Therapeutic Instrumental Music Training and Sensory-Enhanced Motor Imagery in Chronic Post-Stroke Upper-Extremity Rehabilitation: A Randomized Controlled Trial

by

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Faculty of Music
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Abstract

Objectives: To investigate the effectiveness of Therapeutic Instrumental Music Performance (TIMP) training, with or without motor imagery, in upper-extremity rehabilitation for individuals with chronic, post-stroke hemiparesis. Secondary objectives investigate effects of interventions on cognition and affect.

Methods: Two baseline assessments, a minimum of one week apart; one final assessment. Nine interventions (3x/wk for 3 wks), facilitated by a qualified Neurologic Music Therapist. Thirty participants were randomized to one of three groups: 45 minutes of active TIMP; 30 minutes of TIMP followed by 15 minutes of metronome-cued motor imagery (TIMP+cMI); 30 minutes of TIMP followed by 15 minutes of motor imagery without cues (TIMP+MI). A selection of acoustic and electronic instruments was used.

Results: Thirty participants completed the protocol, ten per arm [14 women; mean age= 55.9; mean time post-stroke= 66.9 months]. Pooled group baseline measures did not significantly differ. There were significant improvements from pre-test 2 to post-test for all groups on the Fugl-Meyer-Upper Extremity (FM-UE) and the Wolf Motor Function Test-Functional Ability Scale (WMFT-FAS), and for TIMP and TIMP+MI on the Motor Activity Log (MAL)-Amount of Use Scale. Comparing percent change differences between groups, TIMP (mean rank = 21.05) scored significantly higher than TIMP+cMI (mean rank = 11.00, $p = .032$) on the FM-UE. There were no significant percentage change differences between TIMP and TIMP+MI.

The TIMP+MI group showed a significant change on the Trail Making Test (TMT)–Part B. The TIMP group showed a significant increase on the Multiple Affect Adjective Checklist (MAACL) Sensation Seeking scale and the Valence and Dominance portions of the Self-Assessment Manikin (SAM); TIMP+cMI showed respective increases and decreases in positive and negative affect on the MAACL, as well as an increase in Valence, Dominance, and Arousal portions of the SAM. There was no statistically significant association between cognitive and affective measures.

Conclusions: Implementation of TIMP-based techniques led to significant improvements in paretic arm control. TIMP and TIMP+MI showed greater benefits than TIMP+cMI, suggesting that synchronizing internal and external cues during cMI may pose additional sensory integration challenges. TIMP+MI appeared to increase mental flexibility, while active TIMP interventions appeared to enhance positive affect.

Trial Registration: ClinicalTrials NCT03246217

Dedication

In loving memory of my parents,

John Edwin Haire and Ethel Margaret Gudlaugson Haire

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Table of Contents

Acknowledgments .... *v*

List of Tables .... *ix*

List of Figures .... *x*

List of Appendices .... *xi*

Chapter 1 Introduction *1*

1.1 Purpose **1**

1.2 Background Context **1**

1.3 Rationale **4**

1.3.1 Neurological and Physiological Responses to Musical Behaviour 5

1.3.2 Processes in Nonmusical Behaviour and Neurological Function 7

1.3.3 Mediating Influence of Music on Nonmusical Function 8

Chapter 2 Literature Review *14*

2 Hemiplegic Upper Extremity Rehabilitation *14*

2.1 Rehabilitation using Auditory Stimuli **14**

2.1.1 Bilateral arm training with rhythmic auditory cueing 14

2.1.2 Rhythmic auditory cueing without BATRAC 17

2.1.3 Music-based approaches using Neurologic Music Therapy interventions 18

2.1.4 Additional music-based approaches 29

2.1.5 Neural changes associated with behaviour 32

2.1.6 Secondary effects on cognition and affect 33

2.2 Rehabilitation without Auditory Facilitation **34**

2.2.1 Graded Repetitive Arm Supplementary Program 34

2.2.2 Repetitive task training 35

2.2.3 Neurodevelopmental and Bobath concept approaches 37

2.2.4 Constraint-Induced Movement Therapy 38

2.2.5 Strength training 41

2.2.6 Range of motion and stretching programs 43

2.2.7 Trunk restraint 44

2.3 Simulation Mode **46**

2.3.1 Action Observation 50
2.3.2 Mental Practice with Motor Imagery 52

Chapter 3 Methodology........ 62

3 Materials and Methods........ 62

3.1 Hypotheses........ 62

3.2 Participants 63

3.3 Study Design and Procedures 67

3.4 Assessments 69

3.4.1 Motor Assessment Tools........ 70
3.4.2 Cognitive Assessment Tools........ 71
3.4.3 Affective Assessment Tools 71

3.5 Data Analysis: 72

Chapter 4 Results 73

4 Results of Motor, Cognitive, and Affective Measures 73

4.1 Fugl-Meyer Assessment – Upper Extremity........ 74

4.2 Wolf Motor Function Test 77

4.3 Motor Activity Log 81

4.4 Trunk Impairment Scale 83

4.5 Digit Span Test........ 84

4.6 Trail Making Test 85

4.7 General Self-Efficacy Scale........ 87

4.8 Multiple Affect Adjective Checklist 89

4.8.1 Positive Affect 89
4.8.2 Negative Affect 95

4.9 Self-Assessment Manikin 100

4.10 Borg Rating of Perceived Pain........ 106

4.11 Non-parametric Correlation Analyses 106

Chapter 5 Discussion 109

5 Review of Results..................... 109

5.1 Primary Outcome Measures 109

5.1.1 Impairment-based Measures..................... 109

5.1.2 Function-based Measures..................... 114

5.2 Secondary Outcome Measures 118

5.2.1 Cognitive Outcomes..................... 118

5.2.2 Affective Outcomes..................... 120

5.2.3 Motor Imagery Conditions..................... 123

5.3 General Discussion..................... 125

5.3.1 Rhythmic Auditory Cueing – More than a Mechanism for Planning Movements?..................... 126

5.3.2 Motor Learning Principles..................... 129

5.3.3 Motor Imagery Practice 132

5.3.4 Study Limitations 134

5.3.5 Future Directions 134

5.3.6 Conclusion..................... 135

Appendices 136

References 152

List of Tables

Table 1. Demographic characteristics ……….……………………………………………66

Table 2. Baseline measures ………………………………………………………………..73

Table 3. FM-UE pre-test 2 – post-test by group …………………………...…………...…75

Table 4a. WMFT – FAS pre-test 2 – post-test by group ……………………………....…....78

Table 4b. WMFT – Weight, Grip strength ……………………………………………...80

Table 5. MAL – AS pre-test2 – post-test by group ……………………………....................82

Table 6. TIS pre-test2 – post-test by group ………………………………………….……84

Table 7. DST pre-test2 - post-test by group ..……………………………………………...…85

Table 8. TMT – Part B pre-test2 – post-test by group ..………………………………...…86

Table 9. GSE pre-test2 – post-test by group …………………………………………...…..88

Table 10a. MAACL – PASS pre-test2 – post-test by group ……………………………...…..89

Table 10b. MAACL – PA pre-test2 – post-test by group ……………………….………...91

Table 10c. MAACL – SS pre-test2 – post-test by group ……………………..……….…...93

Table 10d. MAACL – DYS pre-test2 – post-test by group ……………………..……...…95

Table 10e. MAACL – A pre-test2 – post-test by group ………………………..…….………97

Table 10f. MAACL – D pre-test2 – post-test by group …………………………………………99

Table 10g. MAACL – H pre-test2 – post-test by group ……………………….……...…100

Table 11a. SAM – V pre-test2 – post-test by group ……………………………………...…101

Table 11b. SAM – A pre-test2 – post-test by group ……………………………………......102

Table 11c. SAM – D pre-test2 – post-test by group ……………………………………...104

Table 12a. Non-parametric comparisons within primary and secondary measures ……….....106

Table 12b. Non-parametric comparisons between primary and secondary measures …………107

List of Figures

Figure 1. Consort diagram for participant screening and enrollment …………………………..65

Figure 2. FM-UE data points, medians, difference scores, and percent change comparisons…..75

Figure 3. FM-UE difference scores for subsections: Parts A, B, C, and D …….……………….76

Figure 4a. WMFT – FAS individual data points, medians……………………………….......78

Figure 4b. WMFT-FAS pre-test 2 – post-test difference scores; percent change comparisons....80

Figure 4c. WMFT – Weight and Grip strength difference scores; Grip strength across groups...79

Figure 5. MAL – AS individual data points, medians and difference scores ……………...……82

Figure 6. TIS individual data points, medians …………………………………………………..84

Figure 7. DST individual data points, medians ………………………………………………….85

Figure 8. TMT individual data points, medians and difference scores …………………………87

Figure 9. GSE individual data points, medians ………………………………………………….88

Figure 10a. MAACL - PASS data points, medians, difference scores, group comparisons …....89

Figure 10b. MAACL – PA individual data points, medians, group comparisons ………………92

Figure 10c. MAACL – SS individual data points, medians and difference scores ……………..94

Figure 10d. MAACL – DYS individual data points, medians and difference scores …………...96

Figure 10e. MAACL – A individual data points, medians and difference scores ………………98

Figure 10f. MAACL - D individual data points, medians ………………………………………99

Figure 10g. MAACL – H individual data points, medians ……………………………...…..100

Figure 11a. SAM – V individual data points, medians and difference scores ………..……......101

Figure 11b. SAM – A individual data points, medians and difference scores …….…………...103

Figure 11c. SAM – D individual data points, medians, and difference scores ………………...105

List of Appendices

Appendix A: Definitions of Terms 136

Appendix B: Protocol for TIMP Study 140

Appendix C: Detailed Protocol 143

Chapter 1
Introduction

This study has been undertaken with a view to extending the research base vis-à-vis the clinical use of music in upper extremity stroke rehabilitation, with a focus on persons at the chronic stage post-stroke. The overall aim, context, and research rationale will be addressed.

1.1 Purpose

The purpose of this research was to investigate the efficacy of therapeutic instrumental music performance (TIMP) with sensory-enhanced motor imagery in improving therapeutic outcomes for persons with chronic post-stroke upper extremity hemiparesis. The primary outcome measures assessed post-intervention changes from baseline in participants' motor impairment and functional abilities in each of three conditions. Secondary outcome measures assessed therapeutic effects of interventions on cognition and affect. Participants were randomly assigned to one of three experimental arms: Therapeutic Instrumental Music Performance (TIMP); TIMP with sensory-enhanced motor imagery provided through metronome cues (cMI), or TIMP and motor imagery (MI) without sensory enhancement.

1.2 Background Context

Stroke is a global health concern, and with over 80 million survivors worldwide, a leading cause of disability (Johnson et al., 2019). With life expectancy increasing in most countries (Kyu et al., 2018), more people are living to ages where they have greater susceptibility to neurological disorders, placing additional strain on existing services and resources (Feigin & Vos, 2019). According to a recent analysis of the Global Burden of Disease Study 2016 (Feigin et al., 2019), stroke was found among all neurological disorders to contribute the largest proportion of disability-adjusted life-years (42.2%). Despite declining incidence in most regions, improved survival rates are contributing to higher chronic stroke prevalence (Johnson et al., 2019). As millions of individuals live longer with functional health loss (Hay et al., 2017), the economic burden due to post-stroke care continues to rise (Rajsic et al., 2019).

In Canada it is anticipated that the prevalence of individuals living with the effects of stroke will continue to increase (Krueger et al., 2015). Although there has been a decline in age-standardized mortality rates due to stroke (Statistics Canada, 2017), the number of individuals surviving stroke continues to grow due to a combination of decreasing stroke mortality rates, population growth, and aging (Public Health Agency of Canada, 2017). There are currently an estimated 405,000 Canadians living with the effects of stroke (Heart and Stroke Foundation of Canada, 2018). Annual costs to the Canadian economy are estimated to be in excess of $3.6 billion, encompassing medical costs, lost wages, and lost productivity (Heart and Stroke Foundation of Canada, 2014).

Chronic stroke is a disabling condition affecting the individual, their family, and society at large. Measures of activity and participation of individuals minimum six months post-stroke revealed that 39% experienced limitations in self-care activities; 54% reported restrictions on instrumental activities of daily living (IADLs), including meal preparation, housework, and use of telephone; and 65% reported restrictions on reintegration to normal community living (Mayo et al., 2002). Approaching disability from a biopsychosocial perspective, the World Health Organization's International Classification of Function, Disability and Health (ICF) (2001) emphasizes three components of health: body function and structure (impairment), whole person (activities), and societal level (participation). This move towards a components-of-health model has implications for establishing comprehensive assessment practices in rehabilitation, with a more holistic view taken of the individual and greater emphasis placed on health-related quality of life (Herndon, 2006). Analyses of Canadian Community Health Survey data sets revealed that people living with the effects of stroke scored consistently low on life satisfaction, perceived health, and health-related quality of life (HRQoL), underscoring the need for effective interventional programs to ease the burden of chronic illness (Usuba et al., 2019).

While there may be a number of sequelae following a stroke, including depression and mood disorders, post-stroke cognitive disorders, aphasia, and perceptual disorders (Teasell et al., 2018), the most common post-stroke impairment is motor impairment, involving loss or restriction of function in muscle control or mobility (Langhorne, Coupar, et al., 2009). Major obstacles to functional recovery include paralysis or paresis and loss of coordination or dexterity, as well as changes to muscle length and increased stiffness (Carr & Shepherd, 2010). Volitional movements such as reaching can become segmented, slow, and indirect (McCrea & Eng, 2005).

Arm paresis is a strong predictor of activity of daily living (ADL) outcomes (Verbeek et al., 2017). Upper limb impairments make ADLs more challenging, especially those involving coordination of upper limbs and fine finger movements (Pollock et al., 2014). If a functional threshold of recovery is not reached, the affected individual may resort to compensatory movements (Schweighofer et al., 2009), and learned non-use may ensue (Taub et al., 2006). This in turn may diminish sense of well-being, and limit social participation (Pollock et al., 2014).

While younger persons may have more physical capability for recovery from stroke than older individuals, functional outcomes are often poor (D'Anci et al., 2019). Kwakkel and colleagues (2003) reported complete functional recovery of the upper limb in only 11.6% of patients at six months, with 38% achieving some dexterity in the paretic arm. One year post onset 57.2% of affected individuals were found to have given up activities, including IADLs, they were engaged in pre-stroke (Hartman-Maeir et al., 2009). Spontaneous neurologic recovery occurs in the first few weeks following a stroke (Kwakkel et al., 2006), and rehabilitation is thought to modulate this recovery, presumably by interacting with underlying biological processes such as neural plasticity (Kwakkel et al., 2004). Since modifications to movement representations in the primary motor cortex are use-dependent (Nudo et al., 1996), it is critical for persons at the chronic stage, when recovery is often thought to have plateaued, to continue to engage in rehabilitation, using novel modalities and techniques to overcome adaptive states and facilitate neuromuscular improvements (Page et al., 2004). Evidence has shown significant treatment effects for persons undergoing upper extremity rehabilitation more than six months post-stroke (Teasell et al., 2012).

Post-stroke effects on cognition and mood may also impact functional abilities (Pollock et al., 2014). Sveen and colleagues (1999) found that at the chronic stage, arm motor function and cognitive function - in particular visuospatial constructional ability, correlated most strongly with self-care and engagement in social activities, pointing to the need for therapy focusing on upper extremity function and visuospatial abilities. Furthermore, close to one third of persons recovering from stroke may be affected by depression. A systematic review found that at any time-point up to five years following a stroke 31% of survivors experienced depression (Hackett & Pickles, 2014). A possible reciprocal relationship between post-stroke depression and functional independence has been observed (Brown et al., 2012), as well as negative effects of depression on physical and cognitive function (Robinson & Jorge, 2016). While levels of moderate depression appear to decrease with time, levels of anxiety seem more persistent and stable (Morrison et al., 2005). A study assessing anxiety in participants with arm dysfunction six months following a stroke found that anxiety was a stronger predictor than depression of overall HRQoL, with greater upper limb dysfunction also associated with poor HRQoL (Morris et al., 2013).

