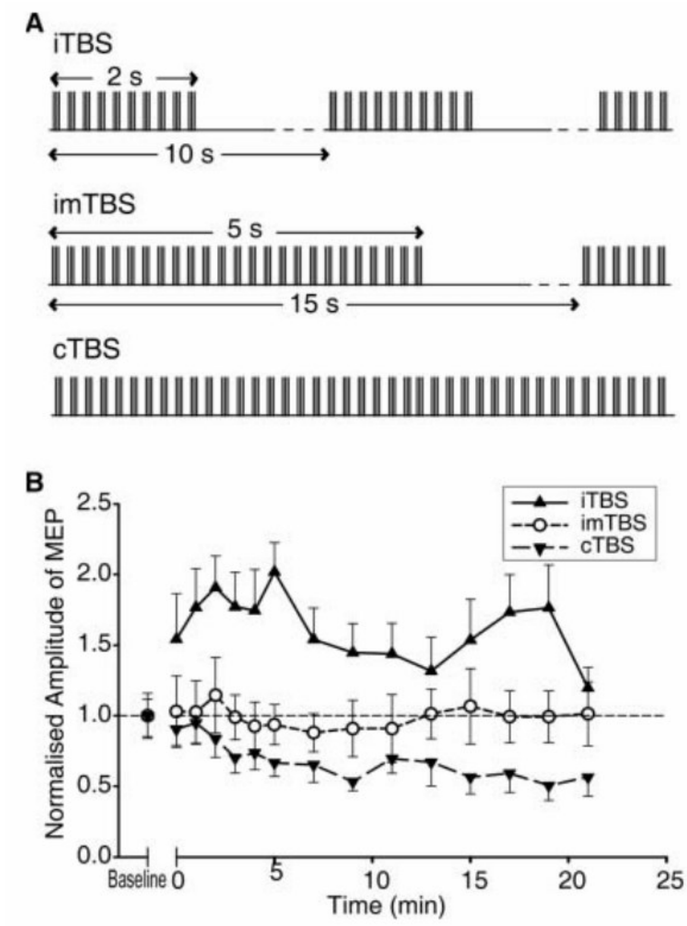

Figure 8. Theta burst stimulation protocols (iTBS, imTBS*, and cTBS) as illustrated in Huang et al. (2005). Each protocol involves three-pulse bursts at 50Hz spaced at different intervals according to each protocol (A). Theta burst can be facilitatory (iTBS), as the resulting MEP amplitudes are increased from baseline following stimulation, or inhibitory (cTBS), as the resulting MEP amplitudes are supressed compared to baseline following stimulation. MEP amplitudes following cTBS remained suppressed at 45 minutes and returned to baseline by 60 minutes (not shown).

**Note: imTBS refers to intermediate theta burst stimulation that was used as a control manipulation in Huang et al., (2005), which does not result in any changes in MEP amplitude.*

While cTBS and other TMS protocols represent an ideal approach to probing the role of the parietal cortex in MI, few studies have employed these techniques. One study conducted by de Vries et al. (2009) found that MI ability was disrupted following low-frequency rTMS of the left superior parietal cortex. However, it is difficult to interpret these findings in the context of MI-based skill acquisition as, along with many other tasks previously employed in the MI literature, the task involved imagination of simple repetitive wrist extension/flexion movements and did not include an objective and quantifiable behavioural outcome. Further, MI ability was assessed subjectively using questionnaires and mental chronometry, consistent with what is typically employed in the MI literature. Thus, while this study provided insight into the involvement of the parietal cortex in MI, its role in MI-based learning has yet to be determined.

CHAPTER 3 RESEARCH OBJECTIVES AND HYPOTHESES

Collectively, the evidence presented in Chapter 2 suggests that little is known about the efficacy of MI alone for skill acquisition, and how this translates to its purported use in neurorehabilitation. Due to the challenges of assessing MI independent of PP as well as the observed differences in activation patterns, including the suggested reliance on parietal regions involved in visuospatial processes, it remains unknown whether MI is an effective form of practice when performed alone. Although studies have demonstrated that the use of MI as a tool for neurorehabilitation is promising, the evidence is limited and conflicting in the literature. As the impact of brain damage on MI-based learning may contribute to this conflicting evidence, probing the contribution of these regions to MI-based learning may provide insight into the effectiveness of MI for neurorehabilitation. Understanding the efficacy of MI alone as a tool for skill acquisition is critical for the use of MI in disciplines in which PP is not possible.

The current work thus seeks to examine the use of MI in facilitating skill acquisition by first implementing an MI-based ISL paradigm that allows for skill acquisition via MI independent of PP. Specifically, as the training phase involves only imagery of the sequence, improved performance can be solely attributed to MI. Secondly, the current work seeks to investigate the role of the parietal cortex in skill acquisition via MI. Understanding the efficacy of MI is critical to employing MI as a modality for skill acquisition. Further, knowing the impact of parietal cortex damage on MI may facilitate the identification of candidates that would benefit from using

MI as an adjunct to PP for rehabilitation. In addressing these aims, this work also endeavours to further our understanding of the mechanisms underlying MI-based skill acquisition. Ultimately, this research will extend the literature regarding the efficacy of MI as a modality for skill acquisition.

3.1 EXPERIMENT ONE: SKILL ACQUISITION VIA MI

As outlined above, while MI has been previously shown to be a useful adjunct to PP in skill acquisition and for improving motor performance (Jones & Stuth, 1997; Malouin et al., 2013), the lack of a robust, objective paradigm to assess the outcome of MI-based skill acquisition makes it difficult to examine changes due to MI alone. Specifically, prior exposure to PP and the lack of control for overt muscle activity in MI protocols are primary challenges in MI research.

Thus, the purpose of this experiment is to demonstrate skill acquisition via MI independent of PP by addressing the challenges associated with MI research noted above. Secondly, learning that results following MI-based practice will be characterised in the context of PP of the same skill. Implicit sequence learning (Nissen & Bullemer, 1987) will be utilized to allow for performance outcomes to be measured without prior exposure to PP. Specifically, no physical task familiarization or physical pre-test will be included in the paradigm (described in detail in Ch.4). Further, the use of EMG will ensure the absence of muscle activity during the MI-based practice. The use of an MI-based ISL paradigm coupled with rigorous monitoring of muscle activity represents a unique opportunity to assess the efficacy of MI-based skill acquisition.

Skill acquisition that occurs as the result of MI-based practice will be compared to skill acquisition that occurs as the result of PP of the same task. This comparison will allow for any decrement in performance to be characterised, thus informing future applications of MI-based practice in lieu of PP. Hypotheses related to Experiment One include:

1. Skill acquisition will occur following MI-based practice, as demonstrated by successful acquisition of the implicit sequence
2. MI-based practice will be characterised as inferior to PP, as demonstrated by enhanced learning outcomes, including general practice effects, following PP in comparison to MI

3.2 EXPERIMENT TWO: PARIETAL INVOLVEMENT IN MI-BASED LEARNING

Recently, MI has been proposed and applied as an adjunct to physiotherapy for neurorehabilitation, including post-stroke (Johansson, 2011; Sharma et al., 2009, 2006). The premise for the effectiveness of MI as a form of recovery is that MI drives activation in brain regions akin to that of PP, thus facilitating skill acquisition in the absence of PP. While overlapping brain regions are indeed activated during MI and PP, additional involvement of parietal regions, commonly damaged post stroke, have been observed during MI (Burianová et al., 2013; Hétu et al., 2013; Kraeutner et al., 2014). Further, it is suggested that the parietal cortex may be more critical to MI than PP due to its role in attentional and visuospatial processes (Rushworth et al., 2001, 2003). Thus, parietal integrity may be necessary for MI to be utilized in neurorehabilitation.

As the contribution of the parietal cortex to MI-based skill acquisition is not clear, this experiment seeks to investigate the role of this region in skill acquisition occurring via MI. The ISL task utilized in Experiment One will be employed. The role of the parietal region will be probed via the creation of a transient virtual lesion in non-disabled individuals via cTBS prior to the MI-based practice. This protocol will thus allow for limitations associated with lesion studies, such as lesion location and size, to be controlled for.

Inhibition of brain regions involved in visuospatial processing will further inform the mechanism underlying skill acquisition via MI. Secondly, knowing the impact damage to parietal regions has on MI-based skill acquisition will allow clinicians to identify candidates that would benefit from using MI as an adjunct to PP for neurorehabilitation. The hypothesis related to Experiment Two is:

1. rTMS of the parietal cortex will prevent skill acquisition via MI

Experiments One and Two, as outlined above, are presented and interpreted in the following chapters (Chapter 4 and 5, respectively). Collectively, the findings from this work are summarized in Chapter 6.

CHAPTER 4 EXPERIMENT ONE

4.1 INTRODUCTION

Acquisition of a motor skill is associated with plasticity in sensorimotor systems resulting from repetitive practice coupled with feedback (Newell, 1991). While physical practice (PP) is recognized as the primary approach to skill acquisition, motor imagery (MI), the mental rehearsal of a motor task (Jeannerod, 1995), has been demonstrated a useful adjunct to facilitate skill acquisition in numerous disciplines (Moran, Guillot, MacIntyre, & Collet, 2012; Wulf, Shea, & Lewthwaite, 2010). The basis for this effectiveness is that MI drives brain activation similar to that of PP, as evidenced by neuroimaging studies reporting that MI engages brain areas that largely overlap with PP (Burianová et al., 2013; Hanakawa, Dimyan, & Hallett, 2007; Kraeutner et al., 2014; Lange, Roelofs, & Toni, 2008; Porro et al., 1996). For example, Burianova and colleagues showed that during MI and PP of a simple finger-movement task, an overlap of activation was observed in premotor, supplementary motor, and parietal cortices, as well as the cerebellum (Burianová et al., 2013). Further, in their scoping activation likelihood estimation meta-analysis, Hétu et al. (2013) concluded that the brain network underlying MI included many regions that overlapped with actual physical execution (Hétu et al., 2013).

While neuroimaging investigations provide support for the basis of the effectiveness of MI for skill acquisition, much of the rationale for the use of MI as an adjunct to PP in facilitating skill acquisition is derived from its application in sport and music (Brown & Palmer, 2013; Driskell, Copper, & Moran, 1994; Jones & Stuth, 1997; Moran et al., 2012; Schuster et al., 2011; Wulf et al., 2010). Although MI has been shown to be most effective when paired with PP (Bovend'Eerdt, Dawes, Sackley, & Wade, 2012), performance gains from MI-based practice independent of PP have also been shown, (Bovend'Eerdt et al., 2012; Jackson, Lafleur, Malouin, Richards, & Doyon, 2003; Malouin, Jackson, & Richards, 2013; Zhang et al., 2011) indicating that MI is better than no practice, and may be of benefit in situations when PP is not possible (Zhang et al., 2011). Indeed, many injured athletes have previously employed MI in order to aid the rehabilitation process and as a replacement to PP in situations where the athlete is physically unable to perform (Jones & Stuth, 1997).

Owing to the concealed nature of MI, many tasks employed in the MI literature do not include an objective measure of performance (e.g., a behavioural measure) that is quantifiable in nature. Specifically, MI performance is assessed using subjective self-report such as the Kinaesthetic and Visual Imagery Questionnaire (KVIQ; Malouin et al., 2007) or mental chronometry (Malouin, Richards, Durand, & Doyon, 2008). Thus, to assess the effectiveness of MI for skill acquisition, it is critical to be able to assess MI performance via objective measures, independent of subjective, self-report techniques.

The concealed nature of MI presents a further challenge to assessing its effectiveness for skill acquisition independent of PP. Specifically, behavioural changes resulting from MI-based practice are typically determined based on differences between values derived via physical execution before and after the MI-based practice. While permitting the assessment of MI performance via an objective measure, bookending MI-based practice with PP prevents isolating the impact of MI alone on skill acquisition. In addition, studies examining MI independent from PP typically include an initial bout of PP before the MI is performed (Jackson et al., 2003). This ordering of PP before MI may be a prerequisite for MI-based learning in that the prior physical exposure to the skill to be learned generates the initial motor representation, which is subsequently reinforced via MI (Munzert & Zentgraf, 2008). Thus, it is unknown if MI may simply be an elaboration of PP, reinforcing learning that has already occurred, or whether MI alone is sufficient to generate and update the motor representation necessary for skill acquisition to occur. Although previous studies have stated that MI can facilitate acquisition of a novel skill (Jackson et al., 2003; Wohldmann et al., 2007), the resulting skill acquisition may have been influenced and in part driven by the prior physical exposure (Kraeutner et al., 2014).

Additionally, MI studies do not always control for muscle activity (Hétu et al., 2013). Previous work investigating brain activation associated with MI demonstrated that different activation maps were generated when trials with and without muscle activity were included (Kraeutner et al., 2014). Taken together, the resulting learning is influenced by prior physical exposure or driven in part by actual movement (Kraeutner et al., 2014). Collectively, this evidence suggests we know little about the efficacy of MI alone for skill acquisition. Having a paradigm that captures performance outcomes independent of PP is key to investigating MI-based learning.