Post-stroke care continues to rely on rehabilitation training to reduce motor impairments (Hatem et al., 2016), and many diverse approaches have been developed to treat arm dysfunction (Pollock et al., 2014). Interventions must be evidence-based, to ensure there is research evidence supporting potential therapeutic benefit, and applicable in a global context, in order to be accessible in regions where health-care resources may be more limited (Langhorne, Sandercock, et al., 2009). Given the importance of upper extremity function to well-being, there is an ongoing need for research into effective neurorehabilitation strategies that will reduce the burden of disability, and improve post-stroke therapeutic outcomes in a timely and cost-efficient manner. Music has the potential to access and effect change in multiple domains simultaneously, including physiologic, psychological, cognitive, behavioural, and social, through evidence-based interventions facilitated by a credentialed therapist (Dileo & Bradt, 2009), and may constitute a valuable medium for addressing rehabilitative goals. By engaging a multisensory and motor network linking diverse brain regions, music exerts multimodal effects on individuals which may be used for therapeutic purposes in neurorehabilitation (Altenmüller & Schlaug, 2012). Neurologic music therapy (NMT), defined as “the therapeutic application of music to cognitive, affective, sensory, language, and motor dysfunctions due to disease or injury to the human nervous system” (Thaut & Hoemberg, 2014, p. 2), is a research-based approach to the use of music in rehabilitation, with a number of specifically-designed techniques. One of these techniques is Therapeutic Instrumental Music Performance (TIMP), which focuses on retraining functional upper extremity movement through active instrumental music playing. The efficacy of TIMP in promoting therapeutic benefits in persons at the chronic post-stroke stage will be explored in this study.

1.3 Rationale

The primary aim of rehabilitation efforts is to promote recovery of impaired movement and corresponding functions, yet in most cases approaches do not target a specific pathophysiological process (Langhorne, Coupar, et al., 2009). There is an ongoing need for theory-based interventions in neurological rehabilitation to help people with post-stroke disabilities realize their potential (Dobkin, 2004), instead of relying primarily on task completion activities, which often foster recruitment of compensatory movements (Kitago et al., 2013). Carefully designed music interventions may serve to mediate and remediate nonmusical brain and behavior functions, thereby reducing underlying impairment. The mechanisms for such mediation, the behaviours and processes they are targeting, and potential for clinical translations provide rationale for the current investigation. The format for the rationale is based on the first three components of the Rational-Scientific Mediating Model (R-SMM) (Thaut, 2000; Thaut & Hoemberg, 2014), which progresses logically from musical response models, through parallel non-musical response models, to mediating models examining the effects of music on non-musical behaviour. The final step in the R-SMM framework, translational clinical research models, is addressed in the literature review.

1.3.1 Neurological and Physiological Responses to Musical Behaviour

Beat perception and synchronization appear to have a special affinity with the auditory system (Patel et al., 2005). It is natural for a person to want to tap to a rhythmic auditory event but not to a visual one, suggesting an inherent, time-referenced link between auditory and motor systems (Zatorre et al., 2007). This natural ability to tap to a beat is not dependent on prior training or skill development (Large et al., 2002). For instance, researchers found all participants, with or without musical training, were able to synchronize tapping to auditory stimuli presented as either strongly metrical patterns or isochronous sequences; however, they had difficulty synchronizing their movements with visual rhythms (Patel et al., 2005). Increased asynchrony was exhibited, however, when participants were asked to tap to auditory rhythms that were increasingly complex or non-metric (J.L. Chen et al., 2008). Researchers found that visual beat sensitivity increased when primed by identically structured auditory sequences, though the reverse was not true (Grahn et al., 2011). In addition, researchers found faster reaction times to auditory than to visual stimuli (Shelton & Kumar, 2010), and lower latencies for correcting movements from auditory than from visual targets (Holmes & Dakwar, 2015).

A distributed set of circuits underpin rhythmic auditory entrainment abilities, with motor regions in the brain active during both rhythm perception and production (Chauvigné et al., 2014; Grahn

& Brett, 2007; Janata & Grafton, 2003; Konoike et al., 2012; Merchant et al., 2015; Thaut, 2003; Zatorre et al., 2007). Importantly, neuroimaging analysis showed both musicians and non-musicians engaging the same motor areas to the same extent in auditory-motor synchronization, namely the supplementary motor area (SMA), pre-supplementary motor area (pre-SMA), dorsal premotor cortex (dPMC), dorso-lateral prefrontal cortex, inferior parietal lobule, and cerebellum lobule VI; these regions were also found to be functionally connected, with temporal correlations involving the planum temporale in the auditory cortex (J.L. Chen et al., 2008). Furthermore, the recruitment of motor regions occurred even during rhythm perception that did not involve overt movement (J. L. Chen et al., 2008). Corticospinal excitability, as measured by motor-evoked potentials, is also modulated by isochronous rhythms delivered at a participant's preferred tempo, indicating that the effects of rhythmic input on the motor system extend from the primary motor cortex through to the spinal cord (Michaelis et al., 2014).

Sensorimotor synchronization occurs at both conscious and subconscious levels, with ventral prefrontal areas engaged during subconscious motor adaptations, and the dorsolateral prefrontal cortex engaged in fully conscious motor control (Stephan et al., 2002). The limbic and auditory systems also have strong connections, with music modulating activity in several brain structures governing affect, including the amygdala, hippocampus, hypothalamus, striatum, insula, cingulate cortex, and orbitofrontal cortex (Koelsch, 2014). Recruitment of brain regions governing higher cognition and affect during sensorimotor synchronization may facilitate far transfer to cognitive and affective processes in addition to facilitating primary movement goals.

There is considerable neurophysiological evidence indicating that the predictive action required to synchronize movement with auditory rhythm relies on communication through oscillatory activity (Arnal & Giraud, 2012; Buzsaki & Draguhn, 2004; Engel et al., 2001; Fries, 2005; Fujioka et al., 2009; Fujioka, Trainor, et al., 2012; Fujioka, Ween, et al., 2012; Lakatos et al., 2019; Schoffelen et al., 2005; Zoefel et al., 2018). Researchers found periodic stimulation led to a periodic pattern of beta modulation, which did not occur with an irregular stimulus, providing a mechanism for predictive timing which spanned auditory and motor systems. Furthermore, this temporally correlated beta modulation occurred in auditory and motor-related brain areas even without movement (Fujioka, Trainor, et al., 2012). Neuronal entrainment through phase-specific alignment of brain rhythms to a regular temporal context allows for dynamic prediction and processing in accordance with current goals. This entrainment is top-down controlled, such that a stimulus stream may be either attended to or ignored, allowing the brain to prioritize sensory input and prevent alignment of neuronal oscillations with irrelevant input, thereby eliminating effects of random interference and allowing more stable representations to be formed. In addition, neuronal entrainment to stable, predictable rhythmic input allows for a central timing mechanism to which other processes can align. Communication through coherence across brain regions is facilitated due to the supramodal nature of entrainment (Lakatos et al., 2019), with synchronization of local and distant networks requiring less energetic cost (Buzsaki & Draguhn, 2004). Altenmüller and colleagues (2009) found increased beta band coherence following music-based interventions, suggesting greater interregional communication post-treatment.

Neuroplastic reorganization is strongest when learning involves task-specific training (Ohl & Scheich, 2005). Cortical representations are highly dynamic and may be induced and modified by motor learning (Sanes & Donoghue, 2000), providing a critical substrate for neurological recovery (Mulder, 2007). Functional neuroimaging following music-supported training revealed modifications in brain organization in healthy older adults, with increased synchronization between stimuli and beta and gamma oscillations. There were also training-related effects in a chronic stroke patient on gamma oscillation synchrony with a rhythmic stimulus, improvements in digit separation, and a posterior-anterior shift in centre of activity in somatosensory areas (Jamali et al., 2014). Previous research had indicated cortical reorganization in the beta-band networks of three chronic post-stroke individuals who underwent music-supported training, as well as an enhanced event-related beta decrease accompanied by functional arm/hand improvements (Fujioka, Ween, et al., 2012). Restitution of auditory-motor connectivity following application of music-supported training was found in chronic stroke individuals with slight to moderate motor deficits (Ripollés et al., 2015), as well as changes in motor cortex representation and increase in excitability of the corticospinal tract (Amengual et al., 2013). Salience is an important component of experience-dependent plasticity; motivation and attention are essential ingredients for task engagement (Kleim & Jones, 2008), and may be fostered through a music-based approach (Schneider et al., 2007).

1.3.2 Processes in Nonmusical Behaviour and Neurological Function

Neuromuscular impairments following stroke include paresis, abnormal synergies, and agonist/antagonist coactivation (Shumway-Cook & Woollacott, 2012). Reaching movements take longer, are less direct, and require more corrective sub-movements, possibly due to neuromotor noise reducing transmission capacity for motor commands (McCrea & Eng, 2005). Neuromotor noise refers to uncontrolled variability or unpredictable noise in the motor system (De Jong & Van Galen, 1997). Motor planning and execution are impacted, leading to the adoption of more conservative options, including greater reliance on feedback control and reduction in velocity (McCrea & Eng, 2005). Gemperline and colleagues (1995) found inefficient muscle contraction in paretic muscles arising from abnormal motor unit recruitment and reduced discharge rates, possibly underlying impairments and contributing to higher levels of effort and fatigue during voluntary force generation. Reduction in muscle activation patterns was found to correlate significantly with alterations in segmental kinematics and functional ability (Massie et al., 2012). With insufficient power in the typical agonists comes greater reliance on compensatory movement; weaker muscles were recruited to a greater extent and movement path was altered when saturation occurred in the paretic anterior deltoid during a reaching task (McCrea et al., 2005). Abnormal synergies, mass patterns of movement in which there is loss of fractionated movement and single joint actions occur coincidentally with other joints, emerge as part of an incremental sequence of motor recovery post stroke (Brunnstrom, 1966; Twitchell, 1951). Such changed motor patterns may be adaptive rather than pathological in atypical populations, reflecting efforts to optimize movements within current system confines (Latash & Anson, 1996). This behavior is in accordance with Bernstein's (1967) theory of co-ordination as "the organization of the control of the motor apparatus" (p. 127), in which at the outset of acquiring a motor skill redundant degrees of freedom are eliminated. The advantage of this basic approach to motor control may be a reduction in energetic cost as well as more accurate movement despite constraints (Kwakkel et al., 2004). Agonist/antagonist muscle coactivation may represent an initial, unrefined mode of coordination (Shumway-Cook & Woollacott, 2012). Researchers found a lack of sufficient recruitment of agonists, rather than increased activity in antagonists, led to inability to complete a movement task, suggesting that rehabilitation efforts focus on facilitating motoneuron recruitment rather than reducing antagonist activity in arm retraining (Gowland et al., 1992).

1.3.3 Mediating Influence of Music on Nonmusical Function

Motor control is based on sensorimotor transformations, which are circuits involving motor outputs and sensory inputs. The sensorimotor system forms a loop, with motor commands that cause muscles to contract, generating sensory consequences, and sensory consequences that influence motor commands (Wolpert et al., 2003; Wolpert & Ghahramani, 2000). The two processes, motor control (an inverse model) and prediction (a forward model) together comprise internal models. These models represent the relationship between the motor system and its external context. Sensory representations serve to shape the actions of the motor system, providing a framework for the system to plan, coordinate and execute the programs which drive voluntary movement (Wolpert et al., 2013). The formation of internal representations of anticipated efferent and afferent consequences is facilitated by prior knowledge of the sensory information that will be available (Elliott et al., 2010). Advance knowledge of a rhythmic cue period through provision of a stable rhythmic temporal framework provides a coordinative constraint which serves to optimize motor planning and execution (Thaut, 2013; Thaut, 2015; Thaut et al., 1999). This rhythmic entrainment is frequency, or period driven, rather than phase-locked to the occurrence of the auditory beat. Matching a cyclical movement period to a predictable, externally-cued rhythmic period affects the spatial-dynamic parameters of the entire movement trajectory. Provision of a stable period as a time reference enables the brain to compute the amount of time left to complete a task, allowing for adjustments of velocity and acceleration parameters throughout the trajectory. This leads to greater consistency in movement path and muscle recruitment, allowing the brain to develop internal models based on movements that are smoother and more energy efficient. Entrainment to the period of a rhythmic template, rather than exact synchronization to a beat, facilitates formation of optimal motor representations, as well as optimal planning and execution.

Sensory inputs during movement provide information about errors arising from unpredictable systemic noise, inaccuracies in internal model representations, or environmental contextual changes. While error signals help to inform and shape motor commands, feedback control, which is error driven, is noisy and slow. Predictive processes help to offset the adverse effects of feedback delays (Wolpert et al., 2013). Individuals with stroke, on the other hand, rely extensively on feedback control (McCrea & Eng, 2005; Trombly, 1992). Rhythmic cueing of movement within a stable temporal context, in contrast, provides the brain with a mechanism for optimal predictive calibration of kinematic parameters throughout the movement period.

Crasta and colleagues (2018), examining the effects of auditory priming on auditory-motor entrainment in healthy young adults, found that neural oscillations produced by predictable auditory stimuli drive entrainment, and even a short period of priming prior to movement onset is sufficient to increase neural efficiency during sensorimotor synchronization. This finding has clinical implications for persons with stroke, whose inefficient motoneuron recruitment in the presence of increased neural noise may underlie impairment (Gemperline et al., 1995; McCrea & Eng, 2005).

Researchers found auditory rhythmic entrainment led to statistically significant improvements in hemiparetic spatiotemporal arm control and significant reductions in arm kinematic variability (Thaut et al., 2002). Importantly, these changes occurred within the initial two to three repetitions of a trial; Thaut and colleagues (1998) had previously noted the brain's ability to quickly acquire and adjust to temporal templates. In addition, in spite of retention of some synergistic movement pattern, researchers noted a significant increase in elbow range of motion – an increase that could not be attributed to shoulder displacement - in the rhythmic synchronization condition compared to the no-rhythm condition (Thaut et al., 2002). Predictive compensation for interaction torques has been found in the central control signals sent to muscles (Gribble & Ostry, 1999), compensation which may benefit from provision of an anticipatory rhythmic template.

There is a monotonic slowing of preferred event rate (tempo), revealed through measures of spontaneous motor tempo and preferred perceptual tempo, over the course of a person's lifetime. In addition, the entrainment region, an area of optimal adaptivity around a person's preferred period, narrows with advancing age. Within this region stable performance can be maintained; however, outside the upper and lower limits of this region variability in period matching increases (McAuley et al., 2006). It is critical, therefore, to ascertain an individual's preferred period for movement within a given spatial context, and to adjust the tempo of an exercise accordingly. Findings also indicate that tempo mediates the extent to which motor-related circuitry is involved in beat perception (McAuley & Jones, 2003). Functional activity in the striato-thalamo-cortico network decreases when the implied beat is at a slower (1,500 ms) rather than a faster (600 ms) tempo. Other areas more active in the 600 ms tempo condition include the bilateral superior temporal gyrus, necessary for rhythm perception and synchronization (J. L. Chen et al., 2008). Because the speed of movements is slower in persons with stroke (McCrea & Eng, 2005), use of a slow preferred tempo may reduce beat perception and hence engagement of motor areas. Patel and colleagues (2005) found tapping variability was lower when participants, asked to tap to an isochronous beat at 800ms, heard subdivisions at 400 ms. The benefit of this subdivision disappeared when it was increased to 200 ms, where variability did not differ from the 800 ms condition without subdivisions. Beat induction at a tempo that will engage motor regions of the brain and be within an individual’s entrainment region is critical for successful sensorimotor synchronization. The protocol for this study is based on participants’ preferred tempi for each activity, with the basic beat subdivided where necessary to facilitate sensorimotor integration and synchronization.

Principles of motor learning, including repetition, task orientation, active learning, shaping, and motivation may be addressed through music-based interventions in therapy (Hoemberg, 2014). Amount of repetition is a critical factor in retraining motor skills (Bütefisch et al., 1995; McFadyen et al., 2009; Shumway-Cook & Woollacott, 2012; Sterr et al., 2002). While repetitive training leads to expansion of cortical representation of areas subserving specific motor functions (Herholz & Zatorre, 2012; Karni et al., 1995), lack of training maintenance leads to contraction of cortical representation (Liepert et al., 2000) . Plasticity is experience-dependent (Kleim & Jones, 2008); however, repetitive activity without skill acquisition is insufficient to promote motor cortex plasticity. Tasks requiring the learning of new skills will induce neuroplastic changes; repetition without learning will not (Nudo et al., 1996; Plautz et al., 2000). As changes occur in the state of the limb, internal models need to be continually revised and updated (Krakauer, 2006). TIMP-based exercises allow for adjusting tasks according to the present needs of the individual. Spatiotemporal constraints tailored to current limb capacities provide a consistent framework for planning movement, optimizing execution, and developing and refining internal representations; these constraints may be adjusted over time to reflect a limb’s changing state. Furthermore, some variability in practice may promote generalization to new tasks (Krakauer, 2006). Improvisation, using instruments selected according to the abilities of the individual, provides an opportunity for creative problem solving and consolidation of prior learning. Learning experiences need to be salient to enhance plasticity (Kleim & Jones, 2008). TIMP exercises that are carefully crafted to meet individual needs and goals may be perceived as rewarding and motivating, prompting participants to continue to engage in rehabilitative training.

In addition to potential therapeutic benefits on motor learning and control, music-based exercises with a consistent temporal referent may also have effects on cognition and affect. Perceptual structure, using rhythmic sequences structured into phrases, has been found to constrain attention in both auditory and visual domains (De Freitas et al., 2014; Grahn, 2012). In Dynamic Attending Theory, internal oscillations (attending or driven rhythms) entrain to external events such as a musical driving rhythm, focusing attentional energies on anticipated time points (Jones, 1976; Large & Jones, 1999). Oscillatory entrainment may be a substrate for selective attention, in which sensory representations and perception of selected stimuli are enhanced (Calderone et al., 2014). Music-based interventions may also influence executive function, including attention and cognitive flexibility, through training-induced far transfer effects on cognitive capacities (Loui & Guetta, 2019). Furthermore, neuroimaging studies have revealed a wide range of cortical and subcortical regions activated during perceived and induced emotional responses to music (Juslin & Sakka, 2019). As well as anatomical correlates of affective responding to music, research involving either positron emission tomography (PET) or peripheral biomarkers has revealed neurochemical, peripheral hormonal, and immune biomarker responses to musical stimuli, along with concomitant functional changes (Koshimori, 2019). As depression and mood disorders may develop following a stroke (Pappadis et al., 2018), these findings suggest that music-based therapeutic approaches may have a potential role in modulating affective responding.

Neuroimaging research has shown that motor regions of the brain are engaged during simulation of movement using motor imagery (Jeannerod, 2001; Lafleur et al., 2002; Roth et al., 1996; Stephan et al., 1995). Motor imagery is a dynamic state involving internal activation of specific motor representations without overt motor output (Mulder, 2007). Cortical plasticity has also been induced following cognitive rehearsal of physical actions (Bajaj et al., 2015; Page, Szaflarski, et al., 2009; Sun et al., 2013). These findings have important implications for post-stroke neurorehabilitation, where paresis may limit voluntary movement and the ability for active retraining (Lotze & Cohen, 2006). Motor imagery provides a safe, cost-effective means of extending repetitions of task-specific practice (Page, Levine, et al., 2009), without incurring additional fatigue - a common post-stroke sequela that can reduce capacity for practice and impede progress (Lanctôt et al., 2019). The combination of overt and covert practice may promote skill acquisition (Feltz & Landers, 1983; Pascual-Leone et al., 1995). Braun and colleagues (2010) distinguish between structural learning, in which the general form of rules for a given task set are extracted, and parametric learning, in which particular maps governing current tasks are acquired. A primary function of the brain is to derive structure (Levitin, 2009), with rhythm functioning as the core organizing structure for music (Thaut, Trimarchi, et al., 2014). As provision of a stable auditory template has been shown to facilitate and optimize motor execution (Malcolm et al., 2009; Thaut et al., 2002), adding a predictable auditory cue to motor imagery of a previously practiced movement, cued at the same tempo, may provide a mechanism to support structural learning in the course of mental rehearsal, thereby facilitating later transfer between tasks.

Chapter 2
Literature Review

2 Hemiplegic Upper Extremity Rehabilitation

Many interventions have been undertaken in an effort to remediate impairment and associated function of the upper extremity following a stroke, yet there is an ongoing need for evidence-based research (Langhorne, Coupar, et al., 2009; Pollock et al., 2014) and for innovative approaches to enhance motor recovery (Buma et al., 2013). This literature review will be based on the fourth step in the R-SMM, Clinical Research Models, and will focus on current methodological approaches to upper extremity stroke rehabilitation, with connections to the current TIMP study. Trials using auditory stimuli will be reviewed first, followed by interventions without auditory stimuli, and interventions using action simulation.

2.1 Rehabilitation using Auditory Stimuli

Approaches using auditory stimuli comprise those using a rhythmic auditory cue without music (e.g. Bilateral arm training with rhythmic auditory cueing), and music-based interventions with or without rhythmic auditory cueing (e.g. Neurologic Music Therapy). These approaches will be reviewed in turn, and specific examples provided for each.

2.1.1 Bilateral arm training with rhythmic auditory cueing

Bilateral arm training with rhythmic auditory cueing (BATRAC) is an approach to upper extremity rehabilitation that uses a rhythmic auditory cue in combination with a bilateral training approach. It is based in part on motor learning principles, including repetition, goal-setting, and feedback. In the protocol, an external auditory cue serves as a conscious attentional and feedback mechanism, as well as a subconscious entrainment mechanism. The method employs a table-top device with T-bar handles for each hand that move on separate tracks perpendicular to the client. Training involves repetitive movements of shoulder flexion/protraction with elbow extension, critical for developing forward reaching control. A chest guard prevents trunk compensation, and the end stop may be adjusted for each individual. Participants are asked to time their reaching of the proximal and end stops with a metronome cue, which is set to the participant’s preferred period for executing the movement. There are four five-minute training sessions interspersed with ten-minute rest periods within the one-hour time frame. Two of the four training sessions involve in-phase bilateral pushing/pulling; these are alternated with two sessions of antiphase movement. Training takes place over six weeks. The target population is people with primarily moderate to severe hemiparesis (Whitall & Waller, 2013).

A number of studies have been undertaken using the BATRAC approach, with mixed results. Early indications were promising. A single group pilot study assessed the efficacy of six weeks of BATRAC training on 14 participants at the chronic post-stroke stage (Whitall et al., 2000). Of the 14 participants, half were classified as having minimal impairment on the Orpington Prognostic Scale, one as severe, and the remaining as moderate. Participants were assessed at three time points: pre-test, post-test, and retention test two months after training. Several significant results were obtained. On the Fugl-Meyer Upper Extremity (FM-UE) motor performance section gains of 18% and 26% were found from pre-test to post-test and retention tests respectively, with effect sizes of 0.41 and 0.66. The Wolf Motor Function Test (WMFT) performance time mean scores also improved significantly – 12% and 13% respectively, with small effect sizes of 0.20 at each post-test time point. There were no significant differences on the quality of function or weight portions of the WMFT, though trends were positive. Significant improvements were found on the University of Maryland Arm Questionnaire for Stroke (UMAQS), which assesses paretic arm use in Activities of Daily Living (ADLs). However, changes on measures of range of motion (ROM) and strength were for the most part temporary, indicating large muscular conditioning did not take place as a result of training.

A subsequent study that also did not use a control group yielded results that were less promising. A condensed, two-week training schedule of BATRAC, 2.25 hours per day, four days per week was used with 14 chronic post-stroke participants. Non-significant post-test results on the FM-UE and WMFT were obtained, though modest improvements in amount of use were reported on the Motor Activity Log (MAL) (Richards et al., 2008). With a mean change of 0.50 (SD = 0.70) these changes were of minimal clinically important difference (MCID) (van der Lee et al., 2004; van der Lee et al., 1999). Improvements were also noted in post-test kinematic measures, including smoothness of curve, hand path curvature, and peak velocity; the latter two kinematic variables correlated positively with post-test functional measures (Senesac et al., 2010). This corresponded with previously reported positive changes in spatio-temporal control, including movement units and smoother hand paths, following BATRAC training (McCombe Waller et al., 2008). The lack of significant changes on the FM-UE and WMFT may have been attributable to the condensed time frame. Distributed practice with rest periods interspersed has been found to benefit performance and learning (Krakauer, 2006).

Results of two large RCTs comparing versions of BATRAC with control groups were equivocal. A trial using the original protocol with 111 chronic post-stroke participants randomized to receive either BATRAC training or DMTE obtained comparable results on the FM-UE and WMFT at post-test and four-month retention, though satisfaction was higher with BATRAC (Whitall et al., 2011). The Upper Limb Training After Stroke (ULTRA) trial, which involved 60 participants one to six months post-stroke, compared three interventions: a modified version of BATRAC for wrist movement (mBATRAC), modified constraint-induced movement therapy (mCIMT), and dose-matched conventional treatment (DMCT) (van Delden et al., 2009). Three training sessions were provided per week over a six-week period, with a focus in mBATRAC and mCIMT on wrist and finger extensor control (van Delden et al., 2013). Participants in the mBATRAC condition received training using a modified BATRAC apparatus in which the hands were fixed vertically to handgrips on a flat surface, allowing only wrist flexion/extension. Exercises over a one-hour period were in three-minute sets with five-minute rest periods in-between – twenty-one minutes in total, and involved in-phase flexion, antiphase, extension, and hand tapping with the wrist on the table. Metronome beats ranged from 0.8 to 1.4 Hz; the hand-tapping activity was paced to a song with a constant frequency within this range. Participants assigned to the mCIMT group received graded repetitive task practice over a one-hour period, resulting in training on a variety of activities with unspecified rest periods, possibly resulting in a different amount of time on task from mBATRAC. Similarly, DMCT involved training for one-hour periods based on existing guidelines, presumably using a variety of activities, with the exclusion of mBATRAC and mCIMT elements, and without specified training/rest intervals (van Delden et al., 2009). There were significant gains on the Action Research Arm Test (ARAT) and post-test and six-week follow-up for all three groups, with no between-group differences. Participants were instructed to practice on their own, according to their specific training protocol; however, compliance was not well-documented, and assumptions of practice-time equivalency were reliant on verbal reports from staff.

The BATRAC approach is based on the notion that bilateral practice in conjunction with an auditory cue may facilitate motor learning. The idea was to retain the principle of forced use with task specificity, as advanced by Taub and colleagues (Liepert et al., 1998; Taub et al., 1998;

Taub et al., 1993), without constraining the nonparetic arm (Whitall et al., 2000). However, evidence now exists refuting the idea that bilateral arm training may be superior to unilateral training (Iruthayarajah et al., 2018). The approach was also based on rhythmic auditory cueing, as well as motor learning principles, including repetition, feedback and goal-setting (Whitall & Waller, 2013). The addition of an auditory cue appeared to increase the number of repetitions per session, with repetition fundamental to experience-dependent plasticity (Kleim & Jones, 2008). Provision of an auditory cue at each end of the movement period was thought to promote attentional focus and encourage goal setting, consciously synchronizing cues with movement endpoints using anticipatory feedforward processes and receiving auditory feedback. No beat was provided during the course of the trajectory, however, which may have facilitated anticipatory planning and online adjustments. Whitall and McCombe Waller (2013) reasoned that the auditory cue would cause passive entrainment by aligning oscillatory systems. However, in some cases training speeds may have been too slow both to promote beat induction and to recruit motor areas during beat perception. McAuley and colleagues (2012) found reduced beat induction at a slower tempo (1,500 ms), accompanied by a reduction in striato-thalamo-cortico involvement. In the modBATRAC study, training speeds ranged from 40 (1500 ms) to 96 beats per minutes. However, much of the training appears to have taken place at the lower end of this spectrum (Richards et al., 2008), where auditory-motor coupling may not have been facilitated, ultimately impacting potential for neuroplastic remodeling in motor regions of the brain. In the ULTRA trial as well, frequencies ranged from 0.8 to 1.4 Hz (based on research showing the least amount of synchronization variance at 0.8 Hz (Woodrow, 1932). Since preferred tempi were slower for some participants, subdivisions of the beat may have aided auditory-motor coupling, providing greater support for movement planning and enhancing underlying plasticity. In the TIMP study, trainers ascertained the participant’s preferred tempo for an exercise, then subdivided the beat for slower tempi to provide consistent support and promote auditory-motor coupling.

2.1.2 Rhythmic auditory cueing without BATRAC

The effects of rhythmic auditory cueing on upper extremity rehabilitation without using the BATRAC approach have also been investigated at the acute and chronic post-stroke stages. Rhythmic auditory cueing, visual cueing, and conventional treatment were compared in a randomized-trial sample of forty-five participants at the acute stage of post-stroke recovery

(Chouhan & Kumar, 2012). Participants received gait imbalance, gross motor and fine motor training, which took place for up to two hours, three times a week for three weeks. Outcome assessments were the Dynamic gait index, and the FM-UE. Both cued conditions, auditory and visual, were effective in improving the gait and UE parameters. There were no significant differences between these two groups. There were, however, significant differences between each of the cued groups and the conventional treatment approach, suggesting enhanced efficacy with rhythmic cueing. Further testing would be required, with a larger sample size and preferably while spontaneous recovery is not occurring, to distill differential effects of auditory and visual cueing.

Using a cross-over design, researchers investigated the effects of intensive precision grip training on hand function in a pilot study involving 10 chronic hemiparetic participants (Dispa et al., 2013). Volunteers were randomly allocated to begin with either bilateral or unilateral training, both with rhythmic auditory cueing. One-hour training sessions took place three times a week, with four weeks allocated for each condition. Exercises involved manipulation of wooden blocks; the same exercises were used in both conditions. The tempo was set at the maximal speed at which the participant could properly accomplish the task during a test trial, with a minimum tempo of 24bpm. There were no significant changes on any of the grip-lift parameters or measure of digital dexterity following the eight weeks of repetitive, cued training. However, the training tempo, as indicated above, may have been too slow to promote auditory-motor coupling; subdivision of the beat may have facilitated entrainment. Furthermore, participants were required to exercise at their maximum rather than their preferred speed. Interviews with individual participants indicated that they were tired following training, and would not have wanted or been able to increase the number or duration of sessions. This underscores the need to work within a person's preferred entrainment region (McAuley et al., 2006). TIMP study training took place using the participant's preferred rather than maximal tempo for each exercise, and participants did not complain about being overly fatigued.

2.1.3 Music-based approaches using Neurologic Music Therapy interventions

Neurologic Music Therapy (NMT) is the "therapeutic application of music to cognitive, affective, sensory, language, and motor dysfunctions due to disease or injury to the human nervous system" (Thaut, McIntosh, et al., 2014, p. 2). It is based on the Rational Scientific

Mediating Model, an epistemological framework generating knowledge concerning the relationship between music and therapy (Thaut, 2000), and uses a transformational design model to translate research findings into clinical practice (Thaut, 2005). To that end, basic research findings are reviewed first, followed by studies of clinical translations.

The effects of rhythm on hemiparetic arm reaching control were examined in a sample of twenty-one chronic post-stroke participants (four to nineteen months since onset) with mild to moderate impairment (Thaut et al., 2002). Trials involved reaching forward and back in a saggital plane between two touch-sensitive sensors. Reaching movements were either cued at the participant's preferred tempo, or not cued, with the order of trials counterbalanced between participants. A number of relevant findings were obtained. First, reduced temporal variability, evident in airborne travel times, occurred at the outset of the cued trial, while without cueing temporal variability remained at a higher level. Second, wrist trajectories revealed a more consistent path with cueing than without, and the improvements were highly correlated with temporal improvements, not found in the no-rhythm condition. Third, there was a statistically significant increase in elbow angles in the rhythm but not the no-rhythm condition; shoulder displacements were comparable in both conditions and therefore did not contribute to the significant finding. Fourth, the number of reversal peaks in the wrist velocity curve were reduced or eliminated, particularly during deceleration, in the rhythmic cueing condition. Fifth, optimization models of peak acceleration, with minimal peak absolute acceleration the criterion, yielded significantly less deviation in the acceleration curve in the rhythm than in the no-rhythm condition. Sixth, period synchronization revealed smaller time deviations than phase synchronization, indicating that for all participants periodicity coupling provided accessible, stable time information with which to counteract deviations in paretic arm time control. These data suggest that the provision of structured time information lends significant stability to kinematic parameters during hemiparetic arm reaching, thereby increasing the effectiveness of training, enhancing the acquisition and consolidation of optimal internal models, and reducing energetic cost during movement.