One approach to investigating MI-based learning independent of PP is through implicit sequence learning (ISL), a form of learning in which an individual repeatedly practices a seemingly random motor sequence in which a repeating sequence is embedded (Goschke & Bolte, 2012; Nissen & Bullemer, 1987). Interestingly, RT decreases with practice for the repeating but not random sequences despite the fact that participants are not explicitly aware of the sequence that repeats. The ISL task is thus well-suited to studying MI without PP, because no PP of the sequence task is required prior to beginning MI training.

Previous work has utilized an MI-based sequence paradigm to demonstrate the efficacy of MI in skill acquisition (Wohldmann, Healy, & Jr., 2007). MI-based practice of novel four-digit sequences resulted in improved typing ability, with maintenance of this improvement at a three-month follow-up. Participants were provided actual typing practice prior to the training however, and thus it remains unclear whether MI can be used to acquire a novel motor skill in the absence of PP. Moreover, it has yet to be demonstrated how effective MI-based practice is in comparison to PP.

The current study compares the efficacy of MI (with no associated PP) or PP (with no associated MI) in an ISL task. If MI leads to skill acquisition through elaboration of prior PP with the task, then it is possible that MI alone will not lead to ISL. However, if the sensorimotor systems engaged by MI can lead directly to motor learning, then some degree of ISL might occur even with no prior PP. Moreover, monitoring of muscle activity throughout MI-based practice will allow us to conclude that changes in performance were driven solely via MI. We hypothesize that MI will facilitate motor skill acquisition in the absence of PP as demonstrated by decreased RTs of the implicit compared to the random sequences. We further hypothesize that while effective, MI-based practice will be inferior to motor skill acquisition occurring via PP, evidenced by decreased RTs after physical compared to MI-based practice. Establishing that MI alone drives skill acquisition will provide support for the use of MI in facilitating the acquisition of motor skills in domains wherein PP is not possible, as well as providing further support for its use as an adjunct to PP.

4.2 METHOD

4.2.1 PARTICIPANTS

Sixty-four right-handed subjects (42 female, 22.1 ± 5.3 years) agreed to participate in the study. Handedness was demonstrated by a score of ≥40 on the Edinburgh Handedness Inventory (Oldfield, 1971). All were healthy and free of neurological disorder, and provided written, informed consent. All participants self-reported to have normal hearing and verbally confirmed they understood the instructions prior to the study onset. The study received approval from the research ethics board of the Capital District Health Authority. Prior to the onset of the study, participants were randomly assigned into an imagery- (MI) or physical- (PP) practice group.

4.2.2 EXPERIMENTAL TASK

The experiment involved four blocks of training followed by a physical test and a verbal report test to infer skill acquisition. The training task was an implicit sequence learning (ISL) task involving button presses with the non-dominant (left) hand. All participants performed the task sitting at a chair in front of a computer screen oriented at eye-level, with both arms resting comfortably and the left hand placed on the keyboard. Participants were oriented to four keys (V, C, X, Z) numbered 1-4 from right to left, representing the index, middle, ring and little finger respectively. During the four blocks of training, participants in the MI group were instructed to close their eyes and imagine themselves performing the button presses that were cued auditorily through noise-cancelling headphones. If participants in the MI group pressed a button during the training blocks, an auditory error tone was played and the response was recorded. Participants in the PP group were instructed to close their eyes and physically press the buttons that were cued auditorily. If participants in the PP group did not respond to the cues during the training blocks, an auditory error tone was played. If participants in the PP group made an incorrect response to the cues during the training blocks, no tone was played in order to mimic the lack of explicit feedback associated with MI. Each individual keypress event (i.e., one imagined or physical button press) lasted 1.5s based on the time separating consecutive auditory cues. Each training block consisted of 250 keypresses, with a 5-minute rest block provided between each.

A repeating sequence was embedded within the training blocks (Goschke & Bolte, 2012) consisting of ten digits (constrained such that no two consecutive digits repeated) unique to each participant. The implicit sequence repeated 20 times during each block, thus constituting 80% of the total keypressing events. Repeating sequences were interspersed with five random ten-digit sequences constituting the remaining 20% of keypressing events. The order in which the sequences appeared was randomized throughout each block. Participants were not informed that there was a repeating sequence in the task, and were simply instructed to respond to each auditory event consistent with their group assignment.

4.2.3 EXPERIMENTAL PROCEDURE

Participants in the MI group first completed the KVIQ (Malouin et al., 2007) to establish their ability to perform MI prior to the MI-based training. Ability to perform MI was based on achieving a score on the KVIQ within the range previously reported for healthy control subjects (Malouin et al., 2007). The KVIQ is an assessment of imagery ability that involves the performance of five body movements, followed by imagery of these movements. The KVIQ has high internal reliability and validity in both healthy controls and clinical populations (Malouin et al., 2007). Participants in the MI group then completed a familiarization block. During this familiarization block, participants listened to an audio recording describing the type of MI to be performed (kinaesthetic), and the task to be performed/imagined. Kinaesthetic MI involves imagining the motor task from the first-person perspective, and encompasses sensory aspects of the movement such as the feel and timing of the movement. Kinaesthetic MI was selected for use in the study as this type of MI is suggested for use in tasks involving motor control as opposed to tasks involving judgements and/or those that focus on position and/or form, as these latter tasks are best sub-served by visual imagery (Féry, 2003). Moreover, kinaesthetic MI has been proposed to better facilitate basic motor skill learning (Stinear, Byblow, Steyvers, Levin, & Swinnen, 2006). In addition to instructions related to imagining the physical movement (i.e., the button presses), the audio recording also emphasized the poly sensory aspects of MI, directing the participants to attend to sensory information related to task performance such as the feel of the structure or temperature of the object to be interacted with, as well as the feel of the movement being made, all of which has been shown to facilitate MI performance (Braun et al., 2008). For this study specifically, examples of the script provided to participants included that they should think about "how each button feels as [they] press it" and "how long each movement takes". Participants in the PP group did not complete the KVIQ or the familiarization block.

To detect inappropriate muscle activity during MI-based practice, the electromyogram (EMG) was obtained from the left flexor and extensor muscles of the digits (anterior and posterior aspects of the forearm respectively) of participants in the MI group only. The EMG signal was acquired using self-adhering electrodes (1 x 3 cm; Q-Trace Gold; Kendall-LTP, USA) in a bipolar configuration with a 1 cm inter-electrode distance, sampled at 1000Hz with a bandpass of 25-100 Hz (1902 and Power 1401; Cambridge Electronics Design, UK) and stored for offline analysis.

Immediately following the training, all participants performed two tests to measure performance and infer learning. The first test measured RT in a shortened version of the practiced task, wherein the implicit and random sequences of equal length appeared 10 times each (i.e., a 1:1 ratio) for a total of 200 trials. The order that the sequences appeared was again randomized. Conditions were the same as that of the training blocks, except that participants in both the MI and PP groups were instructed to respond 'as quickly as possible' by physically pressing the indicated key. In this test block, each cue was presented immediately following the previous response and an auditory error tone was played if participants provided an incorrect response (e.g., pressed the '4' key when the '2' key was cued). Responses and the corresponding RTs were recorded for offline analysis. As in the training blocks, participants were not informed about the repeating sequence in the task.

The second test was a verbal report, the purpose of which was to determine whether participants were explicitly aware of the repeating sequence. Participants were first informed that the purpose of the training was to teach them a 10-digit sequence. Participants were then asked to respond to the question "Do you think you learned a sequence during the training blocks"? For a "yes" response, participants were asked if they could report the sequence that they learned (i.e., the 10 consecutive numbers). For a "no" response, participants were also asked if they could report the sequence to further confirm their negative response. Participants were instructed "it was okay if they did not think they learned a sequence".

4.2.4 DATA ANALYSIS

Participants that demonstrated explicit learning were excluded from further analysis, as different processes have been shown to underlie explicit and implicit learning (Keele, Ivry, Mayr, Hazeltine, & Heuer, 2003). Explicit learning was characterised via the verbal report task as to whether or not participants could correctly identify the sequence (Eimer, Goschke, Schlaghecken, & Stürmer, 1996; Kantak, 2012; Rünger & Frensch, 2010). Specifically, participants that answered "yes" to the question of whether or not they thought they learned a sequence and who correctly reported more than 50% of the sequence (i.e., 5 consecutive sequence elements), were excluded from further analyses.

Analysis of the responses made during the MI training blocks was performed to identify and remove participants who had actually performed button presses and had thus experienced a degree of PP during the MI-based training. Participants that made responses greater than 2% (20/1000 responses total) of the time across all training blocks were excluded from further analyses.

Analysis of the EMG data obtained during MI was performed to further identify and reject participants that demonstrated PP during the MI-based training. Data were first rectified and a low-pass filter of 10 Hz was applied. Similar to the approach of Mochizuki et al. (2010), the absence of activity in the left flexor and extensor muscles of the digits during MI was determined by calculating the average amplitude across 15 second envelopes of the EMG signal during each training block, and comparing each to a 15 second envelope acquired during the familiarization block (during which participants were at rest). The EMG threshold was defined as the average rest amplitude plus 2 standard deviations. Participants were excluded from further analysis if greater than 15% of the comparisons exceeded the threshold.

For the RT task, the first element of each sequence was omitted from analysis as per Wohldmann et al. (2007) due to its role in motor initiation vs. motor execution (i.e., the first element of a sequence is a perceptual cue for the movement about to be performed). RTs for trials that occurred before 100 ms and after 1300 ms were removed from analysis to control for anticipatory and outlier responses

(Rüsseler, Hennighausen, & Rösler, 2001). RTs for trials in which an incorrect response was provided were also removed from analysis. The RTs for all remaining trials as well as error rates were then averaged for both the implicit and random sequences for each individual. RT differences (dRT) between the implicit and random sequences (average RT random minus average RT implicit) were also calculated.

A 2 (sequence type) x 2 (group) mixed ANOVA was conducted to analyze the effects of sequence type (implicit vs. random) and type of practice (PP vs. MI) on RT. An alpha value of 0.05 was used. To further characterise learning in both the MI and PP groups, effect sizes were computed for both sequence types and the dRT using the corresponding average standard deviation. Throughout, mean values are reported followed by standard deviation.

4.3 RESULTS

Using the criteria outlined above, 22 participants were excluded leaving a total of 42 participants in the behavioural analysis (24 and 18 in the MI and PP groups respectively; Figure 9). From the MI group, two participants demonstrated explicit knowledge by accurately reporting more than five consecutive implicit sequence elements on the verbal report task; one participant made 54 button-press responses during MI-training; and four participants were excluded due to the presence of muscle activity during the MI training that exceeded our threshold. Of the remaining MI participants, the average number of responses made across all 1000 of the MI-based training trials was 1.48 ± 2.97. From the PP group, 15 participants demonstrated explicit knowledge by accurately reporting more than five consecutive implicit sequence elements on the verbal report task and were thus excluded from further analyses. A summary of the participants in the study is shown in Figure 9.

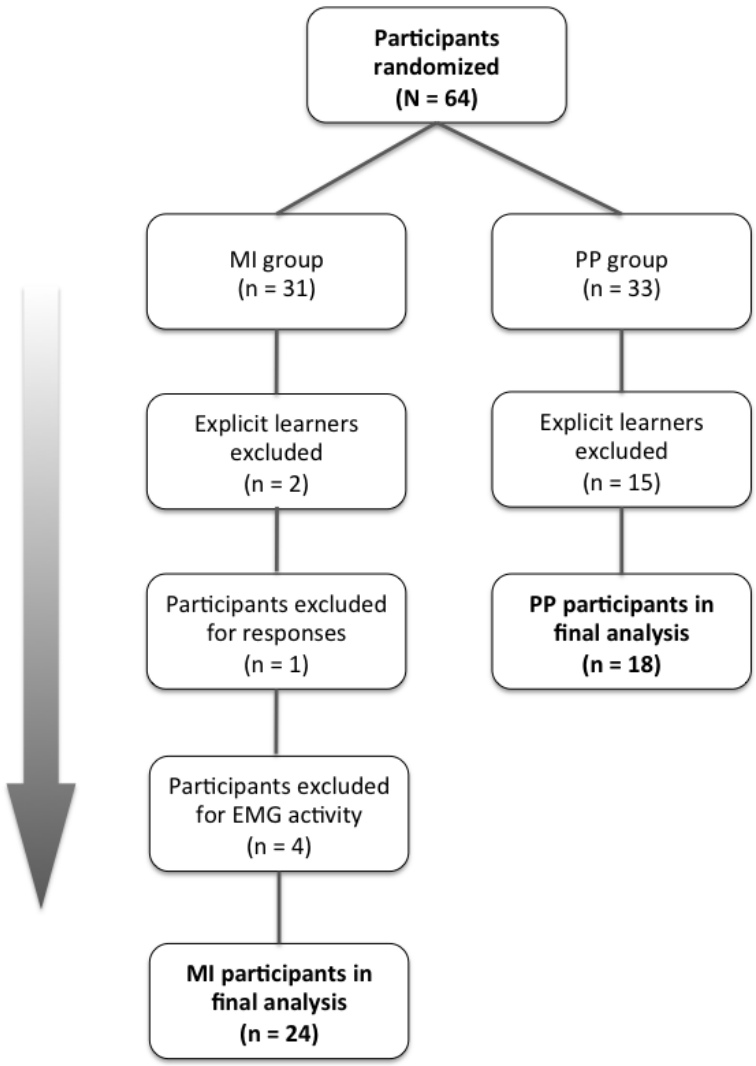

Figure 9. Summary of participant inclusion and exclusion. Following PP or MI-based training of the implicit sequence paradigm, participants were excluded from the final analyses using these criteria: 1) demonstrating explicit knowledge; 2) execution of button-press responses (MI group only); or 3) presence of EMG activity exceeding threshold during MI. As depicted in the figure, a total of 7 participants were excluded from the MI group, and a total of 15 participants from the PP group.