A second exploratory basic study investigated the effects of rhythmic auditory stimulation (RAS) on changes in muscle activation and co-contraction, as well as elbow motion during hemiparetic arm reaching in a pilot study involving 16 participants (Kim et al., 2014). Reaching trials were completed at one-minute intervals with the affected arm, with or without RAS. Preferred auditory stimulation frequency for the RAS condition was based on a one-minute reaching task using the affected arm. Trial order was determined by coin toss. A three-dimensional motion analysis system was used to capture elbow movement kinematics, including movement speed, measured from start of movement to target; range, defined as maximum elbow extension during target reaching; and smoothness, movement units divided by changes in angular acceleration. Electromyography (EMG) recorded triceps and biceps brachii activity. The percent maximal voluntary isometric contraction (%MVIC) indicated how much of the muscle's capacity was used in task execution. The ratio of root mean square (RMS) of the agonist triceps brachii to the antagonist biceps brachii provided the co-contraction ratio. There were significant decreases in movement time; number of movement units, indicating greater smoothness; and significant improvements in elbow range of motion (ROM) during RAS-guided reaching. Similarly, %MVIC in the triceps brachii increased significantly during RAS, while remaining stable in the biceps brachii. The co-contraction ratio significantly decreased with RAS, indicating better agonist/antagonist coordination. These results are highly encouraging as they indicate not only improvements in kinematic stability, making movements more energetically efficient, but also positively impact muscle activation and coordination, contributing to increased elbow ROM during reaching.

Two pilot studies assessed the effects of individualized rhythmic auditory-motor entrainment interventions on arm rehabilitation in clinical settings. In one trial, five participants with mild to moderate impairments at the chronic post-stroke stage were recruited (Malcolm et al., 2009). A pre-test–post-test design was used, and both kinematic and functional outcome measures obtained. Participants trained for three hours a day over a two-week period. One hour of onsite training was completed three days a week, followed by two hours of home-based training on these days. The other two days participants completed three hours of home-based training. A template with 28 consecutively numbered targets was fixed to a table and used to practice reaching movements in sagittal, frontal, and diagonal planes. Auditory cues based on the participant's preferred tempo were generated using a digital metronome. Difficulty was modulated by changing the frequency of the cue or the target array. Significant reductions were found at post-test in compensatory trunk movement, as well as significant increases in shoulder flexion but not elbow extension. Movement time and reach velocity were both positively impacted. Functional measures indicated a significant decrease in time on the WMFT, and significant increases on the FM-UE and the MAL. It appears rhythmic cueing reduced reliance on compensatory strategies, improving not only quality of movement but also functional capacity.

A second small exploratory trial used Therapeutic Instrumental Music Performance (TIMP) to examine treatment effects of Neurologic Music Therapy in addition to a current rehabilitation training program (Yoo, 2009). There were three participants at the chronic post-stroke stage (>3 years post onset) with moderate to severe impairment; one participant had also been diagnosed with Parkinson's Disease. Training took place over two weeks in six 35-minute sessions, and was delivered in addition to a regular exercise program. Participants engaged in functional arm exercises using a variety of rhythmic instruments, including a drum kit, practicing arm flexion/extension, forward reaching, shoulder abduction/adduction, lateral rotation, wrist flexion/extension, hand pronation/supination, as well as bilateral arm movement. Musical facilitation was provided by one therapist, using familiar and preferred songs at an appropriate tempo, and providing spatial (melodic) and force (harmonic) cues as required. A second therapist facilitated functional arm movements. A paired sample *t*-test indicated a significant improvement on the wrist/hand portion of the FM-UE. Other functional measures had modest but non-significant improvements. Similarly, MIDI data indicated positive but non-significant changes in movement time, variability of movement time, and force over the two-week period, suggesting an overall increase in arm control. Both of these trials involved small, heterogeneous samples, and while results appeared encouraging, it is clear that larger, randomized-controlled trials are needed to better understand the therapeutic effects of TIMP interventions on hemiparetic arm control.

Use of rhythmic auditory stimulation (RAS) in group rehabilitation programs has also been investigated. Jeong and Kim (2007) incorporated principles of rhythmic auditory stimulation (RAS) into a community-based music and movement program for persons more than six months post-stroke. Thirty-six participants were randomized to either the experimental condition or the control; both programs involved two hours per week for eight weeks and were delivered in a group setting. The music program used familiar songs with a strong rhythmic quality for exercising both upper and lower limbs, as well as small, hand-held percussion instruments that were played after first listening to the rhythm of the song. Rhythm was emphasized as being central to each activity. Participants were encouraged to practice the activities at home, and were provided with rhythmic music tapes to assist in this process. The control group did not receive an exercise program, but instead were provided with information regarding care opportunities in the community. There were improvements in degree of shoulder flexion, as measured with a goniometer, and shoulder flexibility, as assessed with a back-scratch test, in the experimental group but not the control. While the researchers considered dynamic rhythm to be the main intervening variable, the combination of music, exercise, and social interaction makes understanding the relative contributions of underlying component mechanisms challenging. The lack of an adequate dose-matched control is also a limitation, and it appears that the amount of time spent on home-based practice for members of the experimental group was not consistently recorded.

Lim and Miller (2011) investigated how TIMP, as compared to traditional occupational therapy (TOT), affected in-patients levels of endurance, self-perceived fatigue and self-perceived exertion in upper extremity exercise. There were eight persons with stroke amongst the 35 participants randomized to the two conditions. Sixteen participants completed TIMP exercises on Day 1 and TOT on Day 2, while 19 participants completed the procedure in the reverse order. Identical exercises were used in each, with the difference being the use of instruments and a rhythmic auditory cue set to the participant's preferred pace in the TIMP condition. To keep the focus of the study on the outcomes of interest, participants were asked to exercise using their strongest arm. There were no measures of arm impairment or function included, as the experiment involved participation in only two sessions. Descriptive data indicated higher mean frequency of repetitions during TIMP (n =65) than TOT (n = 58), with mean duration for TIMP (89 sec.) shorter than for TOT (92 sec.). Paired sample t tests, however, indicated non-significant differences in mean frequency ($p = 0.134$) and mean duration ($p = 0.679$). Perceptions of fatigue and exertion, assessed using rating scales, were, however, significantly lower for TIMP than for TOT. Information regarding the time since onset and side of lesion was not provided for the participants with stroke. Research has shown recovery of ipsilateral dexterity during the first six months, though there may be some persistent apraxia-related impairment in those with left hemispheric lesions (Sunderland, 2000). More efficient movement execution during the rhythmically-cued TIMP condition may have led to increased endurance and reductions in perceived fatigue and exertion for the 8 participants with stroke. Also, by attending to audiomotor synchronization, participants' foci may have shifted from sensations of fatigue and exertion, thereby extending their exercise tolerance and increasing endurance levels.

Recognizing the need for further studies involving TIMP, researchers designed a crossover study to determine the effectiveness and the feasibility of delivering home-based interventions using TIMP to provide post-stroke upper extremity training to participants discharged from community rehabilitation (Street et al., 2015). Twelve training sessions were offered in total, twice weekly for six weeks. There was no provision for home-based exercises outside of these facilitated training sessions. Eleven participants, more than three months post stroke, were randomized to either wait list or treatment condition. One person allocated to the waitlist group withdrew before participating; ten participants ultimately completed the protocol, four of whom had been randomized to the waitlist condition (Street et al., 2018). Statistical inferences could not be made due to the small sample size. Structured interviews conducted by the interventionist yielded qualitative data indicating that despite some initial skepticism, participants found the interventions to be motivating and facilitative of target movements, with high tolerance and low fatigue levels indicated.

A team of researchers investigated the feasibility and acceptability of including NMT in a multidisciplinary acute stroke rehabilitation setting (Street et al., 2020). Over a period of two years, 117 patients participated, receiving an average of 4.8 sessions. Referrals came primarily from speech and language therapy and physiotherapy. Patients, family members and staff rated NMT as 'helpful,' with a trend towards being 'very helpful,' particularly in the areas of motivation/mood, concentration, and arm/hand. In addition to the sessions facilitated by a qualified Neurologic Music Therapist, rehabilitation assistants were shown how to assist patients with exercises using music software on iPads to extend practice opportunities, especially during times when other treatment options were not available.

2.1.3.1 Music-supported therapy

Music-supported therapy (MST) was developed to investigate the therapeutic potential of active musical instrument playing in post-stroke upper-extremity rehabilitation, adopting many of the approaches used in TIMP, but with a German name that was later translated into English (Altenmüller et al., 2009; Schneider et al., 2010; Schneider et al., 2007). The MST protocol takes place over three weeks, with participants receiving three individually-administered 30-

minute sessions per week. Two input devices are used – a keyboard for fine motor skills and a drum set for gross motor skills. The MIDI-piano is set so the participant can play only eight white keys. Similarly, the drum pads, arranged by numbers one through eight, emit the same pitches. Participants sit in a chair without arm rests. The height and proximity of drum pads are adjusted to suit the needs of the individual. Exercises are first modelled by the instructor, and then repeated by the participant. The instructor provides support for the affected extremity if required. The participant plays the exercise first with the paretic extremity, and then again using both hands. The difficulty level of the exercises is adjusted according to the needs of the individual, with degree of difficulty progressing incrementally through 10 set levels. At the most difficult stages, participants play the beginnings of children's or folk songs, and then entire songs using five to eight tones with the affected hand.

The first two experiments using MST involved participants at the subacute stage with moderate upper extremity motor impairment (Altenmüller et al., 2009; Schneider et al., 2007). Participants in the music groups but not the control groups made significant improvements on functional measures (Action Research Arm Test, Arm Paresis Score), measures of dexterity (Box and Block Test, Nine Hole Pegboard Test), measures of frequency and velocity (computerized movement analysis), as well as quality of movement parameters. As the control groups for these studies did not receive dose-matched therapy, an additional smaller group of participants was recruited to control for this potential confound. Fifteen participants received functional motor training using constraint-induced therapy (CIT) principles for fifteen 30-minute sessions in addition to conventional therapy to match the music group in terms of training time. The CIT group was comparable to the other two groups at baseline and was assessed using the same behavioural measures. Participants in the music group had substantial improvements relative to the other groups on functional measures. Objective measures of movement quality using computerized movement analysis indicated MST was more efficient than CIT over a comparable period of time in improving movement frequency and smoothness of finger movements. Outcomes from conventional therapy, which was not dose matched, did not indicate improvement in most areas (Schneider et al., 2010).

The effects of MST on hemiparetic arm control at the chronic stage have also been investigated. Rojo and colleagues (2011) conducted a single-case study, in which the participant received 20 sessions of MST over four weeks. The researchers found non-statistically significant improvements on subtests of the ARAT, and statistically significant improvements on quality of movement parameters involving frequency, smoothness, and amplitude of hand and finger movements. Twenty chronic post-stroke participants with moderate impairment were recruited to explore the neurophysiological effects of MST (Amengual et al., 2013). A group of 14 healthy participants served as controls. Participants in the patient group received twenty 30-minute MST training sessions over four weeks. This resulted in significant gains on the Action Research Arm Test (ARAT), as well as improvements in frequency of hand/finger tapping and quality of movement. However, the sample size of 20 participants was small, and the study lacked a control group of chronic stroke participants engaged in a dose-matched standard treatment program for comparison purposes.

Subsequent studies addressed the lack of dose-matched control issue. To clarify the effects of MST with respect to conventional physical therapy (CPT), a randomized-controlled trial was conducted in which 28 chronic post-stroke participants were assigned to either MST or GRASP (Graded Repetitive Arm Supplementary Program) (Fujioka et al., 2018). While a larger sample size had been planned, due to recruitment challenges the sample was small and heterogeneous; however, adherence was excellent. Results on motor assessment measures were modest. The pooled group of participants had a significant improvement on the Chedoke-McMaster Stroke Assessment (CMSA) Impairment Inventory at the post2 timepoint (immediately after 10 weeks of training), with a non-significant tendency for improvement in the MST group. Task completion time for MST on the ARAT also approached significance. A study contrasting MST with dose-matched conventional therapy at the subacute stage yielded significant improvements in both groups on motor outcomes, but there were no significant between-group differences (Grau-Sánchez et al., 2018). There was a positive correlation, however, between capacity to enjoy musical activities, particularly with a strong sensorimotor component, and improvement on the ARAT, the primary motor outcome.

The time course of gains from motor deficits in a chronic stroke participant was investigated using a reversal ABAB design and the MST protocol (Grau-Sánchez et al., 2017). Treatments administered during the B period were four weeks in length, with three 1.5-hour sessions of MST per week. Motor function was assessed weekly for 16 weeks, with follow-up at three months. Treatment on drum pads and keyboard was designed to increase range of motion, coordination and speed. The participant had only slight paresis of the left upper extremity. Findings included initial fast task acquisition during the first sessions, with generalization occurring at the end of a four-week training session. During withdrawal some gains were maintained or improved while others were lost; generalization to ADLs occurred during the second four-week training period. Interestingly, there was no Minimal Detectable Change (MDC) on the Fugl-Meyer Upper Extremity; however, results on the Chedoke Arm and Hand Activity Inventory (CAHAI), administered only at five timepoints to assess ability to perform ADLs, showed sustained improvements throughout, maintained at follow-up. It is possible that the MST approach contributes more to functional gains than to addressing underlying impairment.

MST was developed based on principles derived from previous motor learning and rehabilitation research, including repetition, audio-motor coupling, shaping, and emotion-motivation (Rodriguez-Fornells et al., 2012). Altenmüller and colleagues (2009) compared MST to constraint-induced movement therapy (CIMT), which is based on repetitive massed practice, and noted the larger effect sizes in the MST protocol, suggesting mechanisms in addition to repetition could underlie its efficacy. Auditory-motor coupling, established during learning and training, was suggested as one such mechanism; the other was external auditory feedback, which provides immediate information regarding movement outcome. To better understand the role of music in improving post-stroke motor outcomes, a study was designed in which thirty-three participants at the sub-acute stage with moderate impairment were randomly assigned to either an audible music group (n = 15) or a mute control condition (n = 18), in addition to conventional treatment (Tong et al., 2015). Both conditions used the MST protocol, with 20 training sessions over four weeks. Participants were assessed using the FM-UE and the Wolf Motor Function Test (WMFT). While participants in both groups had significant improvements at post-test, there were significant between-group differences on the WMFT, with the music group improving more. Between-group differences on the FM-UE approached but did not reach significance. This would tend to support the previous observation that the effects of MST may be greater for functional improvement than for reducing impairment, although movement analyses in previous studies revealed some improvements in movement parameters(Altenmüller et al., 2009; Amengual et al., 2013; Schneider et al., 2007). Interestingly, 87% of the participants in this study were diagnosed as having proprioceptive disorders. These participants were unable to gauge the strength and accuracy of their movements in the mute musical instrument and conventional therapy conditions, but appeared to regulate upper limb movement much better in the music condition, possibly due to pitch feedback in addition to rhythm aiding spatiotemporal control.

While the previous study found there were greater improvements in the music group versus the no-sound control group, Van Vugt and colleagues (Van Vugt et al., 2016) sought to determine whether it was auditory feedback that aided motor learning and hence rehabilitation, or whether music may have been responsible for other factors, such as increasing motivation. Participants at the subacute stage (n = 34, maximum time post stroke three months) were randomly assigned to one of two groups: MST with immediate auditory feedback, or MST with jittered delay. A total of 10 half-hour training sessions took place over three to four weeks. The jittered auditory feedback was below the perceptual threshold for delay detection. Both groups improved on measures of fine motor control, indicating that auditory feedback did not influence the rehabilitation outcome. It is worth noting that participants were at the early subacute stage, and although baselines were comparable, spontaneous improvement may have played a role in outcomes; however, the totality of the data in this intervention appears to suggest that auditory feedback was not the underlying mechanism.