4.3.1 IMAGERY ABILITY

For the MI group, the mean scores for visual and kinaesthetic MI were 20.0 ± 4.7 and 19.3 ± 3.6 respectively. Values for visual and kinaesthetic MI were within ranges previously reported for healthy controls (Malouin et al., 2007).

4.3.2 REACTION TIME

For the MI group, mean RT for the implicit and random sequences were 583 ± 84 ms and 632 ± 86 ms, respectively (Figure 10). Mean error rate (%) for the implicit and random sequences were 1.92 ± 2.00 and 2.62 ± 2.68. For the PP group, mean RT for the implicit and random sequences were 532 ± 73 ms and 589 ± 70 ms, respectively (Figure 10). Mean error rate for the implicit and random sequences were 3.44 ± 2.01 and 5.33 ± 3.38.

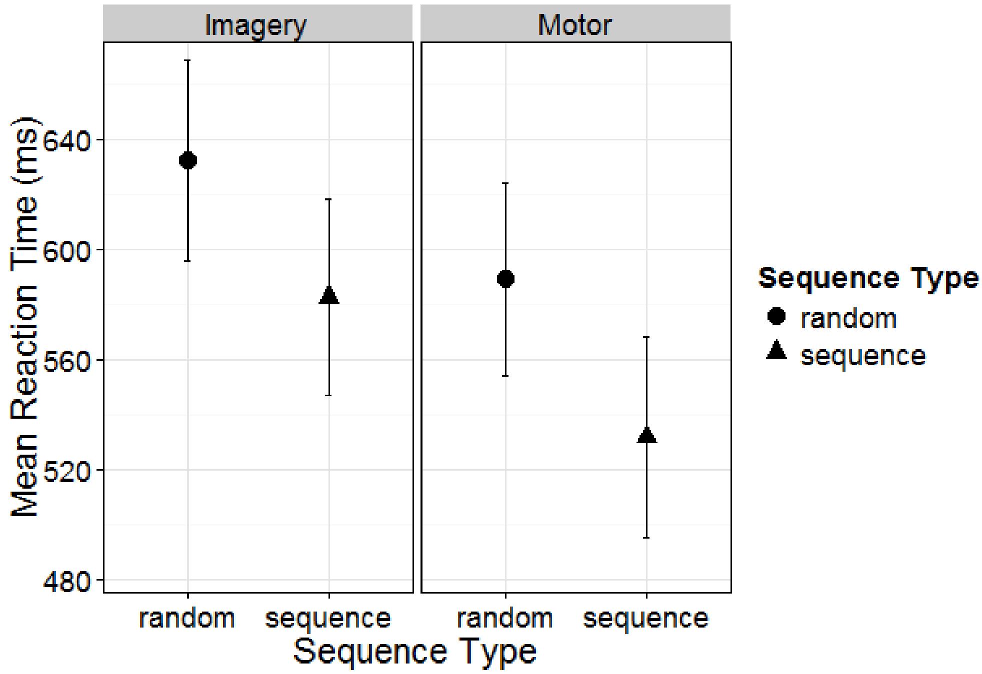

Figure 10. Group averaged reaction times across sequence types (error bars depict 95% CIs). RTs of the implicit sequence were faster than RTs of random sequences ($p < 0.05$) for both the MI and PP groups. RTs for both sequence types were faster following PP in comparison with MI ($p < 0.05$).

4.3.3 MI VS. PP-BASED TRAINING

Overall, there was a significant main effect of sequence type [$F(1,40) = 47.58$, $p < 0.001$], where RTs were significantly faster to sequence numbers than to random numbers. While there was no significant main effect of group detected [$F(1,40) = 3.97$, $p = 0.053$], the results were trending in this direction (further detailed below). There was no significant interaction between block type and group [$F(1,40) = 0.239$, $p = 0.628$].

Comparison of the RTs for the implicit and random sequences within each group resulted in an effect size of 0.59 and 0.80 for the MI and PP groups respectively. Following the trend of the ANOVA results, the magnitude of difference observed in effect size for the MI and PP groups indicates the presence of a group effect (Kelley & Preacher, 2012). In fact, participants in the PP group had faster RTs to both sequence and random numbers compared to participants in the MI group (Figure 10), as a group difference for RTs of the implicit sequence was observed with an effect size of 0.645 (Figure 11). A comparison of random sequence RTs between groups yielded an effect size of 0.551. Lastly, the dRT (random minus implicit) was calculated across groups and no difference was observed between the MI and PP groups (*d* = 0.152; Figure 11).

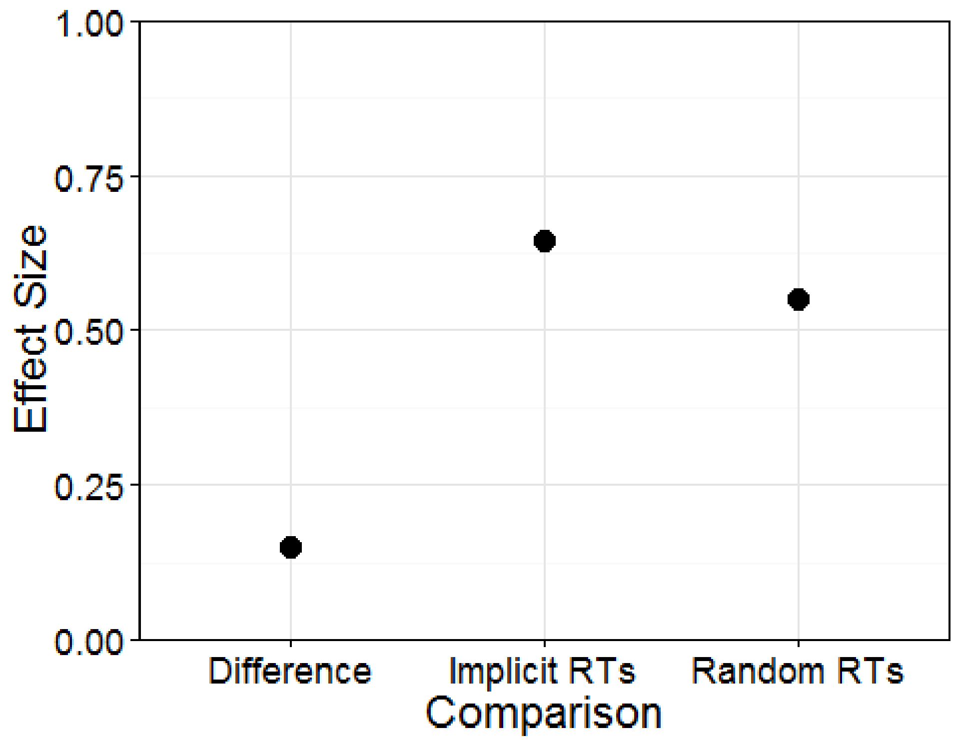

Figure 11. Effect sizes for a between-group comparison of the RT difference between sequence types, RTs of the implicit sequence, and RTs of random sequences. The magnitude of the difference between RTs of the implicit and random sequences did not differ between groups. In comparison with MI, RTs for both sequence types were faster following PP.

4.4 DISCUSSION

The primary objective of this study was to examine the efficacy of MI for motor skill acquisition with no associated PP. A secondary objective was to characterize the effectiveness of MI-based practice relative to PP, the gold standard for skill acquisition. Following MI-based practice, RTs were decreased for the implicit compared to random sequences. Thus, motor skill acquisition was facilitated via MI in the absence of PP. Compared to MI-based practice, RTs for implicit and random sequences were decreased following PP. Thus, while MI-based practice alone was sufficient to produce motor learning, it was inferior to PP. However, this finding needs to be interpreted in the context of the type of learning examined. Below we discuss these findings and their implications for the use of MI in skill acquisition.

4.4.1 MI-BASED SKILL ACQUISITION

Acquisition of a motor skill is associated with refining a motor plan through repetitive practice coupled with feedback (Newell, 1991). Specifically, the sensorimotor system uses sensory feedback to identify errors in performance through comparison of reafference (i.e., response-produced feedback) relative to a forward model guided by an efference copy (i.e., predicted sensory consequences; Therrien & Bastian, 2015). As MI is typically performed following PP, it is unknown whether the subsequent MI simply reinforces the motor plan that is generated through the prior physical exposure. Interestingly, while previous research has demonstrated that MI can improve motor performance in conjunction with PP for established tasks (i.e., those tasks that a participant is already familiar with, such as a high-jumper performing MI of a high jump; Olsson, Jonsson, & Nyberg, 2008) as well as those that are novel to the participant (for review see Malouin et al., 2013), it is thought that MI does not generate the feedback necessary to update the motor plan based on an error detection and correction mechanism (Annett, 1995). This lack of feedback during MI may provide an explanation for why PP remains the gold standard for motor learning, and why it may be necessary to couple MI with PP to facilitate learning.

Interestingly, research indicates that MI-related brain activity parallels that of PP (Hétu et al., 2013), including cerebellar activation that underlies error detection/correction (Lacourse et al., 2005). Thus, MI may be able to both generate and update these motor representations independent of PP. Without a way to objectify errors made during MI in the current paradigm however, whether MI may have its own mechanism of error detection/correction remains unknown. Here we show that MI-based skill acquisition occurs without prior PP, suggesting that the motor plan necessary to execute a skill can be generated and strengthened independent of PP.

4.4.2 MI VS. PP

The effectiveness of MI-based practice was characterised by evaluating MI-based results in the context of PP-based performance. Importantly, the magnitude of the dRT did not differ between groups (Figure 11). Thus, it is suggested that MI and PP are equally effective in facilitating ISL. However, overall RTs were faster in the PP group, as demonstrated by decreased RTs of the implicit and random sequences relative to RTs for the MI group. Though not statistically significant, the RTs of the random sequences between groups differed as evidenced by effect size (Kelley & Preacher, 2012). The finding of decreased RTs for both sequence types suggest that PP resulted in a generalized practice effect (Deroost & Soetens, 2004; Kim, Johnson, Gillespie, & Seidler, 2014; Meehan, Randhawa, Wessel, & Boyd, 2011). Thus, it is suggested that beyond ISL, PP is more effective as a modality for skill acquisition due to the associated error detection and correction mechanism, and support is provided for PP as the primary mode of motor learning relative to MI.

The observation of a main effect for condition (implicit vs. random) and group (MI vs. PP) suggest that there may be different mechanisms underlying the type of learning that occurred. It is well established that ISL (and learning in general) has both perceptual and motor components (Rosenbaum, Carlson, & Gilmore, 2001; Willingham, Nissen, & Bullemer, 1989). Consistent with the paradigm utilized, we assume that successful learning of the ISL task involved both components (Willingham et al., 1989). Specifically, participants needed to map perceptual cues to the appropriate motor response, thus necessitating what we more generally refer to as perceptual-motor learning. Interestingly, implicit perceptual learning has been demonstrated to occur independent of motor practice (Gheysen, Gevers, Schutter, Waelvelde, & Fias, 2009; Remillard, 2003). For example, Gheysen et al. (2009) demonstrated implicit perceptual learning of a colour sequence using a colour matching task, where the order of each colours presented corresponded to its position in the sequence, that did not involve a motor sequence. As such, it is possible that ISL in the MI group may have been facilitated by perceptual learning to a greater extent than in the PP group. However, while few studies have directly compared perceptual to motor ISL (Deroost & Soetens, 2004; Dirnberger & Novak-Knollmueller, 2013; Gheysen et al., 2009; Gheysen, Opstal, Roggeman, Waelvelde, & Fias, 2011), it is thought that perceptual compared to motor ISL occurs more slowly and dRTs increase with more training (Dirnberger & Novak-Knollmueller, 2013; Gheysen et al., 2011). In contrast to these findings, the present results show similar magnitudes of dRTs between the MI and PP groups and thus we speculate that MI-based practice did not result in purely perceptual learning. As discussed above, the generalized practice effect observed in the PP group likely demonstrates greater reliance on motor vs. perceptual learning processes. Interestingly, while activation patterns between MI and PP largely overlap, MI is associated with more widespread activation in comparison to PP (Hétu et al., 2013; Kraeutner et al, .2014), with increased activity observed in parietal and premotor regions during MI vs PP (Burianová et al., 2013). These differences in brain activation may further suggest disparity in the mechanisms that underlie MI and PP. However, as we utilized an ISL task to address the challenge of eliminating PP effects in MI-based learning, the perceptual vs. motor components cannot be elucidated. Future work should investigate the role of the perceptual and motor systems in MI-based learning.

4.4.3 TRANSFER EFFECTS

While MI is a useful adjunct to PP in skill acquisition, it remains unknown how MI-based learning of an implicit perceptual-motor skill will transfer to skill learning in other domains. While the task employed in the current study was well-suited for the investigation of MI-based learning in the absence of PP, its simplicity limits our understanding of how these results translate to more complex tasks. Sequence learning is however recognized as a critical aspect of human behaviour. As indicated previously, similar improvements in performance have been demonstrated following MI-based training (albeit with prior PP) relative to PP in tasks of greater complexity (e.g., a golf bunker shot; Smith, Wright, & Cantwell, 2008). This past evidence suggests that MI may well be as effective as PP for sequence learning of more complex tasks. Further, it is well established that implicit learning is critical for motor skill acquisition (Orrell, Eves, Masters, & Macmahon, 2007; Rosenbaum et al., 2001; Willingham et al., 1989), as some components of a motor skill cannot be verbalized (Rosenbaum et al., 2001). Indeed, the present results lead us to a more general question regarding the nature of MI-based learning. Imagery of motor sequences may only consolidate the internal motor representation of the skill (i.e., the part that cannot be verbalized), and therefore MI has little impact on the actual execution component of a skill. Perhaps the explanation for the generalized practice effect observed for the PP group in the current results is thus also attributable to the nature of MI-based learning. As implicit learning is implicated in acquiring motor skills in non-disabled individuals (Rosenbaum et al., 2001) and following neurological injury (e.g., post-stroke; Boyd & Winstein, 2001; Boyd & Winstein, 2004; Orrell et al., 2007; Siengsukon & Boyd, 2009), MI-based practice that leads to learning of the implicit components of motor skills may have useful applications in rehabilitation and beyond. Future work should investigate transfer effects associated with MI-based practice.

4.4.4 EXPLICIT LEARNING

Given there are multiple domains in which sequence learning occurs, the removal of participants with explicit knowledge of the embedded sequences allowed for control of confounds introduced by explicit learning and ensured investigation of the implicit aspect of the learning that occurred. Previous research indicates that implicit knowledge is associated with skilled performance, as explicit knowledge is critical in learning involving higher levels of cognition (Sun, Merrill, & Peterson, 2001; Sun & Zhang, 2004), and relies on a different underlying neural network (Eimer et al., 1996; Keele et al., 2003; Yang & Li, 2011). Interestingly, more participants from the PP group demonstrated explicit knowledge compared to those in the MI group. This finding is likely attributable to the length of the response-stimulus interval (i.e., the duration of time between each presented cue) used (1.5s) to allow for imagination of the movements to occur. Previous research indicates that explicit learning improves with increasing response-stimulus intervals (Destrebecqz & Cleeremans, 2001). To match the training conditions across groups, we did not shorten this interval in the PP group. Thus it follows that more participants were excluded for explicit knowledge of the implicit sequence in the PP vs. MI group.

4.4.5 EMG MONITORING

It has been previously shown that brain activation patterns differ when MI trials with muscle activity are eliminated from analysis (Kraeutner et al., 2014). Surprisingly, a meta-analysis of neuroimaging studies (Hétu et al., 2013) noted that only two of 75 studies utilized EMG in addition to visual monitoring to control for muscle activity during MI. It follows then that MI-based learning may be driven in part by actual movement that goes unnoticed to the observer (Kraeutner et al., 2014). Excluding participants in whom muscle activity (measured via EMG) exceeded a particular threshold allowed us to control for this confound and conclude that learning indeed resulted from MI-based practice.

4.4.6 LIMITATIONS

To mitigate potential confounds associated with prior exposure to the experimental task we did not include a baseline assessment of RT for either the MI or PP group. Not including a baseline assessment of RT introduces a study limitation in that we could not establish the absence of pre-existing group differences in RT. Knowing this limitation a priori, we attempted to control the potential for a group difference in RT in two ways. First, participants were randomly placed into either the MI or PP group, and thus, while the possibility of pre-existing group differences cannot be completely eliminated, the use of random assignment greatly reduces the likelihood. Second, the participants included in the study were all within an age range that demonstrate similar RTs to previous ISL and/or simple RT tasks (Anstey, Dear, Christensen, & Jorm, 2005). While minimal differences in simple RT have been demonstrated between a cohort of adults between the ages of 40-44 and 20-24, latencies in simple RT are generally associated with adults over the age of 60 (Anstey et al., 2005; Kray & Lindenberger, 2000). As participants in the current study were on average aged 22.1 ± 5.3 years, with only two participants over the age of 40 (aged 41 and 47, one each in the MI and PP groups), the possibility of any such pre-existing group differences that may have influenced RT is unlikely.

4.5 CONCLUSIONS

Motor imagery is a form of practice used to facilitate skill acquisition by driving plastic changes in the brain akin to those of PP (Jeannerod, 1995; Wulf et al., 2010), yet it is unknown whether MI requires prior PP of the skill to allow for MI-based learning to occur. By addressing challenges associated with typical MI training paradigms and rigorously monitoring muscle activity during training, the current study demonstrates skill acquisition resulting from MI-based practice alone. This research also characterises the effectiveness of MI-based practice by directly comparing MI-based performance outcomes to those resulting from PP. Motor imagery-based practice was shown to be as effective as PP in facilitating acquisition of an implicit perceptual-motor skill, yet inferior to PP for skill acquisition as PP further resulted in generalized motor practice effects. Ultimately, this work further informs applications of MI in motor skill acquisition. Future work should investigate perceptual vs. motor components of MI-based practice, as well as the nature of learning promoted via MI.

4.6 SUMMARY TO CHAPTER 4 AND TRANSITION TO CHAPTER 5

Experiment One (Chapter 4) investigated MI-based skill acquisition using an ISL paradigm that allowed for performance outcomes (i.e., learning) to be captured independent of any PP. The results of this first experiment demonstrated that MI-based practice without prior physical exposure effectively facilitated acquisition of an implicit perceptual-motor skill. Thus, it was concluded that the motor plan necessary to execute a skill can be generated and updated independent of PP. Establishing that MI alone can effectively facilitate skill acquisition provides support to its application in rehabilitation following neurological injury such as stroke, wherein PP is not always possible.

In order for MI to be an effective form of neurorehabilitation however, it is critical to understand how damage to brain regions often affected post-stroke impacts on skill acquisition occurring via MI. Although brain activity observed during MI parallels that of PP, previous studies also suggest that MI relies on a more widespread neural network including the consistent activation of left parietal regions that are commonly affected post-stroke (Burianová et al., 2013; Hétu et al., 2013; Kraeutner et al., 2014). It is therefore possible damage to these areas may impact on one's ability to utilize MI for skill acquisition. Thus, the following chapter investigates the impact of left parietal cortex damage via non-invasive brain stimulation in MI-based skill acquisition.

CHAPTER 5 EXPERIMENT TWO

5. 1 INTRODUCTION

Motor imagery (MI), the mental rehearsal of a motor task (Jeannerod, 1995), has been shown to be a useful adjunct to physical practice (PP) to aid skill acquisition in numerous domains (Moran et al., 2012; Wulf, Shea, & Lewthwaite, 2010). Recent work from our laboratory has demonstrated that MI, independent of PP, is an effective means of facilitating the learning of implicit perceptual-motor skills. Establishing that MI alone can effectively drive learning lends support to its use in disciplines wherein PP is not always possible, including rehabilitation following neurological injury such as stroke (Johansson, 2011; Sharma et al., 2009, 2006). Due to the reported parallels in brain activation (Hétu et al., 2013; Kraeutner et al., 2014; Zhang et al., 2012), MI is thought to drive brain plasticity akin to that of PP, thus providing the basis for why MI is effective as a form of practice (Jeannerod, 1995, 2001; Wulf, Shea, & Lewthwaite, 2010). What is not entirely clear in the literature examining MI is how stroke-related brain damage impacts its effectiveness as a modality for skill acquisition. Determining how brain damage impacts on MI-based skill acquisition is critical to understanding its role in post-stroke rehabilitation.

Damage to parietal regions, commonly observed post-stroke, is suggested to affect the ability to perform MI (McInnes, Friesen, & Boe, under review). Buch et al. (2012), studying stroke-related lesions, sought to assess structural and functional morphology relating to imagery of a grasping task. Connectivity between premotor and posterior parietal regions was shown to correspond with successful task performance. Thus, the authors suggest that parietal integrity may be necessary for MI (Buch et al., 2012). Other work has shown that damage to the parietal cortex impairs the generation of movement representations via MI, evidenced by increased time to imagine vs. execute a movement (i.e., mental chronometry; Sirigu et al., 1996). Lastly, parietal cortex damage was recently shown to impair or altogether prevent the performance of MI, based on the findings of 23 studies that provided a measure of ability to perform MI (McInnes et al., under review). As it seems the ability to perform MI is impaired following parietal cortex damage, it stands to reason that so to would MI-based skill acquisition. While these aforementioned studies show MI to be compromised to varying degrees following parietal cortex damage, all assessed MI ability using subjective rating scales rather than measuring the outcome of MI, which in most instances is skill acquisition or learning. As such, it has not been possible to identify the effect of parietal cortex damage on MI-based skill acquisition. Further, the results of these lesion-based studies are difficult to interpret due to the limited number of cases and the variability in lesion location and size (Rorden & Karnath, 2004).

Results from neuroimaging studies support the involvement of the parietal cortex in MI, demonstrating that regions within the parietal cortex are activated to a greater extent in MI relative to PP (Burianová et al., 2013; Hétu et al., 2013). While parietal cortex involvement in MI is attributed to the recruitment of stored motor representations (Cooke, Taylor, Moore, & Graziano, 2003; Hétu et al., 2013), the left parietal cortex specifically, including the inferior parietal lobule (IPL), is suggested to be involved in processes related to motor attention that are critical for movement selection, planning, and visuospatial integration, due to its involvement in the dorsal visual pathway (Rizzolatti & Matelli, 2003; Rushworth et al., 2001, 2003). Indeed, the left IPL has been shown to be active during MI in numerous studies (for review see Hétu et al., 2013). For instance, a study involving MI and PP of simple finger movements using both hands demonstrated that the left IPL was more involved in MI compared to PP regardless of the hand that was imagined. Further, Kawamichi et al. (1998), investigating the time course of activation patterns during an MI-based hand rotation task, demonstrated that the IPL was a critical region of information processing between visual and premotor areas. Taken together, the evidence suggests that the left IPL plays a key role in MI, although the nature of this role as well as the impact of damage to the IPL in MI-based skill acquisition remains unknown.

Based on the above-noted evidence, damage to regions within the parietal cortex (notably the IPL) may limit the effectiveness of MI for skill acquisition, rendering it impractical for aiding functional recovery after stroke. The current study thus seeks to identify the effect of damage to the IPL on MI-based skill acquisition through the use of non-invasive brain stimulation to induce a virtual lesion prior to MI-based practice of a novel skill. Skill acquisition will be determined using an MI-based implicit sequence learning (ISL) task, for which we have previously demonstrated learning via MI without prior PP, whereby faster reaction times (RTs) to a practiced sequence indicates successful learning (Kraeutner et al., under review). If the IPL is indeed critical to MI performance or MI-based skill acquisition, inhibition via brain stimulation should impair learning. As such, we hypothesize that following inhibition of the left IPL, skill acquisition will be impaired relative to those receiving sham or no stimulation. Demonstrating that inhibition of the left IPL diminishes MI-based skill acquisition will provide important information related to how MI should be applied in post-stroke rehabilitation. Importantly, these results provide an opportunity to explore the nature of the role of the left IPL in MI-based skill acquisition.

5.2 METHOD

5.2.1 PARTICIPANTS

Twenty-seven right-handed (Oldfield, 1971) participants (17 female, aged 21.9 ± 4.1) naïve to any form of brain stimulation took part in the study. All were healthy and free of neurological disorder, and each provided written, informed consent. All participants could clearly hear study instructions prior to the study onset, although a formal assessment of hearing was not required, and each was free of contraindications to transcranial magnetic stimulation (TMS; Rossi et al., 2009; see Appendix III). The study received approval from the research ethics board of the Capital District Health Authority. Prior to the onset of the study, participants were randomized into a Sham or TMS group. To contextualize the findings, data from the Sham and TMS groups was compared to that of a control group (N = 24; 16 female; aged 23.6 ± 5.3 years; see Chapter 4.2) collected as part of a previous study that compared MI-based practice of the ISL paradigm to PP of the same task (see Chapter 4). Participants in this control group completed the experimental procedure as outlined below with the exception of TMS.

5.2.2 EXPERIMENTAL TASK

The experiment involved four training blocks of an MI-based ISL task followed by a physical test block, as outlined in Chapter 4. The task involved MI of button presses with the non-dominant (left) hand. All participants performed the task sitting at a chair in front of a computer screen oriented at eye-level, with their left hand resting comfortably over the keyboard. Participants were oriented to four keys (V, C, X, Z) numbered 1-4 from right to left, representing the index, middle, ring and little finger respectively, and were instructed to close their eyes and imagine themselves performing the button presses that were cued auditorily through noise-cancelling headphones. An auditory tone was played and their response was recorded if participants pressed a button during the training blocks. Each individual imagined keypress event lasted 1.5s based on the time separating consecutive auditory cues. Each training block consisted of 250 trials, with a 5-minute rest block provided between each.

Embedded within the training blocks was a repeated sequence (Goschke & Bolte, 2012) that consisted of ten, non-repeating digits unique for each participant. The implicit sequence appeared 80% of the time throughout each block (20 sequences total) while random sequences of equal length appeared 20% of the time (5 sequences total). The order in which the sequences appeared was randomized. Participants were blind to the fact that sequences were incorporated within each block and were thus naive to the implicit learning nature of the task.