In MST, the therapist models an exercise, which the patient then repeats. There is no external rhythmic template provided to prime the auditory motor system and to serve as a predictable reference point for calibrating kinematic parameters throughout a movement trajectory. In other words, the external periodic referent for anticipating and planning movement, that will act as a driving rhythm at conscious and subconscious levels, is lacking. The movement is first generated by the patient, resulting in auditory feedback, which is delayed information at best, and hence not as useful for rehabilitative purposes. In an entrainment model, it is the provision of a steady beat derived from a predictable rhythmic structure that entrains the motor system, allowing the brain to form stable internal models and compute optimal kinematics in a feedforward manner given the current spatiotemporal constraints. This is the model that was used in the initial pilot studies (Malcolm et al., 2009; Yoo, 2009) and that is used in the current TIMP investigation.

2.1.3.2 Movement Sonification

Researchers conducted a sonification feasibility study to explore the potential of this approach in gross-motor function retraining (Scholz et al., 2015). Noting that MST tends to focus more on fine-motor skills and does not provide continuous real-time feedback, the intent was to create a program that focused exclusively on gross-motor retraining, with real-time auditory feedback of arm movements substituting for potentially lost proprioception. Four inpatients participated, pseudo-randomly assigned to either the experimental movement sonification condition, or to the control condition that replicated the movements in the sonification condition but without auditory feedback. There were nine days of sonification training, with sessions each lasting 30 minutes. All patients concurrently received conventional physiotherapy. Arm movements were sonified in real time, with sensors on the wrist and affected upper arm. Participants were encouraged to actively play and create music by moving their arm in a 3D sonification space. Pitch was mapped onto the *y*-axis, brightness onto the *x*-axis, and volume onto the *z*-axis. The goal was by the end of training to play simple folk songs moving their affected arm in the sonification space. The patients assigned to the experimental group showed improvements on the FM-UE, the ARAT, Box and Block Test (BBT) and SIS. One participant also improved on the Nine-Hole Pegboard Test (9HPT), a measure of finger dexterity. The control group participants did not show any improvement from sham sonification training on measures of motor impairment and function. Using the same protocol, 25 inpatients were subsequently assigned to either the music sonification (n = 15) or sham sonification (n = 10) condition, with an average of 10 days of training (Scholz et al., 2016). On the FM-UE, significant improvements were found in the music group only on the subscale assessing joint pain. There was also a trend toward better hand function on the SIS and improvement in movement smoothness in the music group. A second follow-up study was conducted involving 42 patients at two sites, with a median of 22 training sessions for the treatment group and 16.5 for the control (Nikmaram et al., 2019). There were no significant differences on motor test batteries or on the SIS, and only slight improvements in movement smoothness for the experimental condition. While this approach incorporates goal setting, with the goal of playing a simple folk song in the sonification space, there are no spatiotemporal constraints to facilitate optimal movement planning and formation of motor representations. This approach may have merit if used following an active TIMP training session as a creative and fun means of synthesizing new motor learnings by engaging in improvisational movement patterns.

2.1.4 Additional music-based approaches

2.1.4.1 Piano training program

Noting the resource intensive nature of MST protocols on mixed instruments, Villeneuve and colleagues (2014) sought to examine the benefits of a structured protocol that combined supervised piano training with home practice. Thirteen participants at the chronic stage underwent a three-week formal keyboard training program, three times a week for one hour, with 30-minute biweekly home practice sessions on a roll-up piano. All participants had to have some wrist and finger movement capacity. The training program was structured at three levels of increasing difficulty, with three pieces per level. Training began at a tempo of 30 bpm, with stepwise increases until 60 bpm was reached, again too slowly at least initially for audio-motor coupling to take place. Outcome scores were significantly higher on all evaluations at post-test, and gains were maintained at three-week follow-up. Those participants who had the highest levels of function at baseline showed the greatest improvement. According to the feedback questionnaire, participants found the program enjoyable and motivating. It is unclear, however, whether functional gains may be attributable to musical aspects, or the specificity of the practice with frequent repetitions involving dissociated finger movements. A visual display guided key presses, with the program pausing until the participant pressed the next correct key, so there was no entrainment mechanism involved.

2.1.4.2 Music Upper Limb Therapy-Integrated

A pilot study combining music therapy and occupational therapy in collaborative group music, entitled Music Upper Limb Therapy-Integrated (MULT-I), explored addressing physical, psychological and social components of health simultaneously (Raghavan et al., 2016). The study was based on a Nordoff-Robbins music therapy approach, which focuses on creating a fulfilling musical experience for each participant. Thirteen chronic post-stroke participants completed a six-week, biweekly training program in groups of three for a total of twelve 45-minute sessions. Repetitive isolated upper limb movements were practiced while playing various musical instruments under the supervision of an occupational therapist and music therapist. A second music therapist provided a musical framework from the piano. Accompaniment was adjusted to reflect participant mood, expression and effort, and to encourage smoother movement. Thirty-five minutes was spent in training, with five minutes at the beginning for OT led musically supported warm-up stretches and group discussion, and five minutes at the end for feedback and final thoughts from participants to encourage social participation. Assessments took place on three occasions: pre-intervention, post-intervention, and at one-year follow-up. Significant improvements, retained at follow-up, were found, including on the FM-UE (p = 0.021) and the World Health Organization (WHO) well-being scale (p = .003). Changes on activities of daily living and participation subscales of the Stroke Impact Scale (SIS) did not change significantly from pre- to post-test; however significant changes were found on the activities of daily living score from post-test to follow-up, with a trend toward significance on the participation score. Limitations of this study include small sample size, lack of a control group, and a study design based on synergistic effects of physical, psychological and social aspects, making it difficult to ascertain relative contributions and underlying mechanisms.

2.1.4.3 Electronic music-making activity

Paul and Ramsey (1998) investigated the effects of electronic music-making activity on shoulder flexion and elbow extension on persons with hemiplegia in a nursing facility. Participants were randomly assigned to either experimental (n = 10) or control (n = 10) groups. Mean time post-stroke was 93 days. All participants had been discharged from formal rehabilitation therapies, yet continued to participate in recreation therapies, including games, yoga and tai-chi. The dependent variables were active shoulder flexion and elbow extension, measured with a goniometer before and after the 10-week intervention period. The instruments used were electronic paddle drums on stands, with touch-sensitive signals sent from the drums to a sound-making module programmed to emit sounds of various acoustic instruments within pitches of a particular scale. Participants sat in their wheelchairs in front of the drums, with a trunk restraint to reduce compensatory trunk movement. Drums were set in the participant’s mid-saggital plane, and the height was adjusted to the individual’s maximum range for upward reaching. Group interventions took place twice a week for 30 minutes over the 10-weeks. In the experimental music group, the music therapist sat in front of and facing the participants, with the OT standing beside. Familiar songs were used in sessions to enhance engagement. The music therapist established a basic pulse for the music, then increased or decreased the tempo to focus attention and involvement. The OT ensured participants were executing movements properly and adjusted the height of the drum when necessary. Control-group participants engaged in physical exercises conducted by a recreation therapist for the same amount of time, with exercises also incorporating shoulder flexion and elbow extension practice. Results were analyzed using independent and paired t-tests. There were no significant between-group differences. Two-tailed paired t-tests revealed significant pre-post differences for participants in the experimental group on both shoulder flexion and elbow extension, with differences approaching significance in the control group. Though no formal assessments were conducted, anecdotal reports from participants in the experimental group indicated they enjoyed and felt motivated to engage in the music-facilitated activity. However, the range of activities in the experimental group was limited, much more so than in the control, and fatigue in repetitive practice of upward reaching motions may have affected participants in the experimental group, and ultimately reduced the number of repetitions of movements.

Recent systematic reviews with meta-analyses found evidence to support use of music-based interventions in treating post-stroke motor dysfunction. Zhang and colleagues (2016) found there were significant results for the BBT and Arm Paresis Score (APS), and positive trends for the 9HPT and Action Research Arm Test (ARAT). The researchers recommended on a local scale that persons with stroke be encouraged to consider music-supported therapy for motor rehabilitation. Ghai (2018) found beneficial effects for post-stroke arm recovery from training with rhythmic auditory cueing and/or real-time auditory feedback, based on meta-analyses for FM-UE, Stroke Impact Scale (SIS), elbow range of motion, and WMFT-Time; a training dose of 30 minutes to one hour, with three or more sessions per week was recommended. A recent Cochrane Review took a more cautious approach, finding some support for improved timing of upper extremity function, as well as for gait parameters, quality of life and communication, while indicating a need for high quality RCTs in order to make clinical recommendations (Magee et al., 2017). A number of review articles note the need for high-quality studies to elucidate potential therapeutic effects (François et al., 2015; Grau-Sánchez et al., 2020; Le Perf et al., 2019; Schaffert et al., 2019; Sihvonen et al., 2017; Yoo & Kim, 2016; Zhang et al., 2016). François and colleagues (2015) recommended more RCTs at the chronic stage where there is a stabilization of deficits, and noted that in many studies where the control is conventional treatment, the content of the exercise program needs to be clarified, as this can vary between facilities and countries. In a perspective article, Chen (2018) makes a number of specific recommendations for moving forward. These recommendations include more modeling and exploratory studies to improve understanding of specific mechanisms contributing to therapeutic effects of music in rehabilitation, which will in turn help to identify potential responders and non-responders. As well, stratification using biomarkers to assess corticospinal tract integrity would help to increase statistical power by reducing variability. Agreement on which behavioural outcome measures to use is also needed, supplemented where possible by kinematic and kinetic data to distinguish between recovery and compensation. Statistical significance does not constitute minimal clinical important difference (MCID), which must be reported and met to have meaningful benefit. This provides the basis for a well-executed RCT with comparable control, the need for which has been highlighted above. Final testing involves multiple sites to ascertain effectiveness in real-world settings, requiring extensive buy-in from stakeholders. Much exploratory and clinical research remains to be done to better ascertain the therapeutic benefits of rehabilitation using auditory stimuli.

2.1.5 Neural changes associated with behaviour

A number of studies have used techniques to examine neural changes associated with training-induced behavioural outcome improvements. Using transcranial magnetic stimulation (TMS), motor-evoked potential (MEP) parameters were found to be significantly better following BATRAC (Shahine & Shafshak, 2014) and MST (Amengual et al., 2013; Rojo et al., 2011). These changes included increases in MEP amplitude, decreases in MEP threshold, and increases in ipsilesional motor cortex excitability. The changes in MEP amplitude may represent an increase in strength of synaptic transmission along the corticospinal tract (Amengual et al., 2013). Positive gains on behavioural measures following MST were paralleled by increased event-related desynchronization (ERD) and coherence in the beta band, as revealed by electroencephalogram (EEG) recordings, indicative of increased motor region activity (Altenmüller et al., 2009). Electrophysiological data obtained from two music and two control group participants indicated increased cortico-muscular phase coherence in the ipsilesional hemisphere for music condition participants following sonification training (Nikmaram et al., 2019). Functional magnetic resonance imaging (fMRI) has revealed enhanced auditory-motor region activity and connectivity following MST, with decreased activation in contralesional motor regions (Ripollés et al., 2015; Rojo et al., 2011). Together these findings suggest neuroplastic changes underlying behavioural improvements following interventions using auditory stimuli.

2.1.6 Secondary effects on cognition and affect

Metrics obtained from research studies have indicated some secondary effects on cognition and affect following motor interventions using auditory stimuli. Significant improvements were found following MST interventions on neuropsychological evaluations of visual attention, speed of processing, and rate of learning, using the Trail Making Test (TMT) (Part A), the colour Stroop test, and the Rey Auditory Verbal Learning (RAVLT) tests respectively (Ripollés et al., 2015). Cognitive flexibility, assessed with the TMT- Part B, was found to be significantly improved in music-group participants after five weeks of MST interventions (Fujioka et al., 2018). These findings suggest that music-based interventions designed for motor rehabilitation may have far transfer effects on cognitive processes.

Improvements to affect have also been found in a number of studies following motor rehabilitation interventions using auditory stimuli. Following MST training, significant changes on the positive affect portion of the Positive and Negative Affect Schedule (PANAS) as well as the valence and arousal portions of the Self-Assessment Manikin (SAM) were obtained (Ripollés et al., 2015). There were improvements in mood on face scale ratings (Van Vugt et al., 2016; Van Vugt et al., 2014), on the Beck Depression Inventory (Ripollés et al., 2015), and a positive correlation was found between the capacity to enjoy musical activities and improvement on the ARAT (Grau-Sánchez et al., 2018). Significant reductions in negative affect were found on the short form of the POMS (Van Vugt et al., 2016; Van Vugt et al., 2014) and on the negative affect portion of PANAS in the music group following five and ten weeks of MST training (Fujioka et al., 2018). Mood states, as measured with the Profile of Mood States (POMS), significantly improved following use of rhythmic auditory stimulation (RAS) in a community-based rehabilitation program (Jeong & Kim, 2007); however, while the researchers considered dynamic rhythm to be the main intervening variable, the combination of music, exercise, and social interaction makes understanding the relative contributions of underlying mechanisms challenging. Following NMT interventions in multidisciplinary acute stroke rehabilitation, participants indicated improvements in mood on the Visual Analogue Mood Scale, with significant reductions in sadness and increases in happiness ratings (Street et al., 2020). Street and colleagues (2018) also used structured interviews to ascertain participants' tolerance of a home-based program using TIMP exercises. Qualitative data showed that despite some initial skepticism, participants found the interventions to be motivating and facilitative of target movements, with high tolerance and low fatigue levels indicated. Overall, these results appear to suggest positive effects on affective responding in individuals partaking in music-based motor rehabilitative exercises.

2.2 Rehabilitation without Auditory Facilitation

What is the nature of conventional post-stroke treatment, and how does it unfold? François and colleagues (2015) expressed concern that this can vary from one jurisdiction to the next. Recognizing the ambiguous nature of the term "conventional" and how this might complicate interpretation of study results, researchers conducted a systematic review to explore the issue (Lohse et al., 2018). Based on mean word count in procedures for experimental relative to control conditions, mean references in procedures, and total scores on the Template for Intervention Description and Replication checklist (Hoffmann et al., 2014), the authors concluded that there is a lack of sufficient description for control conditions, and that this lack of transparency threatens the internal validity and generalizability of trial findings (Lohse et al., 2018). A general theme emerging from a systematic review is the notion that therapy needs to be task-specific, intensive and repetitive (Langhorne, Coupar, et al., 2009). The *Canadian Stroke Best Practice Recommendations* (2018) indicate that training needs to be "meaningful, engaging, repetitive, progressively adapted, task-specific and goal-oriented" (Section 5.1), designed to encourage patients to use their affected limb in activities of daily living. Established approaches exemplifying these general principles, in particular treatments that have been used as control conditions in previously discussed studies, will be reviewed, as well as those of a more experimental nature.

2.2.1 Graded Repetitive Arm Supplementary Program

The Graded Repetitive Arm Supplementary Program (GRASP) approach was designed as a patient self-administered program to augment exercise intensity at the subacute stage (Harris et al., 2009). As it has a standardized protocol, it was used as a dose-matched control condition in an MST study of participants at the chronic stage who would not otherwise be accessing physiotherapy or occupational therapy services (Fujioka et al., 2018). In-patients in the original four-week study were randomized to either the experimental GRASP group (n = 53), or the education protocol control group (n = 50). All participants received usual therapy during this time, with a record kept of time spent. There were three GRASP exercise protocols, based on the

FM-UE impairment level (severe, moderate, mild) ascertained during the screening for eligibility process. Each level had an exercise book, providing written and pictorial instructions, and a kit with equipment for exercise practice. Activities included ROM, arm/hand strengthening, gross and fine motor skills, as well as task-based exercises simulating ADLs. The number of repetitions was adjusted according to individual needs, and monitored once a week by the site coordinator. Participants were asked to do their exercise homework for one hour, six days a week, and to track their exercise completion using a log sheet. Upon discharge four weeks into the program, they were provided with additional log sheets as well as the exercise book and kit, and instructed to continue practicing at home until reassessment at three-months follow-up. The control group worked on education modules, and met with the site coordinator for a comparable amount of contact time during the four-week intervention. With higher intensity levels and targeted repetitive exercises, GRASP group participants made significant gains relative to controls on post-intervention behavioural assessments, gains which were retained at follow-up, although due to attrition the retention assessment was under-powered.