To ensure the absence of muscle activity during MI-based practice, the electromyogram (EMG) was obtained from the left flexor and extensor muscles of the digits (anterior and posterior aspects of the forearm respectively). The EMG signal was acquired using self-adhering electrodes (1 x 3 cm; Q-Trace Gold; Kendall-LTP, USA) in a bipolar configuration with a 1 cm inter-electrode distance, sampled at 1000Hz with a bandpass of 25-100 Hz (1902 and Power 1401; Cambridge Electronics Design, UK) and stored for offline analysis.

5.2.3 TRANSCRANIAL MAGNETIC STIMULATION

Neuro-navigated TMS was administered using a Brainsight 2™ (Rogue Research Inc., Montreal, Canada) navigation system and an air-cooled 70mm figure of eight coil connected to a SuperRapid²Plus¹ magnetic stimulator (Magstim, Whitland, UK). Prior to each TMS session, three anatomical landmarks (nasion, right and left pre-auricular points) were digitized for each participant and co-registered with a template brain (MNI152_T1_1mm) to facilitate accurate positioning and orientation of the TMS coil.

Resting motor threshold (RMT) was determined by measuring the peak-to-peak amplitude of motor evoked potentials (MEPs) recorded via surface EMG overlying the right first dorsal interosseous (FDI) muscle. EMG was obtained using vendor-supplied hardware (Brainsight EMG Isolation Unit and Amplifier Pod). Briefly, a 5 x 5 grid with 7.5mm spacing was overlaid on the template brain with the mid-point (location 2, 2) centered on the 'hand knob' of the left primary motor cortex (Kleim, Kleim, & Cramer, 2007). Stimulator output was set to 55% and points on the grid were stimulated starting from 2,2 with the coil positioned tangentially to the scalp with the handle at a 45^0 angle to the posterior, working outwards from the centre in a counter-clockwise manner to determine the location(s) that produced the highest amplitude MEPs for 5 out of 10 stimulations. Once the 'hotspot' was localized, the RMT was determined as the lowest stimulator output where a MEP of an amplitude of ≥ 50 μV was obtained on 5 out of 10 stimulations and confirmed by stimulating grid points around the hotspot again in a counter-clockwise manner with the resultant stimulator output. Following determination of the RMT, inhibitory stimulation was delivered to the left IPL using a continuous Theta Burst Stimulation (cTBS) paradigm following established practices (Huang et al., 2005; Oberman, Edwards, Eldaief, & Pascual-Leone, 2011). cTBS intensity was set at 90% of RMT and delivered in bursts of three stimuli at 50Hz pulses, repeated at intervals of 200ms for a total of 600 pulses (Huang et al., 2005). Activation peaks from a study comparing activation during MI to PP of a similar button-press sequence task (Kraeutner et al., 2014) was used to localise IPL in MNI space (-36, -32, 34). Participants receiving sham stimulation underwent the same procedures as that of the TMS group, with the exception that during cTBS, the TMS coil was placed over the vertex of the head and stimuli were delivered at 15% of RMT.

5.2.4 EXPERIMENTAL PROCEDURE

Following informed consent and TMS screening, participants underwent the TMS procedures as described above. Following administration of the cTBS, all participants completed a MI familiarization block (Figure 12; Chapter 4.2). During this block, participants listened to an audio recording describing the type of MI to be performed (kinaesthetic), and the task to be imagined. Kinaesthetic MI was selected as this type of MI is most commonly used in sport and proposed to better facilitate basic motor skill learning (Stinear et al., 2006). The audio recording emphasized the poly sensory aspects of MI, directing the participants to attend to sensory information related to task performance, which has been shown to facilitate MI (Braun et al., 2008). Upon completion of the familiarization block, participants began the first of the four MI-based ISL training blocks.

TMS/Sham	All Groups						
Stimulation	EMG setup / Familiarization block	MI Training Block	MI Training Block	MI Training Block	MI Training Block	RT Test	Verbal Report
	10 mins	30 mins				5 mins	1 min

Figure 12. Timeline of the single experimental session. A reaction time (RT) test involving physical performance (i.e., keypresses) of the ISL task and verbal report assessment followed MI-based practice.

Immediately following the MI-based training, participants performed two assessments to measure skill acquisition (Figure 12). The first assessment was a RT test. Participants repeated a shortened block of the auditory-cued sequence task but were instructed to respond via actual button-press. During this test, the implicit and random sequences of equal length appeared 10 times each (i.e., a 1:1 ratio) for a total of 200 trials. The order that the sequences appeared was again randomized and an auditory tone was played if participants provided an incorrect response (e.g., pressed the '4' key when the '2' key was cued). Responses and the corresponding RTs were recorded for offline analysis. As in the training blocks, participants remained naive to the implicit sequence nature of the task.

The second assessment was a verbal report, the purpose of which was to determine whether explicit or implicit learning had occurred. Participants were first informed that the purpose of the training was to teach them a 10-digit sequence. Participants were then asked to respond to the question "Do you think you learned a sequence during the training blocks"? For either "yes" or "no" responses, participants were asked if they could report the sequence that they learned (i.e., the 10 consecutive numbers). Participants were instructed "it was okay if they did not think they learned a sequence".

5.2.5 DATA ANALYSIS

Data analysis followed procedures reported in Chapter 4.

Participants that demonstrated explicit learning were excluded from further analysis. Specifically, participants that answered "yes" to the question of whether or not they thought they learned a sequence and who correctly reported more than 50% of the sequence (i.e., 5 consecutive sequence elements), were excluded from further analyses.

Analysis of the responses made during the MI training blocks was performed to identify and remove participants who had actually performed button presses and had thus experienced a degree of PP during the MI-based training. Participants that made responses greater than 2% (20/1000 responses total) of the time across all training blocks were excluded from further analyses.

Analysis of the EMG data obtained during MI was performed to further identify and reject participants that demonstrated PP during the MI-based training (Kraeutner et al., under review). Data was first rectified and a 10Hz low-pass filter applied. The absence of activity in the left flexor and extensor muscles of the digits during MI was determined by calculating the average amplitude across 15 second envelopes of the EMG signal during each training block, and comparing each to a 15 second envelope acquired during the familiarization block (during which participants were at rest). The EMG threshold was defined as the average rest amplitude plus 2 standard deviations. Participants were excluded from further analysis if greater than 15% of the comparisons exceeded the threshold.

For the RT task, the first element of each sequence was omitted from analysis as per Wohldmann et al. (2007) due to its role in perception vs. motor execution (i.e., providing a cue to the movement about to be performed). RTs for trials that occurred before 100ms and after 1300ms were removed from analysis to control for anticipatory and outlier responses (Rüsseler et al., 2001). RTs for trials in which an incorrect response was provided were also removed from analysis. The RTs for all remaining trials as well as error rates were then averaged for both the implicit and random sequences for each individual. RT differences (dRT) between the implicit and random sequences (average RT random minus average RT implicit) were also calculated for the purposes of group comparison.

A 2 (sequence type) x 3 (group) mixed ANOVA was conducted to analyse the between condition effects of sequence type (implicit vs. random) and group (TMS vs. Sham vs. Control) on RT. An alpha value of $p < 0.05$ denoted significance. To assess learning within the groups, an effect size was computed for each group comparing RTs of implicit to random sequence using the average standard deviation between the two sequence types. To characterise group differences, effect sizes were computed comparing dRTs of the TMS vs. Control and Sham vs. Control using the average standard deviation of dRT between groups. Throughout, means values are reported followed by standard deviation.

5.3 RESULTS

Following the criteria above, 7 participants were excluded leaving a total of 20 participants in the behavioural analysis (9 and 11 in the TMS and Sham groups respectively). From the TMS group, 2 participants were excluded as they accurately reported more than five consecutive sequence elements on the verbal report task. Data from one participant was further excluded from final analyses due to an error in the EMG calibration. Of the total remaining TMS group participants, the average number of responses made across all 1000 of the MI-based training trials was 1.44 ± 3.24. From the Sham group, 1 participant accurately reported more than five consecutive sequence elements on the verbal report task; and 3 participants were excluded due to the presence of muscle activity during the MI training that exceeded our threshold. Of the total remaining Sham group participants, the average number of responses made across all 1000 of the MI-based training trials was 1.82 ± 3.92. As noted above, data from 24 participants that performed the same MI-based task were included to serve as a behavioural control group.

5.3.1 REACTION TIME

As reported previously, the Control group produced mean RTs of 583 ± 84 ms and 632 ± 86 ms for the implicit and random sequences, respectively (Figure 12). Mean error rate (%) for the implicit and random sequences within the Control group were 1.92 ± 2.00 and 2.62 ± 2.68 (see Chapter 4.3). For the Sham group, mean RT for the implicit and random sequences were 593 ± 50 ms and 629 ± 51 ms (Figure 13). Mean error rate for the implicit and random sequences were 2.36 ± 2.77 and 2.64 ± 2.84. For the TMS group, mean RT for the implicit and random sequences were 626 ± 73 ms and 634 ± 62 ms, respectively (Figure 13). Mean error rate for the implicit and random sequences were 2.56 ± 1.42 and 2.89 ± 2.76. Mean dRT and effect sizes between the sequence types for all groups is reported in Table 1.

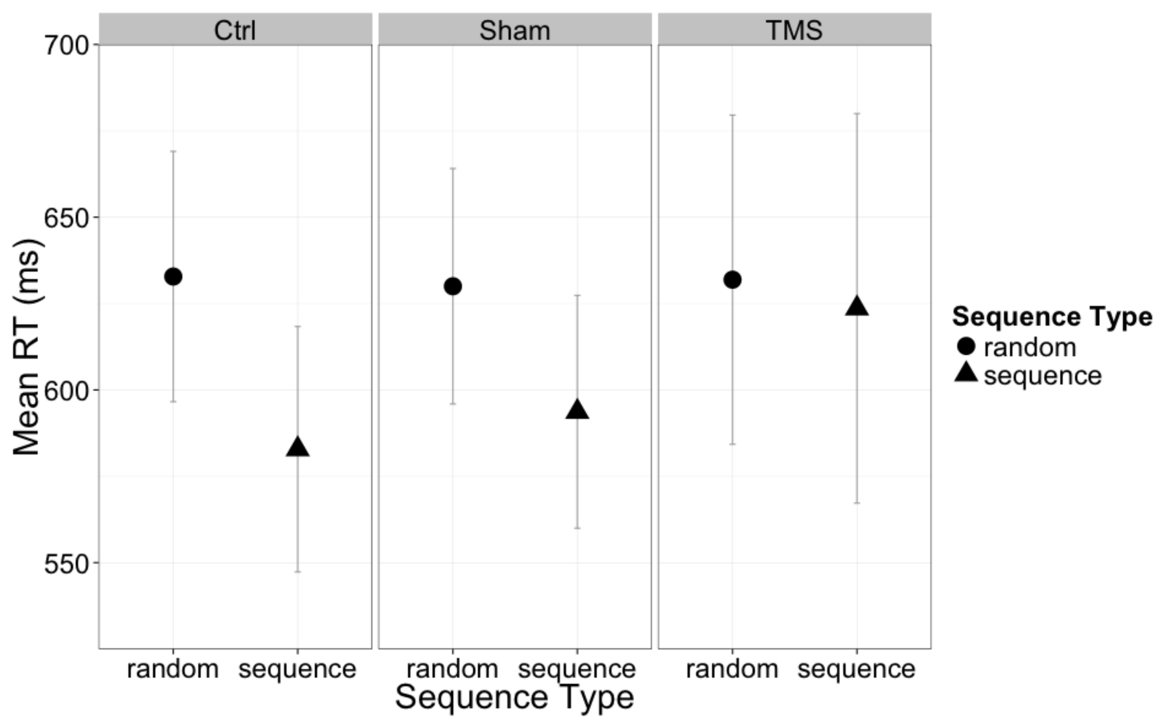

Figure 13. Mean reaction time (RT) for the implicit and random sequences across groups. Error bars denote 95%CIs. Overall RT across group did not differ.

5.3.2 GROUP COMPARISONS

Overall, there was a significant main effect of sequence type [$F(1,41) = 34.52$, $p < 0.001$], where RTs were significantly faster to sequence numbers than to random numbers. There was no main effect of group detected [$F(2,41) = 0.34$, $p = 0.71$]. While there was no significant interaction between sequence type and group [$F(2,41) = 3.21$, $p = 0.051$], the results were trending in this direction (further detailed below).

To characterize the amount of learning that resulted via MI, effect sizes (Kelley & Preacher, 2012) within each group were calculated comparing the RTs of the implicit and random sequences (Table 1). While the Sham and Control group resulted in similar differences between the implicit and random sequences, the TMS group showed no difference (Table 1). Thus, we further investigated observed RTs between the groups. A comparison of dRTs between the Control and Sham groups yielded an effect size of 0.34, while a comparison of dRTs between the Control and TMS groups yielded an effect size of 0.96. Taken together with the within group effects, we conclude the TMS group did not produce similar implicit sequence RTs as that of the Control and Sham groups (Figure 13).

Table 1. Mean different between implicit and random sequences across group.

	Control	Sham	TMS
dRT (*ms*)	49.74 ± 48.70	36.05 ± 28.15	7.67 ± 38.47
Effect size (*d*)	0.58	0.71	0.11

5.4 DISCUSSION

The primary objective of this study was to examine the impact of left IPL damage on MI-based skill acquisition. Following MI-based practice, successful skill acquisition was observed in participants receiving Sham TMS, but not in those receiving real TMS. Similar to that of the previously collected control group, RTs were decreased for the implicit compared to random sequences in the Sham group, whereas no difference in RT was observed between the implicit and random sequences in the TMS group. Thus, we conclude that inhibition of the left IPL via cTBS impaired MI-based skill acquisition. Below we discuss these findings and their implications for the use of MI in skill acquisition.

The current findings demonstrate that inhibition of left IPL impaired MI-based skill acquisition. We assume then, consistent with previous lesion-based research, that inhibition of the left IPL via cTBS disrupted MI ability, and in turn MI-based skill acquisition. As outlined above and based on the prior literature, it is not possible to wholly conclude that MI ability was impacted by damage to regions within the parietal cortex, as the performance of MI was assessed subjectively, with no robust, quantifiable measure of the outcome of MI performance (e.g., skill acquisition). Additionally, variability associated with lesion size and location further confounds the interpretation of previous findings. Here, we established that MI was affected following a virtual lesion to the left IPL, via performance of a robust learning paradigm that did not rely on subjective report. As MI has been previously shown to facilitate skill acquisition utilizing this learning paradigm (Kraeutner et al., under review), and performance following sham stimulation was shown to parallel these results, we conclude that the left IPL is indeed critical to MI performance and, in turn, the effectiveness of MI as a modality for skill acquisition.

5.4.1 IMPACT OF IPL DAMAGE TO MI

As stated above, our results left us to conclude that the left IPL is critical to MI-based skill acquisition. While damage to the left IPL may well hinder the effectiveness of MI as a modality of skill acquisition post stroke, it was previously unclear whether the left IPL was critical to MI performance (i.e., the ability to do MI), or rather processes underlying learning that is mediated by MI. The evidence generated to date would largely suggest that it is impairment in MI ability that prevents learning via MI following IPL damage. First, although subjective in nature, there is a large body of literature showing impaired MI ability in patients with parietal cortex lesions. When coupled with the current findings, the notion of impaired MI ability receives further validation in that we show an inability to learn via MI as assessed quantitatively using a robust learning paradigm that is independent of any PP. Second, neuroimaging work has shown that activity in the IPL during MI occurs prior to that of motor regions, in that the IPL first receives input from visual areas, followed by a bi-directional flow of information with premotor areas (Kawamichi et al., 1998). Thus, while the IPL is an important hub for information processing and transfer, the temporal order of activation during MI (i.e., prior to involvement of regions key to motor learning including pre- and primary motor regions; (Doyon & Benali, 2005; Hikosaka et al., 2002; Ungerleider et al., 2002), suggests a critical role in MI performance rather than motor learning per se.

In addition to that described above, other neuroimaging studies provide a means to understand the impact of IPL damage on MI ability. Research has demonstrated that while parietal regions are critical to explicit motor sequence learning, the network underlying implicit motor sequence learning relies on connectivity between the primary motor cortex, cerebellum and striatum (Destrebecqz et al., 2005; Marvel et al., 2007; Tzvi, Münte, & Krämer, 2014). It follows then that parietal damage does not impact upon implicit learning (in this case ISL), but rather the modality or substrate used to facilitate it. This evidence suggests that the impairment of MI-based learning observed in the current study was in fact due to an inability to perform MI following rTMS of the left IPL.

5.4.2 ROLE OF IPL TO MI

The current findings extend those of previous work that indicate parietal regions, including the left IPL, play a key role in MI ability and thus are more critical to MI-based practice relative to PP. Indeed, while similar brain regions are driven during MI-based practice as in PP (Burianová et al., 2013; Hétu et al., 2013; Kraeutner et al., 2014), MI is suggested to recruit a more widespread and bilateral network, including the consistent activation of left parietal regions (Burianová et al., 2013; Hétu et al., 2013). While the underlying mechanisms involved in MI-based learning remain largely unexplored, we turn to previous work to provide preliminary insight on the nature of the role of IPL in conjunction with the present findings.

Previous research suggests the parietal cortex, including the IPL, is involved in generating motor representations and movement selection (Rushworth et al., 2001, 2003). Specifically, regions in parietal cortex are thought to be responsible for coding properties of objects and intrinsically creating a sequence of movements to execute. Arguably however, the generation of a 'motor map' is equally important for both MI and PP. Thus, the consistent activation of the left IPL during MI may suggest that skill acquisition via MI involves additional processes less critical for skill acquisition via PP, and that these processes are modulated by the IPL.

Numerous studies have demonstrated the involvement of the IPL in visuospatial processes (Chambers, Payne, & Mattingley, 2007; Corbetta & Shulman, 2002; Hilgetag, Théoret, & Pascual-Leone, 2001; Kitadono & Humphreys, 2011; Rizzolatti & Matelli, 2003). In fact, damage to this area often results in spatial attentional deficits (Behrmann, 2004; Vandenberghe, Molenberghs, & Gillebert, 2012). As the IPL is a key structure in the dorsal visual pathway (responsible for visuospatial integration), it follows that these processes may be critical to MI. Further, research suggests that MI improves the implicit or cognitive aspect of the skill being practiced (i.e., MI consolidates the generated motor representation) without improving the actual execution component as, unlike PP, MI does not generate the feedback necessary to update the motor plan (Annett, 1995). Thus, it follows that MI activates regions involved in visuospatial integration and motor attention that are critical to generating the motor representation and consolidating cognitive aspects of the skill more so than regions necessary for movement output, such as the primary motor cortex. Reviewed in the context of the present findings, the implicit nature of MI-based learning may provide an explanation as to why parietal regions, including the left IPL, are critical to MI. To this end, we suggest that these visuospatial processes may be more necessary for MI-based learning compared to skill acquisition occurring via PP.

5.4.3 LIMITATIONS

A limitation of the current study includes the possibility that cTBS of the left IPL disrupted processes involved in actual motor execution, and thus the RTs observed for the implicit sequence would be attributable to impairment in motor execution (i.e., actual button pressing) in the test block. No difference was observed however when comparing the baseline motor response across groups (i.e., RTs of random sequence; see Figure 14). Thus we conclude that actual motor execution was not impaired following inhibition of the left IPL, and that the lack of skill acquisition in the TMS group is attributed to the induced virtual lesion.

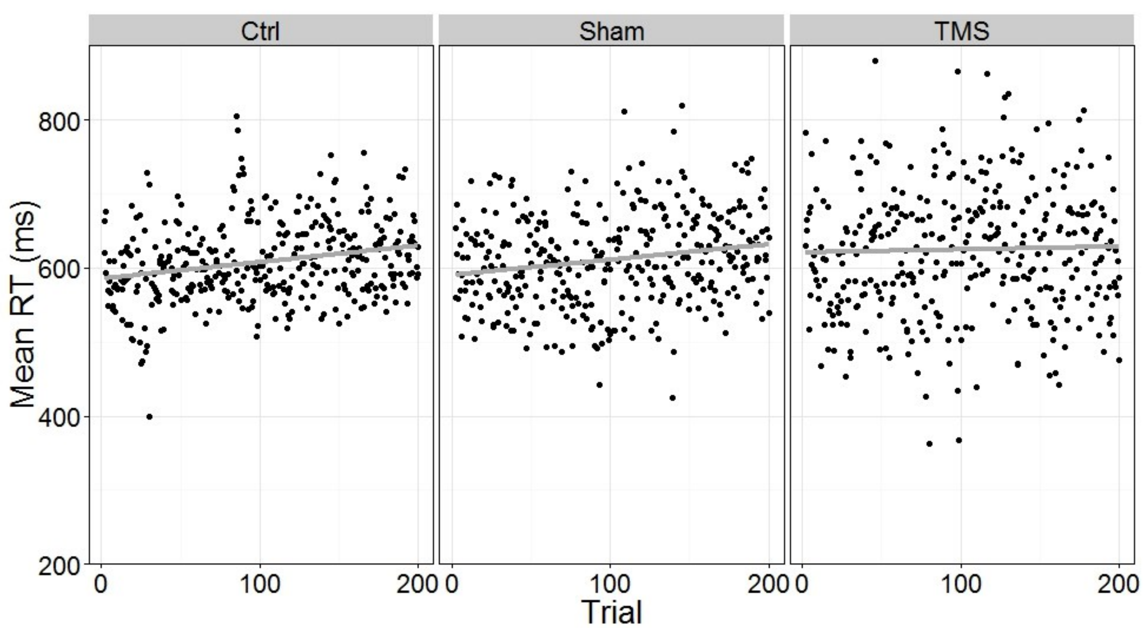

Figure 14. Mean reaction times (RT) for random sequence across test block trials. Random sequence RTs across group did not differ.

A second limitation is that data from our TMS group showed greater variability compared to the Sham and Control groups. In fact, one participant receiving real TMS demonstrated acquisition of the implicit skill. Previous research has demonstrated that some individuals, termed 'non-responders', do not show inhibition following cTBS (López-Alonso, Cheeran, & Río-Rodríguez, 2014). Thus, we suggest that the TMS participant who demonstrated successful skill acquisition was a non-responder. Due to the location of the stimulation site (i.e., a non-motor area), we were not able to assess cTBS effects via MEP amplitude to identify non-responders, but rather depended on behavioural outcomes. Importantly, while removal of this participant's data from the analysis decreased variability (see Figure 15), its inclusion still resulted in a robust effect.

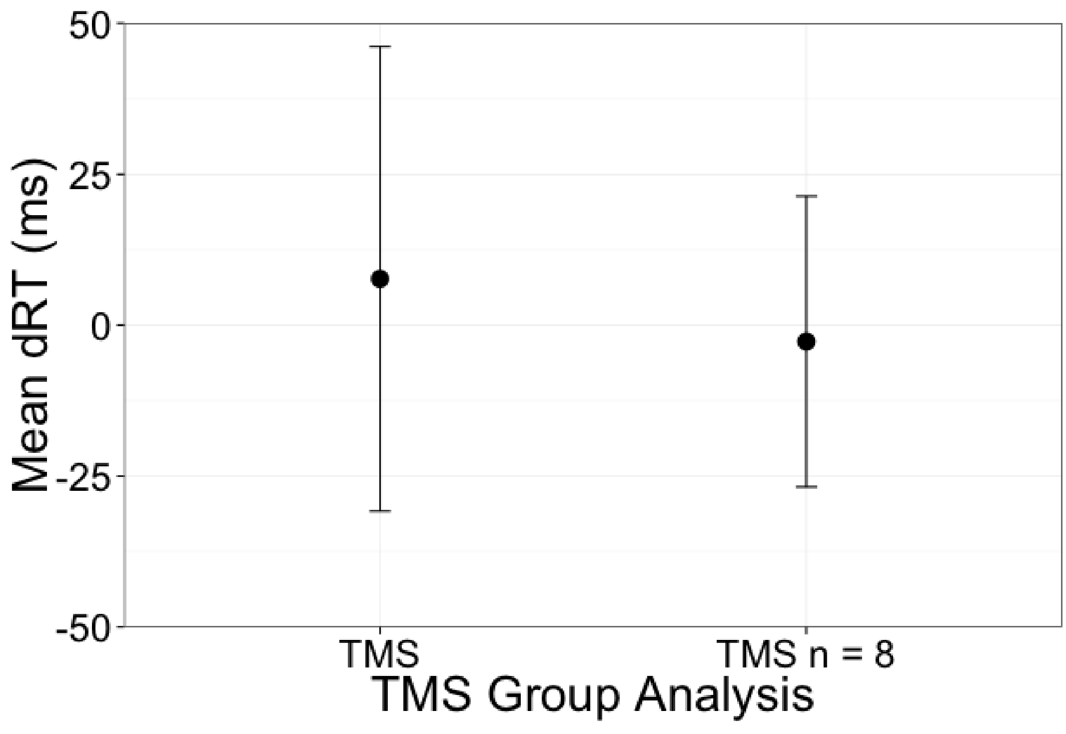

Figure 15. Mean difference between implicit and random sequences (random minus implicit) for the TMS group including and excluding the potential non-responder. Error bars depict SDs.

5.5 CONCLUSION

MI is shown to be a useful adjunct to PP in numerous domains and is emerging as a useful tool for rehabilitation post-stroke, yet it is unknown how stroke-related brain damage impacts on the effectiveness of MI as a modality of skill acquisition. The present study demonstrates that damage to the left IPL impairs acquisition of an implicit perceptual-motor skill through MI, thus providing direct evidence that this region is critical for MI performance, and thus MI-based learning. The involvement of the IPL in visuospatial processes suggests that the IPL may contribute to generating the motor representation and consolidating cognitive aspects of the skill, and that these visuospatial processes may thus be more critical to skill acquisition via MI vs. PP. As parietal cortex function is often impaired following stroke, these results have implications for the use of MI-based skill acquisition in post-stroke rehabilitation. Future work should investigate the mechanisms underlying MI ability.