The *Canadian Stroke Best Practice Recommendations* (2018) recommend consideration of GRASP as a supplementary training program to promote active, functional use of the affected extremity between rehabilitation sessions. The activities have similar goals to those used in TIMP training, which incorporates ROM, gross and fine motor skills, as well as practice of functional movement patterns. By using specific spatiotemporal constraints in TIMP exercises, however, quality of movement is addressed in retraining movement patterns, which does not appear to be the case in the GRASP protocol.

2.2.2 Repetitive task training

Repetitive task training (RTT) involves sequential repetitions of task-specific activities. Based on a review of evidence, researchers recommended that training be relevant, repetitive, randomly ordered to increase generalization, aim towards entire task reconstruction, and positively reinforced (Hubbard et al., 2009). A Cochrane Review (with update) found low-quality evidence that this approach yields benefits for upper limb function, and indicates further research is required to ascertain amount of training, including number of repetitions, as well as the type of training involved (French et al., 2016; Thomas et al., 2017). The *Evidence-based Review of Stroke Rehabilitation* suggests that task-specific training may support some facets of UE rehabilitation, with higher and lower intensity levels possibly having similar effects (Iruthayarajah et al., 2018). The conclusion provided in the *Stroke Rehabilitation Clinician Handbook* states that task-specific training may facilitate motor function, spasticity, ROM and strength, but that it does not improve ADLs, nor does it mitigate stroke severity (R. Teasell et al., 2020).

A number of clinical trials have yielded equivocal results. In a pilot study conducted at the chronic stage, sixteen participants were randomized to receive either repetitive task practice (RTP) or occupation-based intervention, with 55 minutes of treatment provided two days a week for four weeks (Skubik-Peplaski et al., 2017). In the occupation-based group, the focus was on performing the occupation, rather than on intensive repetition, as in the RTP group. Both groups improved on behavioural outcome measures (FM-UE and SIS), with no significant between-group differences. Similar results were found in the ICARE randomized clinical trial (Winstein et al., 2016), which involved 361 patients randomized from 14 to 106 days post-stroke to one of three conditions: structured, task-oriented training using an accelerated skill acquisition program (ASAP), dose-equivalent usual and customary care (DEUCC), or usual customary care (UCC). The ASAP (n = 119) and DEUCC (n = 120) groups received 30 hours additional treatment over 10 weeks, three times a week; however, a number of participants either did not adhere to the therapy or did not complete the program. There were no group differences at 12 months from randomization, as measured by time on the WMFT-Time, with additional treatment time and use of a structured, task-oriented program not translating into meaningful changes in outcomes. Lang and colleagues (2016) specifically examined the effects of treatment dose on results in a group of 85 chronic post-stroke participants. Task-specific training was identical for participants in four groups; however, the number of repetitions varied: either 100, 200, 300, or an individualized number of repetitions. Results on the ARAT indicated no apparent difference in response to task-specific exercises based on dose of training, with modest differences in motor function and small treatment effects. Neither this trial nor the ICARE trial measured the quality of movement following repetitive task training.

Kim and colleagues (2015), on the other hand, measured both impairment and functional changes in a study which contrasted repetitive spatial target reaching training (TRT), involving 150-180 movements per session, with routine physical and occupational therapy. Chronic-stage participants in the experimental group (n = 20) received 30 minutes of TRT with visual biofeedback and 30 minutes of routine therapy, while those in the control-group (n = 20) received one hour of routine therapy. There was a significantly greater improvement on the FM-UE and WMFT, as well as on kinematic measures of speed and joint angle, in the experimental group relative to the control. Research has shown that it is motor skill acquisition as opposed to repetition alone that facilitates cortical reorganization (Plautz et al., 2000). Spatial constraints; variations in size, shape, and weight of targets contacted on the LCD screen; as well as corrective feedback to help minimize compensatory movements may have contributed to greater learning during the repetitive target reaching condition. Cirstea and Levin (2007) found clinical impairment and function improvements stemmed from knowledge of performance (KP) rather than knowledge of results (KR), and this may also have furthered skill acquisition in the Kim et al. (2015) trial.

2.2.3 Neurodevelopmental and Bobath concept approaches

Approaches considered to be neurodevelopmental (NDT) - motor relearning programmes (MRP) and Brunnstrom movement therapy (Iruthayarajah et al., 2018), as well as the Bobath concept (IBITA, 2020) are hands-on treatment approaches. While UE studies using auditory stimuli have not explicitly used NDT as a control, Thaut and colleagues (2007) compared rhythmic auditory stimulation (RAS) to NDT/Bobath in a trial focusing on gait training in patients early post-stroke, and found gains to be significantly higher in the RAS condition. A study contrasting Bobath with MRP at the acute stage found the latter led to superior results and shorter hospital stays (Langhammer & Stanghelle, 2000). A follow-up study also concluded that quality of movement improved more at the acute stage from MRP task-oriented exercises compared to results obtained using Bobath techniques (Langhammer & Stanghelle, 2011). In a multiple baseline study involving 27 chronic-stage participants, paretic hand outcomes improved following repetitive training of isolated movements, improvements that were not seen in a baseline period consisting solely of Bobath treatment focusing on muscle tone reduction (Bütefisch et al., 1995). A systematic review found sufficient evidence (n > 500) indicating Bobath therapy is not superior to other forms of treatment (Hatem et al., 2016). The *Evidence-based Review of Stroke Rehabilitation* suggests that Bobath and MRP may not further UE rehabilitation, and notes that Brunnstrom movement therapy may assist UE function more than MRP (Iruthayarajah et al., 2018). Statistically significant results in favour of the Brunnstrom protocol were obtained when 30 chronic post-stroke participants were randomly assigned to hand rehabilitation based on either the Brunnstrom or the MRP approach (Pandian et al., 2011); however, further research with a larger sample size and more extensive outcome measures is required to confirm results.

Functional movement analysis, skilled facilitation, and clinical reasoning are key to Bobath clinical practice (IBITA, 2020; Michielsen et al., 2019). While the approach focusses on promoting quality of movement rather than compensatory mechanisms during task completion, the facilitative skills of the therapist are critical to successful task execution. In contrast, during a TIMP session, a therapist may support an individual in making a movement they cannot yet make on their own, yet movement within synergies may also be practiced as participants learn to coordinate and regain motor control using any extant degrees of freedom (Bernstein, 1967). Participants' sense of personal agency is fostered as they consciously plan and execute movements within a given template.

2.2.4 Constraint-Induced Movement Therapy

Constraint-induced movement therapy (CIMT) was developed based on research showing increased use of an affected extremity, while constraining the less affected extremity, promoted cortical reorganization and reduced the risk of learned nonuse (Taub et al., 1998; Taub et al., 1993). It involves concentrated task-oriented training, applying motor learning principles of feedback, specificity of practice, repetition, shaping (with movement complexity increased according to need), motivation and reward, delivered in intensive training blocks (Hatem et al., 2016). Use of a transfer package, including a daily motor activity log, diary, problem solving to overcome potential barriers, and behavioural contract, is also incorporated to encourage transfer of gains to real-world settings (Morris et al., 2006). CIMT is typically provided in traditional or modified formats. Traditional CIMT involves two weeks of intensive practice, six hours a day, with the less affected extremity restrained during 90% of waking hours. The modified format (mCIMT) is less intense: constraint time, duration and intensity of training are variable (R. Teasell et al., 2020). A modified form of CIT was added at a later date as a dose-matched control condition for an MST study that had used comparable inclusion criteria to CIMT, but had not initially controlled for time (Schneider et al., 2010).

The Extremity Constraint-Induced Therapy Evaluation (EXCITE) trial was designed to assess the therapeutic effects of two weeks of CIMT, to ascertain the persistence of these effects, to compare results between participants treated at subacute and chronic stages, and to assess the impact that initial level of impairment might have on treatment outcomes (Winstein et al., 2003). To determine the latter, participants were stratified into two groups: inclusion in the higher group required minimum 20 degrees active wrist extension and 10 degrees active metacarpophalangeal joints and interphalangeal joints for all digits, while inclusion in the lower group required at least 10 degrees active wrist extension, and 10 degrees abduction/extension of the thumb and minimum two other digits. Interventions took place for up to six hours/day on weekdays during a two-week period, while the less affected hand was confined to a safety mitt for 90% of the person's waking hours for the full two weeks. Training consisted of tasks adapted and shaped according to individual abilities and practiced in sets of 10 trials, as well as standard activities, such as writing or gift wrapping, performed continuously for 15 to 20 minutes. Participants (n = 222) at seven different sites were randomized to receive either CIMT or customary care, which varied from either no treatment to physiotherapy or pharmaceutical interventions (Wolf et al., 2006). The customary care group was a delayed entry group; CIMT treatment for these participants commenced after one year. Primary outcome measures were the WMFT and the MAL, and secondary outcome measures were the SIS and caregiver completion of the MAL. Results at post-treatment indicated improvements in the CIMT group were significantly greater than the control group on all measures except for the two WMFT strength-based items. At 12 months, significant improvements were found in the experimental group relative to the control in the WMFT-Time, MAL Amount Scale (MAL-AS) and MAL How Well Scale (MAL-HW), as well as for the two strength items. There were no significant between-group differences on the WMFT Functional Ability scale (WMFT-FAS) at 12-months. Long-term secondary outcomes revealed significant gains for the experimental group on the MAL caregiver scale and SIS hand function domain, but there were no treatment gains in other SIS subdomains. Treatment effects for participants stratified at baseline into higher- and lower-functioning groups showed no significant differences. Retention of treatment effects was assessed through 24 months (Wolf et al., 2008). Gains were found to be persistent on primary outcome measures, including significant therapeutic changes on the WMFT strength components. The WMFT-FAS, however, was not administered at 24-month follow-up. Five measurements on the SIS were significantly greater at 24 months than 12 months for the higher functioning group: strength, memory and thinking, ADL and instrumental ADL (IADL), social participation and physical domain, whereas for the lower functioning group significant retention was found only for the social participation domain.

Of the participants originally allocated to receive immediate treatment, 22% had withdrawn at 12 months, and 34% at 24 months, including losses due to mortality or deteriorating health. Finally, the early and delayed treatment groups were compared two years following enrollment (Wolf et al., 2010). Of the participants originally allocated to the delayed-treatment group, 74% began CIMT treatment one year later, 67% completed treatment, and 54% completed 12-month follow-up. Results at 24 months showed no significant between-group differences on the WMFT and MAL measures. SIS reports, however, indicated significantly higher results for the hand function, ADL/iADL, and communication domains for the early-entry group compared to the control.

While these results appear to support use of CIMT at sub-acute and chronic levels in qualifying participants, the impact of earlier administration of CIMT also needed to be investigated. The Very Early Constraint-Induced Movement during Stroke Rehabilitation (VECTORS) trial involved 52 participants at the acute stage, randomized to one of three conditions: traditional UE therapy, dose-matched CIMT, or high-intensity CIMT (Dromerick et al., 2009). Treatment took place five days a week over a two-week period. Control group participants received two hours/day of traditional OT, including strengthening and ROM exercises, as well as compensatory techniques for managing ADLs. CIMT shaping activities were based on exercises from the EXCITE protocol (Wolf et al., 2006). Standard CIMT participants wore the mitten for six hours per day, and received two hours of dose-matched therapy each day. High-intensity CIMT participants wore the mitten 90% of time awake, and received three hours per day of shaping exercises. Contrary to expectations, results revealed an inverse dose-response relationship, with the high-intensity CIMT group underperforming the standard CIMT and control groups on the ARAT, both at 14-day training completion and at 90-day follow-up. This appears to show that higher doses of training, particularly in the early post-stroke stage, may be counterproductive.

Researchers conducting a Cochrane Review assessing efficacy of CIMT found that while CIMT may facilitate limited improvements to motor impairment and function, benefits did not confer a convincing reduction in disability (Corbetta et al., 2015). However, the authors did not distinguish between modes of delivery (CIMT, mCIMT, FU) or stages of recovery in their analyses. According to the conclusion provided in the *Stroke Rehabilitation Clinician Handbook*, CIMT and mCIMT at the chronic phase may benefit motor function and ADLS, and CIMT may improve muscle strength (R. Teasell et al., 2020). The *Canadian Stroke Best Practices* guideline recommends that CIMT or mCIMT be considered for qualifying patients; i.e., those with 20 degrees active wrist extension, 10 degrees active finger extension, as well as normal cognition and minimal sensory deficit (Canadian Stroke Best Practice Recommendations, 2018; Robert Teasell et al., 2020).

To better understand mechanisms underlying functional improvements following mCIMT, a small proof-of-concept study was conducted which included kinematic measures (Kitago et al., 2013). While clinically meaningful gains were recorded on the ARAT, there were no corresponding gains on the FM-UE or kinematic measures, indicating that compensatory strategy use during CIMT may mediate improvements rather than a reduction in underlying impairment. An earlier exploratory study also included kinematic measures, as well as the WMFT and MAL, but not the FM-UE (Massie et al., 2009). Improvements were found on some kinematic measures in addition to functional outcomes, but results indicated CIT may promote compensatory rather than normalized control. In addition, the restrictive inclusion criteria limit the ecological validity of this approach. Participants with a range of abilities, including those with much higher levels of impairment, were admitted to the TIMP study, which was designed, through the use of rhythmic auditory entrainment in conjunction with carefully selected exercises, to promote a reduction in underlying impairment rather than a reliance on compensatory mechanisms.

2.2.5 Strength training

Strength training encompasses both progressive resistance exercises and activities involving repetitive, effortful muscle contractions, which increase motor unit activity and therefore potentially strength (Ada et al., 2006). The *Canadian Stroke Best Practice Recommendations* (2018) suggest that strength training may be considered for improving grip strength in individuals with mild to moderate UE impairment. While strength training is not directly addressed in the TIMP study, exercise 14 in the detailed protocol (Appendix C) indirectly addresses grip strength.

Based on a systematic review, Harris and Eng (2010) determined that strength training can contribute to UE post-stroke strength and functioning without increasing tone or pain. Agni and Kulkarni (2017) conducted a trial to examine the effects of functional UE training combined with strength training. Participants (n = 45), three weeks to six months post stroke, were randomized to one of three groups: strength-training, functional task-related training, or combined strength and functional task-related training. Seventy-minute sessions, four days/week for six weeks included conventional therapy, with stretching, balance and gait training, as well as training in the randomized condition. Strength-training involved resistance exercises using concentric, eccentric or isometric contractions. Functional task training focused on ADLs and iADLs, including grip and grasp training. Participants in the combined group received 40 minutes of strength and 40 minutes of functional task training. Assessments were administered at three time points: baseline, three weeks, and six weeks, with 37 participants completing the study. Each of the groups showed significant improvements on the FM-UE, with no significant between-group differences. The task training and combined groups made significant gains on the Chedoke arm and hand inventory, while the strength and combined groups made significant gains in strength, as evidenced by dynamometer readings. It appears that improvements were greatest in the combined group for both strength and impairment-based measures, although the three conditions do not seem to have been entirely dose-matched.

Researchers compared the effects of a goal-oriented, functional strength-training program with a non-goal oriented, regular strength-training program in chronic, post-stroke participants (Graef et al., 2016). Therapist-supervised interventions took place in the home over a five-week period, three times per week for 30 minutes. Twenty-seven participants were stratified into weak, moderate, and strong categories prior to randomization to ensure sample homogeneity. Sessions began with stretching and physiotherapist-assisted passive ROM; the participant remained seated throughout with their trunk restrained to avoid trunk-related displacements while training. Loads were set at 60% of the participant’s maximum strength as established at baseline. Regular strength-training that was not goal-directed involved repetitive exercises using a dumbbell, with ROM increasing progressively from 60 to 90 degrees, involving shoulder abduction, adduction and flexion. In the functional strength-training group, the previously-established weight for the participant was placed in objects of different sizes and shapes, so that reaching-to-grasp movements could be practiced against resistance. The same progressive shoulder ROM and directions were used as in the regular strength-training group. Assessments took place pre- and post-training, as well as at 10-month follow-up. The primary clinical outcome was The Upper-Extremity Performance Test (TEMPA). Both groups showed significant improvements at post-test, maintained at follow-up; however, the functional training group had significantly greater improvement on the unilateral ADL task analysis at post-test, and combined unilateral and bilateral ADL task scores at follow-up. There were no statistically-significant between-group differences on the FM-UE at either time-point, nor on measures of grip and shoulder flexion strength, or ROM. While both programs yielded positive results, the goal-directed, functional strength training program appeared to promote greater transfer to ADLs, suggesting the importance of purposeful rather than repetitive exercises in retraining functional capacity.