CHAPTER 6 GENERAL DISCUSSION

The primary focus of the current work was to address the challenge of assessing skill acquisition via MI independent of PP, by employing an MI-based ISL task. Within this focus, the efficacy of MI-based practice was also characterised relative to PP, the gold standard for skill acquisition. Experiment One demonstrated that MI-based practice without prior PP is as effective as PP in facilitating skill acquisition, as RT differences observed between the implicit compared to random sequences following MI-based practice were similar to the RT differences observed following PP. However, PP resulted in a generalized practice effect specific to motor performance that was not observed after MI, thus providing further support for PP as the gold standard of skill acquisition. A secondary objective of the current work was to complete a preliminary step in examining the effectiveness of MI for post-stroke rehabilitation by investigating the role of the left parietal cortex, commonly damaged post-stroke, in MI-based skill acquisition through the use of non-invasive brain stimulation. Experiment Two demonstrated that inhibition of the left IPL via cTBS impaired MI-based skill acquisition, as those participants receiving cTBS to the left IPL prior to the MI-based ISL task did not acquire the implicit skill while those not receiving stimulation did.

Collectively this work supports the use of MI as a modality for skill acquisition independent of PP. Specifically, direct evidence is provided for the use of MI in the acquisition of implicit perceptual-motor skills, which is not only important for learning in general, but also a critical aspect of re-learning motor skills post-stroke, which is the foundation for recovery of motor function. While these findings are promising for the use of MI in post-stroke rehabilitation, further research of MI-based learning in stroke populations is necessary to support this claim. Below these findings are discussed in the context of the general nature of learning that results following MI-based practice and their implications for MI as a form for skill acquisition.

6.1 THE NATURE OF MI-BASED SKILL ACQUISITION

As outlined in the preceding chapters, imagery of motor sequences may only consolidate the internal motor representation of the skill (i.e., the implicit aspect or part that cannot be articulated; Annett, 1995; Rosenbaum, Carlson, & Gilmore, 2001). The significance of this notion with regard to skill learning via MI is that MI may well have little impact on learning the actual execution component of a skill. Indeed, Experiment One demonstrated that MI-based practice was as effective as PP in facilitating the implicit (and perhaps perceptual) aspect of a motor skill, but did not impact upon the actual execution component. As discussed in Chapter Four, the lack of feedback associated with MI-based practice may explain this observation in part, in that errors in performance are unable to be identified as no sensory input is received following the imagined movement. Additionally, MI is a form of practice that does not actually engage the 'effector organs' (namely the components of the peripheral nervous system termed the motor unit, including the motor neuron and its corresponding muscle fibres). Unlike actual movement then, the training effects associated with MI include changes associated with network efficiency within the brain and/or those changes related to corticospinal excitability (see Chapter 2.1). It follows then that the contribution of MI in skill acquisition is related to strengthening implicit components of a skill as only regions involved with planning vs. execution within the motor pathway are activated, and that these components consist of the visuospatial aspect of the motor task to be learned. Thus, the implicit nature of learning that results following MI-based practice may indicate that MI-based practice is fundamentally different from PP.

Findings from Experiment One may further support the fundamental differences between MI and PP, in that MI-based practice only supports the internal motor representation of the skill (i.e., the part that cannot be articulated). It was demonstrated that PP of the ISL task resulted in a greater number of explicit learners compared to MI-based practice. Although this finding was attributed to the length of the response-stimulus interval (Destrebecqz & Cleeremans, 2001), it could be speculated that the greater number of explicit learners in the PP group is attributable to the stage of learning that was attained following training. Early learning (i.e., initial generation of the motor plan) requires increased use of cognitive resources to process task-related information and cues (Guadagnoli & Lee, 2004). Conversely, late learning (i.e., once the initial motor plan has been established) is considered to be more 'automatic' in nature, requiring less cognitive resources relative to early learning (Dayan & Cohen, 2011). Interestingly, when contrasting the results of explicit and implicit learners in the PP group, explicit learners showed a greater difference in RTs between implicit and random sequences (Figure 16). Further, explicit learners seemingly made more anticipatory responses (i.e., responses occurring ≤ 100ms of the stimulus; Rüsseler, Hennighausen, & Rösler, 2001) relative to implicit learners (0.01% and 0.0006% of the data, respectively), although the limited number of overall anticipatory responses prevented further investigation of this claim. Thus, as automaticity of the skill was reached following PP but not MI, it is suggested that MI may only support early stages of learning, with establishment of the motor plan for task automaticity requiring PP.

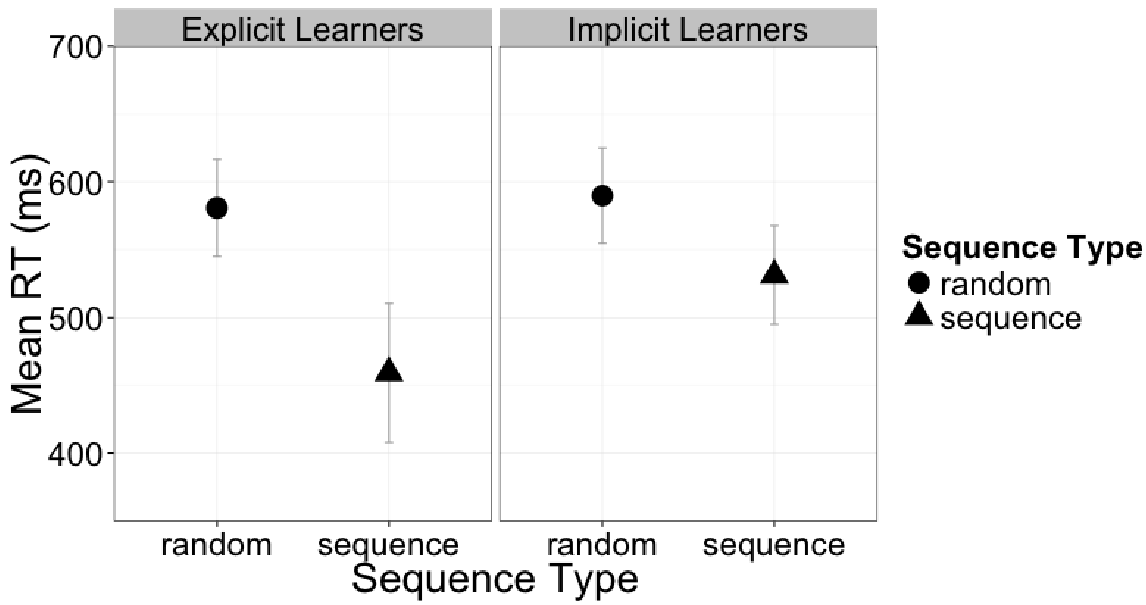

Figure 16. Mean reaction times (RT) for sequence types across type of learners within the PP group (explicit and implicit). Explicit learners were defined as participants who correctly reported greater than five consecutive elements of the implicit sequence and demonstrated decreased reaction times to the implicit sequence. Error bars depict 95%CIs.

Interestingly, a study conducted by Bohan, Pharmer, and Stokes (1999) sought to determine the stage of learning at which implementing MI would be most effective. MI practice was performed following varying doses of PP of a computer-based target-tracking task. Each dose of PP resulted in the learner having achieved an early, intermediate, or late stage of learning. It was demonstrated that MI-based practice in conjunction with the early stage of learning resulted in the most gains.

Thus, MI was demonstrated to have less impact on skill acquisition once the skill had become automated (i.e., the internal motor representation or plan had been established). Reviewed in the context of the current work, it is suggested that the gains observed via MI during the early stages of learning are attributable to the strengthening of the internal movement representation. Once the internal representation of the motor plan is well established however, any improvements in the skill during late stages of learning (i.e., following establishment and maintenance of the motor plan) rely on physical training effects that go beyond the capabilities of MI. Thus, it follows that MI-based skill acquisition may rely more heavily on brain regions critical to generating and updating the internal movement representation (Annett, 1995). Findings from Experiment Two may further support the contribution of these brain regions to MI.

6.2 MECHANISM FOR MI-BASED SKILL ACQUISITION

As demonstrated in Chapter Five, a virtual lesion of the left IPL impaired MI-based skill acquisition. While the specific role of the IPL in MI was unable to be elucidated (i.e., MI performance vs. learning occurring via MI), its role in MI-based skill acquisition was suggested to be related to generating and updating the internal movement representation due to its involvement in the dorsal visual pathway (Binkofski & Buxbaum, 2012; Rizzolatti & Matelli, 2003; Rushworth, Krams, & Passingham, 2001; Rushworth, Johansen-Berg, Göbel, & Devlin, 2003). Thus, if MI-based practice only supports early stages of learning that require these visuospatial processes, it follows that learning did not occur following inhibition of the IPL due to an impairment associated with generating this initial motor representation. On the contrary, when MI-based practice leads to successful acquisition of the implicit aspect of the skill (i.e., the initial motor representation becomes consolidated), it stands to reason that regions critical to generating the initial motor representation become less critical. Interestingly, research examining differences between expert and novice athletes has demonstrated that imagery training resulted in reduced parietal activity in experts when performing MI of a skill specific to their sport (Olsson, Jonsson, Larsson, & Nyberg, 2008). It is suggested that as the motor representation becomes consolidated (i.e., the implicit aspect of the skill improves) the imagery task itself becomes less cognitively demanding (Olsson et al., 2008). Taken together with our findings, we suggest that MI-based practice is indeed fundamentally different from PP with regard to the component of learning it facilitates.

6.3 IMPLICATIONS FOR THE APPLICATION OF MI IN REHABILITATION

The basis for the effectiveness of MI as a modality of skill acquisition is that MI facilitates plastic changes in the brain akin to those that occur following PP (see Chapter 2.2). Notable differences observed during MI and PP of the same motor task (see Chapter 2.4) however, further supports the difference in the nature of learning that results from MI-based practice in comparison with PP. Specifically, differential activation of core motor areas observed during MI (Hétu et al., 2013; McInnes et al., under review) further suggests that MI has little to no impact on the actual execution component of a skill. If MI indeed only contributes to generating and updating the internal movement representation, it is unknown how this mechanistic difference may impact the use of MI in rehabilitation.

Previous literature is in favour of the use of MI as a tool for neurorehabilitation (see Chapter 2.3), however this evidence is preliminary and there is a need for larger scale randomized controlled trials to strengthen the level of evidence for its use. In fact, the effectiveness of MI for promoting functional recovery is contested, with several well-designed (albeit underpowered) studies demonstrating limited efficacy of MI in neurorehabilitation (see Chapter 2.3; Ietswaart et al., 2011; Liu, Chan, Lee, & Hui-Chan, 2004). While the ability to perform MI (see related discussion in Chapter 2.5) as well as variability associated with the brain lesion (e.g., size and location; Chapter 2.7) represent two factors contributing to the conflicting results, it is also possible that the limited efficacy of MI is attributable, at least in part, to the implicit nature of learning facilitated through MI-based practice.

Importantly, while the efficacy of MI for skill acquisition in general may be limited by its implicit nature, prior investigations of motor learning following stroke have demonstrated successful acquisition of implicit skills (Boyd & Winstein, 2003, 2001; Orrell et al., 2007). Thus, as previously mentioned (see Chapter 4.4.3), MI-based practice that results in facilitating implicit components of motor skills may have useful applications in post-stroke rehabilitation, as consolidating the internal motor representation of a skill may be critical to relearning post-stroke. A study conducted by Siengsukon and Boyd (2009) investigated the effects of sleep in motor skill acquisition of a continuous tracking task post-stroke. Researchers demonstrated that compared to equivalent elapsed time between the last practice block and the retention test, spatial and temporal components of the skill were improved following sleep. However, this same enhancement was not observed in a control group of non-disabled individuals (Siengsukon & Boyd, 2009; Song, Howard, & Howard, 2007). Reviewed in the context of the current findings, we suggest that the improvements observed in the stroke group related to the spatial and temporal components is attributed to further consolidation of the internal representation of the movement during sleep vs. the actual execution component, and that the lack of additional improvement in the control group is attributed to having already established the internal representation. Thus, consolidation of the internal motor representation may be more challenging post-stroke, and tools that facilitate consolidation of these representations, including MI-based practice, may be critical to relearning motor skills.

Further, literature suggests that acquisition of implicit skills post-stroke may rely on a compensatory neural network (Meehan, Randhawa, Wessel, & Boyd, 2011; Wadden et al., 2015). A study conducted by Meehan et al. (2011) employed fMRI to investigate functional changes associated with ISL of a tracking task. In healthy individuals, initial task performance was shown to rely heavily on prefrontal regions. Activation in these areas decreased as the skill was acquired, with a parallel increase in activation noted in premotor areas. This shift in activation was thought to be indicative of changing processes underlying task performance. While initial task performance in participants with stroke was also shown to rely on dorsolateral prefrontal areas, the same shift in activation to premotor areas did not occur during acquisition of the skill. Alternatively, acquisition of the implicit skill in participants with stroke was associated with increased activity within the middle frontal gyrus

(BA8). As the middle frontal gyrus is involved in working memory and visuomotor processes (Adam et al., 2003), its involvement further supports the greater reliance on cognitive processes that may be necessary to consolidate the internal representation of the skill in stroke. Thus, understanding the contribution MI has in establishing the internal motor representation of a motor skill is necessary to inform on the use of MI in rehabilitation.