2.2.6 Range of motion and stretching programs

According to the *Evidence-based Stroke Rehabilitation* guidelines, range of motion and stretching programs may improve aspects of UE function and help inhibit contractures; they are therefore encouraged, despite a limited evidence base (Iruthayarajah et al., 2018). Passive and active assisted ROM exercises are recommended in the current Canadian best practice guidelines (Canadian Stroke Best Practice Recommendations, 2018). In the TIMP study, exercises were intentionally designed to promote greater range of motion, with therapists facilitating activities and placement of instruments adjusted according to ROM needs. Provision for a stretching warm-up exercise was also made using the bodhran (Appendix C).

Facilitated ROM exercises appear to yield greater benefits. The effects of a nurse-facilitated ROM exercise program on older chronic post-stroke participants in long-term care were investigated in a three-armed randomized-controlled trial by Tseng and colleagues (2007). Patients in the usual care group (n = 17) did not receive any additional treatment during the study; however, upon study completion were provided with the ROM intervention. Participants in the two experimental groups received treatment twice daily (approx.10-20 minutes), six days a week, for four weeks. Those in the first intervention group (n = 21) were supervised by a Registered Nurse (RN) as they completed the ROM protocol on their own, while participants in the second group (n = 21) were aided physically by the RN, who placed a hand above and below the target joint to safely achieve maximum ROM. Outcome measures included the ADL subscale of the Functional Independence Measure (FIM), which contains 13 items on a seven-point Likert scale; 17 joint angle measurements in six joints; score on the Geriatric Depression Scale (GDS) (Chinese version); and self-reported pain. ADL scores for the intervention groups were statistically significantly different from the usual care group, but there was no significant difference between the two intervention groups. Patients receiving usual care had an average UE joint angle decrease of 5.83°. On the other hand, patients in the first intervention group had an average UE gain of 5.42°, while those in the second group receiving manual ROM assistance had an average UE gain of 12.8°. There was a statistically significant decline in depression for patients receiving the intervention, with no significant between-group differences. In contrast, GDS scores were higher in the usual care group at the conclusion of the study. Similarly, pain scores decreased significantly for the intervention groups, with no between-group differences, while they increased for those receiving usual care. This would appear to indicate that a ROM protocol will help to ease the pain of contractures, lessen depressive symptoms, improve functional status, and increase joint flexibility, with facilitated ROM exercises yielding the greatest benefits. ROM exercises with rhythmic auditory stimulation may help to extend these benefits. Thaut and colleagues (2002) found rhythmic cueing significantly increased elbow angle ranges of motion.

2.2.7 Trunk restraint

The *Canadian Stroke Best Practice Recommendations* (2018) indicate that trunk control retraining needs to accompany functional UE training. In the TIMP study, there are two exercises in the detailed protocol (Appendix C) designed to promote greater trunk control. Exercise 18 focuses on sideways bend, while exercise 19 focuses on trunk rotation. Trunk restraint was not used in the study; however, participants were instructed to keep their back in contact with the chair during forward reaching movements and to refrain from using compensatory trunk movements.

Researchers found that trunk restraint promoted greater elbow and shoulder joint ROM during reaching movements, as well as greater interjoint coordination, caused by increased ROM and improved interjoint dynamic temporal correlation (Michaelsen et al., 2001). A follow-up experiment compared the effects of trunk restraint on reach-to-grasp with verbal instructions to refrain from trunk movement during forward reaching (Michaelsen & Levin, 2004). Chronic post-stroke participants (n = 28) were stratified based on their degree of impairment, according to FM-UE baseline measures, and block randomized to either the experimental trunk restraint or control group. Clinical evaluation measures of impairment (FM-UE), function (TEMPA), and spasticity (Composite Spasticity Index -CSI), as well as kinematic measures, ascertained that the two groups were comparable at baseline. Kinematic measures were obtained at pre-test, at post-test after a one-day training period involving 60 trials, and at retention the following day after a single session. There were no between-group differences in performance outcome measures (velocity peaks, movement time, wrist peak velocity, time to peak velocity) at post-test or retention. However, post-test measures of movement variables revealed significantly less anterior trunk displacement in the experimental group, retained at follow-up. While both groups increased elbow extension with practice, the increase was significantly larger in the experimental group. Significantly more experimental than control group participants exhibited improvements on the Temporal Coordination Index (TCI), based on moment to moment phase angle differences between shoulder and elbow. Shoulder horizontal adduction and flexion showed no statistically significant between-group differences. This data would appear to indicate that limitation of trunk compensatory movements by means of restraint during reach-to-grasp movements had a greater impact on arm reach kinematics and interjoint coordination than verbal instruction.

A double-blind RCT examined the effects of trunk restraint on task-specific training compared to training without restraint (Michaelsen et al., 2006). Chronic post-stroke participants (n = 30) were randomized to receive therapist-supervised training in their homes, three times/week for five weeks, with or without trunk restraint. To balance patient characteristics between groups, randomization was stratified based on impairment, with participants achieving less than 50 on the FM-UE considered to be more impaired. Training in both groups was repetitive and progressive, involving reach-to-grasp tasks with objects that varied in shape, weight and size. Participants were instructed to refrain from trunk movement during practice; however, those in the trunk-restraint group practised with body and shoulder belts attached to the backs of their chairs. Results showed significant increases in elbow extension in the trunk-restraint group compared to control, as well as non-significant greater improvements on the FM-UE and TEMPA. Effects were more pronounced in the subgroups with greater initial impairment. The moderate impairment trunk-restraint subgroup had significantly greater improvement on the FM-UE at follow-up, a significant reduction in trunk displacement at post-test and follow-up, as well as significant increase in elbow extension at both time points. On the other hand, in the control subgroup with moderate impairment, the effect of training was to significantly increase trunk displacement, with decreased shoulder flexion and a tendency towards decreased elbow extension. This group also had a strong correlation between increase in TEMPA and increase in trunk displacement, which was not found in the moderate group practicing with trunk restraint.

This appears to indicate that limiting excessive trunk movement during task-specific training, particularly for participants with moderate to severe impairment, facilitates behavioural and kinematic improvements, while decreasing reliance on compensatory strategies.

Additional approaches to UE rehabilitation recommended in Canadian stroke practice guidelines that are not examined in the context of this paper, as there are no parallels between these approaches and TIMP study techniques, include Functional Electrical Stimulation (FES), mirror therapy, sensory stimulation, virtual reality, and non-invasive brain stimulation (Canadian Stroke Best Practice Recommendations, 2018; Robert Teasell et al., 2020). Yet despite established and novel interventions for UE treatment, stroke remains a leading cause of long-term disability (Benjamin et al., 2018). A recent systematic review has indicated an ongoing need for high-quality studies (D'Anci et al., 2019). Collaborative effort is required to address existing shortcomings and fill the many gaps in the evidence base to better inform clinical practice (Langhorne et al., 2011; Pollock et al., 2014).

2.3 Simulation Mode

Jeannerod’s action simulation hypothesis (1994, 2001) is predicated upon recruitment of similar neural structures during simulation state (conscious, imagined action representations) as during action execution. Furthermore, simulated and overt actions unfold in comparable time frames (Decety et al., 1989). To better understand the nature of shared brain networks, researchers compared and summarized data from motor imagery (MI), action observation (AO), and movement execution (ME) neuroimaging experiments involving healthy adult participants (Hardwick et al., 2018). While similar premotor-parietal networks were recruited for both MI and AO, contrast analyses indicated that MI was more often associated with recruitment of bilateral supplementary motor area (SMA), dorsal premotor (PMd) and ventral premotor (PMv) areas, bilateral inferior parietal lobe, and primarily left superior parietal lobe. In addition, MI was more closely associated with dorsolateral prefrontal cortex (DLPFC), bilateral putamen and cerebellum recruitment. Areas more associated with AO than with MI recruitment included bilateral inferior frontal gyrus and right inferior and superior parietal lobule areas, regions implicated as the human homologues of the mirror neuron system, first identified in non-human primates (di Pellegrino et al., 1992; Fogassi et al., 2005; Gallese et al., 1996; Rizzolatti et al., 1996). Notably, ME relative to MI was associated with left primary motor and somatosensory cortex recruitment. Conjunction analyses between MI and ME indicated consistent bilateral premotor cortex recruitment, including SMA, pre-SMA, PMv, and right PMd, as well as mid-cingulate cortex, bilateral primary somatosensory cortex, and subcortically bilateral putamen, thalamus, and cerebellum lobule VI. AO and ME conjunction analyses indicated bilateral premotor, parietal and sensorimotor network recruitment; however, AO did not consistently recruit subcortical structures. Brain areas involved across MI, AO, and ME in action simulation and performance included bilateral premotor, parietal, and somatosensory areas. In contrast, DLPFC recruitment occurred consistently only during MI, while critically, primary motor cortex recruitment was found consistently only in the ME network. Based on their conjunction analyses showing greater recruitment overlap between MI and ME networks than between AO and ME, Hardwick and colleagues (2018) suggest that use of MI may best support translational research involving action simulation interventions with a goal of ME circuit recruitment. The TIMP study focusses on action simulation using MI, with AO utilized solely for demonstration purposes.

Glover and Baran (2017) posited a motor-cognitive model, which emphasizes the role of central executive functions in motor imagery, as an alternative to Jeannerod's functional equivalence hypothesis. While the action planning stage of motor imagery is matched behaviourally and neurologically with overt action, the motor-cognitive model suggests that overt and covert processes diverge during the action execution stage, with motor imagery relying on conscious executive control mediated primarily by the DLPFC, and overt execution operating largely through automatic processes requiring less conscious online control. In instances where the motor representation is not fully developed, reliance on executive processes during online control increases, with correspondingly greater increases in movement times for motor imagery compared to overt action. This was demonstrated in experiments involving either an interference task or high levels of precision, which took longer to execute in simulation mode. This finding contrasts with the functional equivalence model, which is based on similar neural resources underlying both action simulation and execution throughout the movement cycle, with both unfolding over comparable time frames. Jeannerod (1994) also viewed motor imagery as key to grasping cognitive components of actions and understanding motor representations, and furthermore acknowledged that overt and covert components are not entirely identical due to biomechanical constraints during execution involving the musculoskeletal system and environmental factors that may not be represented centrally; however, he did not specifically distinguish between planning and control phases of movement in his simulation theory.

Mulder (2007) views motor imagery as an embodied, rather than a symbolic, cognitive activity in its activation of sensorimotor regions in the brain. In formulating the *emulation theory of representation*, Grush (2004a) argues that motor imagery goes beyond accessing and activating motor areas of the brain. For motor imagery to occur, efferent cortical motor areas must also drive an articulated emulator of the musculoskeletal system and corresponding sensors. In effect, motor imagery requires an emulator of the body acting within its environment, driven by sensorimotor control centres in the brain, but without engaging the musculature or utilizing the usual sensory inflow. The emulator instead generates a likely proprioceptive and kinesthetic sequence. Biomechanical constraints, such as joint ROM and acceleration properties, may be internalized in an articulated emulator, which has isomorphic parameters to the actual musculoskeletal system, allowing for trajectory predictions (Wilson, 2004). An embodied emulator not only helps overcome problems associated with feedback delay in online processing, but also trains the brain in both on- and offline rehearsal, enabling formation of expectations that facilitate sensory processing (Grush, 2004b).

Researchers found evidence of corticospinal excitability modulated by motor imagery (Fadiga et al., 1998). TMS was used to stimulate the left precentral cortex of six, right-handed, healthy volunteers during motor imagery of proximal and distal UE movement. In the first experiment, participants imagined right forearm extension and flexion, while in the second experiment, opening and closing of the right hand was imagined using thumb opposition to the fingers. EMG recordings were made of the right Biceps Brachialis (BB) and right Opponens Pollicis (OP) for the first experiment, to ascertain if only proximal muscles were involved in imagery of proximal movement. For the second experiment, EMGs were recorded for both OP and Extensor Digitorum Communis (EDC), to determine the effects of motor imagery on corticospinal pathway excitability of agonist and antagonist muscles used during active hand opening and closing. Results for the first experiment showed significantly larger MEP amplitude during forearm flexion than extension, with no significant effects on OP muscle excitability. For the second experiment, there was a significant effect on OP muscle excitability, with larger MEP amplitude during imagery involving hand closing than opening. The EDC muscle excitability pattern, while not statistically significant, was the opposite of the OP muscle pattern for the same task. Results from these experiments indicate the influence of motor imagery on corticospinal excitability, such that it is not a generalized effect that is incurred, but rather one that is specific to the effectors and types of movements that are the target of the simulation.

The specific effects on muscles and movement patterns elicited through motor imagery have been shown to promote skill acquisition. In a randomized controlled trial (Pascual-Leone et al., 1995), 15 participants were randomly assigned to either a physical practice, mental practice[1], or a control group. Baseline TMS mapping of long finger flexor and extensor muscles was acquired, and all participants were taught a five-finger exercise on an electronic keyboard. Subsequently, physical practice group participants were asked to practice the exercise daily for two hours for five consecutive days. Mental practice group participants were instructed to sit in front of the keyboard for a comparable period of time and to visualize the finger movements required for the exercise while imagining the sound produced. There was no practice involved for members of the control group. Results showed no improvement in control group performance, while both physical and mental practice groups showed fewer sequence errors, less variability of interval timing between key presses, as well as greater accuracy, indexed by an overall decrease in mean interval between key presses. The physical practice group had a significant reduction in sequence errors compared to the mental practice group, and there was a trend towards greater accuracy. However, for both practice groups, there was a steady decrease in the TMS activation threshold for finger flexor and extensor muscles, as well as an equal increase in the cortical representation size for the two muscle groups. Mental practice elicited the same neuroplastic changes as physical practice, and with an additional two-hour physical practice session, participants in the mental practice group also attained a comparable level of performance. Therefore, mental practice appeared to lay the groundwork for skill acquisition with a minimal amount of physical practice, as well as facilitate reorganization of underlying neural circuits.

Given the effects of motor imagery in promoting motor skill learning and neural reorganization, there is promising potential for clinical translation to rehabilitative contexts. Mulder (2007) notes

[1]Mental practice is defined here as “the imagined rehearsal of a motor act with the specific intent of learning or improving it, without overt movement output” (p. 1043). While ‘mental practice’ is an umbrella term embracing several aspects of cognitive rehearsal, its use here appears to be more in line with motor imagery.

that patients with lesion incurred movement limitations may be able to preserve motor representation in the brain through mental rehearsal to avoid central reorganization emanating from inactivity or disuse of an affected extremity. Motor imagery provides an alternative means for motor relearning, supplementing physical practice, and increasing time on task that may otherwise be restricted due to physical fatigue. Kleim and Jones (2008) note that intensity and specificity of practice matter for experience-dependent neural plasticity; however, overuse of impaired extremities, particularly at a vulnerable acute stage, may have a negative impact on motor improvement (Dromerick et al., 2009). According to the *Canadian Stroke Best Practice Recommendations* (2018), mental practice used in addition to a structured therapeutic program can improve UE outcomes in suitable candidates, and following an assessment to determine suitability, individuals affected by stroke are encouraged to practice mental imagery to further their UE recovery. However, recommendations for specific assessments to determine suitability are not provided in the guidelines. Action observation and mental practice are recommended in the *Stroke Rehabilitation Clinician Handbook* for priming the motor system (R. Teasell et al., 2020). Some overviews of studies pertaining to action observation and mental practice with motor imagery follow.

2.3.1 Action Observation

According to the *Evidence-Based Review of Stroke Rehabilitation*, action observation may benefit some aspects of post-stroke recovery, including motor function, dexterity, ADLs, and spasticity (Iruthayarajah et al., 2018). Action observation is used in the TIMP+cMI and TIMP+MI conditions at the outset of each motor imagery practice exercise. In TIMP+cMI, the therapist first demonstrates the previously practiced activity using a metronome beat set to the participant’s preferred pace, providing both visual and auditory priming for the participant, while in TIMP+MI the demonstration is provided without auditory cueing. Following each demonstration, the participant engages in motor imagery of that exercise with (TIMP+cMI) or without (TMP+MI) the external cue.