6.4 FUTURE DIRECTIONS

While the nature of MI-based learning remains largely unexplored, the protocol employed in Experiment Two (see Chapter 5.2) may provide a means to further investigate the mechanisms underlying MI-based learning. Establishing the role of the IPL in MI represents the first step in identifying key regions involved in the brain network as well as illuminating the processes underlying skill acquisition occurring via MI. By employing non-invasive brain stimulation to induce a virtual lesion, the role of previously identified 'hubs' critical to motor learning can be probed to further elucidate their contribution to skill acquisition that results from MI-based practice. Specifically, investigating the stages of learning that are achieved following MI-based training may provide a means to address the differences in learning that results following MI-based practice relative to PP.

As previously mentioned, the contribution of MI to the generation and subsequent updating of the internal movement representation suggests that MI supports early stages of learning. It stands to reason then that virtual lesions to brain areas involved in the late stages of learning, including those associated with automaticity such as the primary motor cortices, SMA, and striatum, should have no impact on skill acquisition occurring via MI. While a study conducted by (Pelgrims, Michaux, Olivier, & Andres, 2011) indicated that MI was disrupted following inhibitory TMS to primary motor cortices, the task involved laterality judgements of hand and letter positions, measured by RT of the judgement. However, as the responses recorded were verbal, it is possible that the delay in RT associated with virtual lesions of primary motor cortex were attributable to a disruption of language processes (de Lafuente & Romo, 2004; Yang & Shu, 2012). Further, as a learning paradigm was not employed, the impact of the virtual lesion to primary motor cortex on MI-based skill acquisition remains unknown. Alternatively, probing the role of premotor regions using the same ISL and TMS protocol as employed in the current work (see Ch. 5.2) could generate evidence to further support the contribution of MI to early vs. late stages of learning. Numerous studies have demonstrated that the magnitude of activation and degree of connectivity within the network involving premotor regions is increased during early learning, with subsequent reductions observed as the skill is consolidated (i.e., later stages of learning; Coynel, Marrelec, Perlbarg, & Pélégrini-Issac, 2010; Dayan & Cohen, 2011; Doyon et al., 2002). Therefore, if MI is most effective in the early stages of learning, premotor regions should be more critical to MI-based learning than learning via PP. A study by Lacourse, Orr, Cramer, & Cohen (2005) investigated brain activity during MI and PP of a sequential finger tapping task, before and after five days of PP. Interestingly, while premotor activation decreased between the novel phase of skill acquisition (i.e., day one) and the skilled phase (i.e., day five) during PP, premotor regions were consistently activated during MI (and to a greater extent than during

PP) following the five days of practice. Thus, even as participants reached a later stage of learning, premotor activation was shown to be critical for MI performance and therefore MI-based learning*.* As suggested above, creation of a virtual lesion in premotor regions should impair skill acquisition via MI given the role of this region in early learning. Thus, future research involving inhibition to areas such as the primary motor cortex and premotor regions prior to MI-based practice will provide insight on the claim that MI is involved in early learning.

Investigating transfer effects that result following MI-based practice may further serve as a means to explore the implicit nature of MI-based learning. It has been previously shown that motor skill acquisition via PP in one hand is associated with motor skill improvements (albeit to a lesser extent) in the other, untrained hand (Japikse, Negash, Howard, & Howard, 2003; Perez et al., 2007; Perez, Wise, Willingham, & Cohen, 2007). Interestingly, it is thought that this transfer may arise from the already established visuospatial representation (Rosenbaum et al., 2001). As the hand demonstrating the transfer does not undergo any physical training, it is arguable that the actual execution component is not impacted. Thus, a possible explanation is provided for why intermanual transfer is always proportionate to the hand in which the skill was learned. In light of the current work, by employing MI to facilitate acquisition of implicit components of a motor skill without impacting the actual execution component, intermanual transfer should thus still occur yet also result in a similar magnitude of improvement. Therefore, we suggest that intermanual transfer following MI-based skill acquisition be explored to further inform on the nature of MI-based learning.

6.5 GENERAL LIMITATIONS

6.5.1 CHALLENGES ASSOCIATED WITH THE ISL PARADIGM

While it is thought that ISL involves both perceptual and motor components (Willingham et al., 1989, Rosenbaum et al., 2001), implicit perceptual learning has also been demonstrated to occur independent of PP (Gheysen, Gevers, Schutter, Waelvelde, & Fias, 2009; Remillard, 2003). As the perceptual vs. motor components cannot be elucidated from the task employed in the current work, it is therefore possible acquisition of the implicit sequence via MI-based practice relied solely on the perceptual system, and thus was not representative of motor learning. In Experiment One however, similar magnitudes of dRTs between the MI and PP groups were observed. Thus, it is suggested that MI-based practice did not result in purely perceptual learning, although the lack of a generalized practice effect in the MI group may demonstrate a greater perceptual vs. motor component in MI-based learning. To address this limitation, the ISL paradigm employed in future studies should be modified to test transfer effects associated with perceptual and motor learning to investigate the role of the perceptual and motor systems in MI-based learning.

6.5.2 CHALLENGES ASSOCIATED WITH TMS

Numerous studies have demonstrated that some individuals, termed 'non-responders', do not show inhibition following cTBS (López-Alonso, Cheeran, & Río-Rodríguez, 2014). Typically, non-responders are identified by re-assessing MEP amplitude following inhibitory stimulation to primary motor cortex (López-Alonso et al., 2014). Due to the location of the stimulation site used in the current work (i.e., a non-motor area), we were not able to assess cTBS effects via MEP amplitude to identify non-responders, but rather depended on behavioural outcomes. As noted in Chapter 5, the TMS group showed greater variability compared to the Sham and Control groups. It was suggested that this variability was due to the possibility that some of the participants were non-responders or responded differently to the stimulation. Importantly however, the possible inclusion of non-responders in the TMS group still resulted in a robust effect.

Further, the variability within the TMS group may be attributed to individual differences in the location of the stimulation site. Each participant was co-registered to a template brain based on three anatomical landmarks to facilitate accurate positioning and orientation of the TMS coil. The left IPL was then localised in MNI space according to activation peaks from a study comparing activation during MI to motor execution of a similar button-press sequence task (Kraeutner, Gionfriddo, Bardouille, & Boe, 2014) and further shown to have good correspondence with activation peaks in a number of MI studies (Gerardin et al., 2000; Hétu et al., 2013). However, slight variations in the stimulation site are possible due to individual differences in brain morphology. Moving forward, if TMS is to be employed to probe the role of key regions involved in MI-based skill acquisition, maps generated based on functional imaging techniques may provide a means to more accurately localize each area of interest within individuals.

Importantly, virtual lesions induced via TMS differ from stroke-related brain damage in a number of ways, and interpretation of the TMS-induced effects must be made in the context of these differences. Current produced in the brain via TMS is influenced by a number of factors, including coil orientation and biological properties of the site targeted for stimulation. Specifically, current produced in the brain via electromagnetic induction are dispersed subject to volume and density of the tissue (Wagner, Zahn, Grodzinsky, & Pascual-Leone, 2004). While theoretical models have been developed to describe the effect this current has on cortical neurons (Roth, Cohen, & Hallett, 1991), this spread is unable to be quantified and thus it is impossible to know the extent of neuronal activation or the volume of cortical area affected by each TMS pulse (Bolognini & Ro, 2010; Hallett, 2000). Further, neurological damage following stroke is often diffuse and very rarely is one focal region of the brain affected. Thus, it is important to consider these differences when interpreting the current findings and in future studies employing TMS to explore the impact that stroke-related brain damage may have on behaviour.

6.4 CONCLUSION

Motor imagery is shown to be a useful adjunct to PP in numerous domains and is emerging as a useful tool for rehabilitation post-stroke (Johansson, 2011; Malouin, Jackson, & Richards, 2013; Sharma, Baron, & Rowe, 2009; Sharma, Pomeroy, & Baron, 2006). In showing that MI facilitated skill acquisition in the absence of PP, the current work further supports the application of MI in rehabilitation and beyond. Yet, the effectiveness of MI as a tool for rehabilitation post-stroke may be limited following damage to the left IPL. However, it is suggested that MI-based practice is fundamentally different than PP in that MI may only contribute to implicit components of a skill and relies more heavily on visuospatial processes. Thus, future research should be conducted into the general nature of MI-based learning and the mechanisms underlying MI-based practice. Furthering our understanding of the mechanisms that underlie MI and MI-based learning will ultimately lead to more effective and efficient applications of MI in motor skill acquisition in both non-disabled individuals and following neurological injury.

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APPENDIX I: EDINBURGH HANDEDNESS INVENTORY

Please indicate your preferences in the use of hands in the following activities by putting a check in the appropriate column. Where the preference is so strong that you would never try to use the other hand, unless absolutely forced to, put 2 checks. If in any case you are really indifferent, put a check in both columns.

Some of the activities listed below require the use of both hands. In these cases, the part of the task, or object, for which hand preference is wanted is indicated in parentheses.

Please try and answer all of the questions, and only leave a blank if you have no experience at all with the object or task.

	Left	Right
1. Writing	☐ ☐	☐ ☐
2. Drawing	☐ ☐	☐ ☐
3. Throwing	☐ ☐	☐ ☐
4. Scissors	☐ ☐	☐ ☐
5. Toothbrush	☐ ☐	☐ ☐
6. Knife (without fork)	☐ ☐	☐ ☐
7. Spoon	☐ ☐	☐ ☐
8. Broom (upper hand)	☐ ☐	☐ ☐
9. Striking Match (match)	☐ ☐	☐ ☐
10. Opening box (lid)	☐ ☐	☐ ☐
<u>TOTAL(count checks in both columns)</u>		

Difference	Cumulative TOTAL	Result

Scoring:
Add up the number of checks in the "Left" and "Right" columns and enter in the "TOTAL" row for each column. Add the left total and the right total and enter in the "Cumulative TOTAL" cell. Subtract the left total from the right total and enter in the "Difference" cell. Divide the "Difference" cell by the "Cumulative TOTAL" cell (round to 2 digits if necessary) and multiply by 100; enter the result in the "Result" cell.

Interpretation (based on Result):

below -40 = left-handed
between -40 and +40 =
ambidextrous above +40 = right-
handed

APPENDIX II: MOTOR IMAGERY FAMILIARIZATION SCRIPT

"Motor imagery is the mental performance of a movement – this means that you don't physically perform the movement. Instead you imagine yourself doing it by creating a picture of it in your head. There are two ways you can do motor imagery. The first is by picturing yourself performing the movement, and the second is by picturing someone else doing the movement. For this study we want you to imagine yourself doing the movement.

Doing motor imagery can be difficult at first, but there are a few things that can help you get better at it. One thing you can do is to try and relax – take a couple of slow, deep breaths and let yourself sink into the chair. As you are sitting there think about how the chair feels, and the position of your body. Another thing you can do is to think about how it feels when you actually perform the movement. How is your hand moving? How long does each movement take? All of these sensations can be used to make the picture in your head more vivid.

As we mentioned before there are two ways to do motor imagery. The first is by picturing yourself performing the movement and the second is by picturing someone else doing the movement. For this study we want you to imagine yourself doing the movement. You should be able to see your arm and hand, and your fingers moving up and down as your press each button.

For this study we want you to picture yourself performing the button press task. While you are imagining yourself pressing the buttons, think about what your arm and hand look like and how it feels when you're pressing each of the buttons."

APPENDIX III: TMS SCREENING FORM

V 1.0. 11/07/2012

LABORATORY FOR BRAIN RECOVERY AND FUNCTION

SCHOOL OF PHYSIOTHERAPY

DALHOUSIE UNIVERSITY
Inspiring Minds

TRANSCRANIAL MAGNETIC STIMULATION (TMS) SCREENING FORM

Below is a questionnaire used to determine whether potential participants are suitable for research studies using transcranial magnetic stimulation (TMS). Please complete the questions honestly and to the best of your knowledge. This information, as well as your identity, will be kept completely confidential.

Participants Study ID: ______________________________

Participants Age: ______

PLEASE COMPLETE THE QUESTIONS BELOW

	YES	NO
1. Do you have epilepsy or have you ever had a convulsion or a seizure?	☐	☐
2. Have you ever had a fainting spell or syncope (loss of consciousness)? If yes, please describe on which occasion:	☐	☐
3. Have you ever had a head trauma that was diagnosed as a concussion or was associated with a loss of consciousness?	☐	☐
4. Do you have any hearing problems or ringing in your ears?	☐	☐
5. Do you have cochlear implants?	☐	☐
6. Are you pregnant or is there any chance that you might be?	☐	☐
7. Do you have metal in the brain, skull or elsewhere in your body (e.g., splinters, fragments, clips, etc.)? If so, please specify:	☐	☐
8. Do you have an implanted neurostimulator (e.g., DBS, epidural/subdural, VNS)?	☐	☐
9. Do you have a cardiac pacemaker or intracardiac lines?	☐	☐

	YES	NO
10. Do you have a medication infusion device?	☐	☐
11. Are you taking any medications? (please list):	☐	☐
12. Did you ever undergo TMS in the past? If yes, were there any problems:	☐	☐
13. Did you ever undergo MRI in the past? If yes, were there any problems:	☐	☐

* TMS screening form is from the International Consensus Guidelines:
Rossi S, Hallett M, Rossini PM, Pascual-Leone A, Safety of TMS Consensus Group (2009) Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiol 120: 2008-2039.