The effects of action observation training in addition to standard therapy on UE function were evaluated in a large trial involving 13 centres and 102 early post-stroke participants (Franceschini et al., 2012). Assessments (FM-UE, MAS, BBT, Frenchay Arm Test -FAT, and Functional Independence Measure -FIM motor items) were conducted pre- and post-treatment, as well as at four to five-month follow-up. Both experimental and control participants received twice daily 15-minute sessions in addition to standard rehabilitation for four weeks, five days a week. Experimental group participants watched video clips of specific, goal-oriented activities - one per day, progressing from easiest to most complex over 20 sessions - under the supervision of an OT. Each task was broken into three sequences. The patient observed each sequence for three minutes, then practiced the sequence for two minutes, with assistance and guidance as required from the OT. "Sham" action observation was used as a control treatment, involving observation of static, nonhuman images for three minutes, followed by two minutes of active limb movement, guided verbally by the OT. The OT provided support to control participants as needed, but did not model the action, and there was no interaction with objects in this condition. Both groups exhibited improvements over time on the BBT, FM-UE, FAT, and FIM. However, there was a statistically significant Time x Treatment interaction on the BBT, indicating greater positive effects of action observation on functional dexterity gains.

Zhu and colleagues (2015) examined the effects of action observation in a subacute population on UE function and ADLs. Participants (n = 70) in a rehabilitation hospital were within six months post-stroke; 31 patients in the experimental group and 30 in the control group completed the trial. All participants received standard PT and OT therapy, delivered between two to five hours daily, six days a week for eight weeks. Experimental group participants received an additional 30 minutes of action observation therapy, six times per week for eight weeks. Action observation therapy involved viewing 50 second video clips in which specific UE actions were demonstrated and shown from different angles. The patient then attempted to imitate the action. Videos were grouped according to difficulty level, with six videos per group; the patient progressed to the next set of videos once they were able to perform four or more of the actions. Pre- and post-test results on the FM-UE, Barthel index (BI) and Modified Ashworth Scale (MAS) indicated significant within group improvements for both experimental and control group conditions, as well as significant between-group differences in favour of the action observation group. This appears to indicate that use of an action observation therapy program in addition to standard treatment contributes to improvements in UE function and ADLs, as well as reductions in spasticity.

A pilot study compared action observation with task-oriented training to a control group receiving task-oriented training (Kim & Bang, 2016). Participants at the subacute stage (n = 22) were randomly assigned to either experimental or control condition. In addition to three hours per day of conventional rehabilitation (OT and PT), participants received 20 training sessions, five days a week for four weeks. Experimental group participants began by watching a video for nine minutes. The video was first played at normal speed, then half normal speed, and finally normal speed again, with tasks shown simultaneously from front, side, and top angles. After a one-minute break, the action observation group had 30 minutes of task-oriented training based on the video content. Control group participants practiced the same tasks for 30 minutes without seeing the video beforehand. Results indicated statistically significant improvements for both groups on the FM-UE, BBT, and modified Barthel index (MBI), as well as a statistically significant difference for experimental group participants on the MAS. In addition, there was a between-group statistically significant difference on the FM-UE, BBT and MBI, with action observation group participants exhibiting greater gains. These findings suggest that action observation in addition to task-oriented training furthers functional improvements; however, no provision was made in this pilot study for follow-up assessments.

A 2018 Cochrane Review (Borges et al.) examining the effects of action observation on UE function and motor performance included 12 trials with 478 participants. Using standardized mean differences, reviewers found a small significant effect for impact on arm function, and large significant effects for hand function and ADL outcomes. A 2019 systematic review and meta-analysis (Peng et al.), on the other hand, found a moderate effect size for arm and hand outcomes, and a moderate to large effect size for impact on ADLs. This review was based on 17 articles involving 600 individuals, and used Hedge's *g* for effect size calculations. Both reviews concluded that action observation is beneficial in facilitating post-stroke improvements to arm and hand motor function, as well as ADLs. Given the effects of AO on premotor-parietal networks, including the inferior frontal gyrus, and somatosensory areas (Hardwick et al., 2018), it is thought that AO can be effectively used in the TIMP study to prime the brain for subsequent motor imagery practice.

2.3.2 Mental Practice with Motor Imagery

While mental practice with motor imagery may be used as a supplement to active training at any stage post-stroke, the focus here will be on studies that have examined effects at the chronic stage. What impact does motor imagery have on impairment levels, functional improvements and daily use of the paretic limb, as well as on upper extremity kinematics at the chronic post-stroke stage? Are potential effects impacted by whether motor imagery precedes, follows, or is embedded in active training, or by duration of motor imagery practice? Does neuroplasticity potentially underlie motor imagery-induced changes? Each of these questions will be examined in turn through relevant research findings, and implications for the current research established.

The effects of motor imagery on impairment were examined in a randomized-controlled trial (Page, 2000). Sixteen chronic post-stroke participants were randomized to either OT followed by motor imagery or OT followed by a dose-matched control, with outcomes measured on the FM-UE. OT treatments consisted of NDT techniques and compensatory strategies using the unaffected limb, and were administered three times a week for 30 minutes over four weeks. Following OT, participants in the experimental group received a 20-minute tape-recorded imagery intervention, consisting of five minutes of relaxation, 10 minutes of imagery suggestions related to activities practiced during OT sessions, and five minutes for transitioning back to the room. Control group participants instead listened to 20-minutes of taped instructions and stroke-related information. Both groups had comparable FM-UE means at outset, and while both showed improvements between pre- and post-assessments, the improvement in the experimental group was significantly greater, with a large effect size of 1.39. Results of this study suggest that motor imagery in conjunction with OT may reduce UE impairment more than OT alone.

While the previous study examined the effects of motor imagery on levels of impairment, a follow-up trial focused on measuring functional improvements and changes to the amount individuals used their affected extremity (Page et al., 2005). Eleven participants, over a year post-stroke, who had a minimum of 10° active flexion of the affected wrist and two digits of the affected hand, were randomized to either the mental practice[2] or control group. The MAL and ARAT were used to assess functional use. Two baselines were obtained, one week apart, with one post-intervention assessment. All participants received therapy twice weekly for 30 minutes over a six-week period. Selected ADLs were practiced, in addition to stretching and compensatory exercises. Following therapy, participants in the experimental group engaged in mental practice for 30 minutes using a pre-recorded tape based on the actively practiced ADL.

[2]While ‘mental practice’ is more of an umbrella term, its use is retained here when referencing studies that use this term in lieu of ‘motor imagery.’

The opening five minutes of progressive relaxation exercises was followed by a 20-minute segment with guidance for internal, polysensory images of the affected arm executing previously practiced tasks, whether it was for reaching and grasping an object, turning a book page, or using a writing utensil correctly. The final few minutes were allocated for refocusing back into the room. Mental practice of the ADLs occurred both in the laboratory after active practice sessions, as well as at home. Control group participants received identical motor therapy interventions, and listened to a 30-minute tape of progressive relaxation exercises following their active therapy sessions. Results on the ARAT were significantly higher for participants in the experimental group. Prior to the intervention, none of the participants used their affected limb for ADLs, as revealed by amount of use scores on the MAL. However, post intervention mean change scores in the experimental group were 1.55 for patients and 1.66 for caregivers, while in the control group they were 0.49 and 0.30 respectively. Similar improvements were obtained on the MAL quality of movement scores. These results supported the hypothesis that mental practice would lead to functional improvements and increased use of the affected extremity. A phase two trial was subsequently conducted involving 32 chronic stroke participants (Page et al., 2007). The same protocol was used as in the 2005 (Page et al.) study, with the exception that the ARAT and FM-UE were used as outcome measures. All participants were instructed not to engage in additional physical or mental practice at home over the six-week period. Change scores on the ARAT and FM-UE were significantly higher at post-test for the experimental than for the control group, confirming previous results that the addition of mental rehearsal to physically-practiced tasks substantially improves outcomes on standardized measures of impairment and function.

Researchers also used ARAT and FM-UE to measure the efficacy of mental practice as an adjunct to modified constraint-induced therapy (mCIT) at the post-stroke chronic stage (Page, Levine, et al., 2009; Park, 2015). Page and colleagues (2009) conducted a pilot study with 10 participants randomized to either mCIT or mCIT and mental practice in a multiple baseline study with post-test and three-month follow-up. The researchers hypothesized that the experimental group would exhibit larger reductions of functional limitation on the ARAT, as well as larger decreases in arm impairment on the FM-UE. All participants received 30 minutes of training administered by an OT, three times a week for 10 weeks. The focus of training was on ADLs for

25 minutes and ROM for five minutes, with shaping techniques incorporated for ADLs to advance task difficulty according to individual abilities. The unaffected hand and wrist were also restrained for five hours on weekdays. After each training session, participants in the experimental group also spent 30 minutes engaged in mental practice, using audiotapes modelled on the protocol previously outlined by Page and colleagues (2007; 2005). Participants were instructed not to engage in mental practice outside of the laboratory setting. At post-test, experimental group participants demonstrated significantly larger improvements than controls on both ARAT and FM-UE. All participants made slight additional gains between post-test and follow-up. Results appeared to confirm the hypothesis that mental practice in addition to mCIT facilitates greater overall improvements. In a study modelled on the same mental practice protocol, Park (2015) enrolled 26 chronic, post-stroke volunteers, who were randomized to the two conditions. mCIT consisted of 30-minute individualized training sessions five days a week for six weeks, with the unaffected hand and wrist restrained for four hours on weekdays. Outcome measures were the FM-UE, ARAT, and Korean mBI. There were significant improvements on all three outcome measures for both groups, and significant between-group differences in favour of the experimental group. This supported the previous finding of enhanced treatment efficacy with mental practice added to a mCIT protocol. Collectively, these research findings appear to indicate that the addition of motor imagery to a rehabilitation training program leads to a reduction in overall impairment and in greater functional capacity of the affected extremity.

Are UE kinematics altered following mental practice in addition to ADL training? A pre-post case series involving five chronic post-stroke participants was conducted to investigate mental practice-induced changes using kinematic measures (Hewett et al., 2007). Following six weeks of ADL training, twice weekly for 30 minutes, as well as mental practice modelled on previous protocols (Page et al., 2007; Page et al., 2005), kinematic post-intervention measurements were obtained. Significant improvements were found in reaching distance in a reach-up task, as well as trends towards increased shoulder flexion and elbow extension, and linear hand velocity, indicating use of the combined protocol elicited positive changes on objective, quantifiable kinematic measures.

Does the placement of motor imagery interventions with respect to active practice affect outcomes? The above studies all utilized motor imagery following active training. Feasibility of integrating motor imagery into a standard PT and OT therapy program was investigated by a team of researchers (Bovend'Eerdt et al., 2010). Thirty participants were block randomized to either the imagery or the control condition. All participants continued to receive task-specific PT and OT from their usual therapist. In addition, experimental group participants learned how they could incorporate motor imagery into treatment sessions and outside activities. Therapists were asked to implement imagery, tailored to individual needs, into therapy sessions three times a week for three weeks, and two times during the last two weeks. The control group received usual therapy, as well as information pertaining to task-specific practice and how to implement it outside of therapy. During the latter part of the intervention period, participants in both groups were also encouraged to engage in specific task practice five minutes a day outside of therapy – the control group through active practice, and the experimental group through use of imagery. Goal attainment scaling was used as a primary outcome measure; the Barthel ADL index, Rivermead Mobility Index, ARAT, and the Nottingham Extended ADL scale were used as secondary measures. There were significant improvements on all measures over time, with no significant between-group differences. However, custom-developed questionnaires revealed poor compliance from both therapists and participants with respect to motor imagery implementation and practice. The study was undertaken in a specialist neurologic rehabilitation center and involved a heterogeneous population with complex needs, which may have affected uptake by patients and personnel, as the imagery component replaced time spent during usual therapy sessions, and therapists may have been responding instead to specific in-session needs of patients. Reports from an additional study conducted at the subacute stage indicated that implementation of a flexible, individually-tailored, embedded protocol posed additional challenges for therapists; there were more difficulties than the researchers anticipated in changing professional practice, with variations between therapists in uptake and use of the protocol (Braun et al., 2012; S. M. Braun et al., 2010). These studies highlight the need to ensure that the goals of a protocol align with the goals of all stakeholders. Motor imagery included at either the beginning or end of a training session, or in addition to customary therapy, may have improved overall adherence. A randomized pilot study was conducted to compare the effects of embedded motor imagery with motor imagery added to the end of active practice (Schuster et al., 2012). Both approaches were found to be feasible and beneficial; however, results need to be interpreted with caution due to small sample size.

The effects of brief mental practice sessions preceding standard rehabilitation compared to dose-matched standard rehabilitation have also been investigated in chronic post-stroke participants (Park et al., 2015). Criteria for participation included a minimum 20° active wrist extension and 10° extension of the metacarpophalangeal joint. Training sessions were held once a day for 30 minutes, five days a week for a total of ten sessions. Experimental group participants (n = 14) received standard OT for 20 minutes, preceded by 10 minutes of mental practice. The mental practice session was comprised of two minutes of muscle relaxation training, six minutes imagining practice of the actual task, and two minutes to transition back to reality. The control group (n = 15) spent the entire 30 minutes receiving conventional OT therapy. The ARAT, FM-UE, and modified Barthel Index (mBI) were used as clinical measures. There were significant improvements on all clinical measures in the experimental group relative to the control. These results support the findings of Page and colleagues (2007) in finding reduced impairment and improved function and ADLs with mental rehearsal. It also indicates that incorporating a brief, 10-minute period of mental practice prior to active practice can lead to gains in a relatively short period of time in chronic post-stroke participants. In contrast, a study comparing different durations of mental practice (0, 20, 40, and 60 minutes) following active practice found that each increase in mental practice duration resulted in a correspondingly greater increase on FM-UE score (Page et al., 2011). Results on the ARAT did not yield a similar dose-response effect, with a larger improvement exhibited only in the 20-minute condition. This trial unfolded over 10 weeks, with 30-minute active training sessions three times a week followed by the experimental condition. However, there were four conditions and only 29 participants, so results need to be interpreted with caution. Further studies would need to be undertaken to ascertain the differential effects of motor imagery preceding or following active practice, as well as optimal duration of sessions.

Underpinning potential efficacy of motor imagery interventions are neuroplastic changes, as revealed by several imaging studies. An initial study to examine cortical responses involved ten chronic post-stroke participants who received 30 minutes of ADL-based training three days a week for 10 weeks, followed by 30 minutes of mental practice training (Page, Szaflarski, et al., 2009). Gains on ARAT and FM-UE outcome measures corresponded with significant changes to BOLD fMRI signals. The fMRI motor task consisted of an active condition involving affected wrist flexion/extension, alternating with a “relax” control condition. Although there was no control group, activation changes in this sample were noted ipsilateral and contralateral to the affected hand in the premotor area and primary motor cortex, as well as the ipsilateral superior parietal cortex, suggesting intervention-induced cortical reorganization. Sun and colleagues (2013), however, utilized a control group, which was not dose-matched, in exploring cortical reorganization patterns using fMRI. Motor imagery training plus conventional treatment was compared to conventional treatment alone in 18 severely impaired, chronic post-stroke participants. Treatment was provided three hours a day, five days a week for four weeks, with the experimental group receiving an additional 30 minutes of motor imagery training on each active treatment day. Motor imagery practice involved progressive relaxation, imagining of isolated movements followed by imagining of ADLs, and finally a few minutes to refocus back into the room. Scores on the FM-UE were significantly higher in the experimental group post-treatment. The fMRI task involved a therapist-facilitated passive fist clench. Two cortical reorganization patterns emerged, which included all experimental group participants, and six of the nine control group participants. In one pattern there was increased contralateral sensorimotor cortex activation; while there were no statistically significant between-group changes, this pattern was greater in the experimental group. Correlation analyses revealed a significantly positive relationship between increments in contralateral sensorimotor cortex activation and increments in FM-UE scores. The second pattern, which involved only three experimental group participants and one from the control group, was a decreased, more focused activation in the contralateral sensorimotor cortex, with a corresponding laterality index increase. These findings appear to indicate an association between reduced motor impairment following motor imagery training combined with active practice, and varying patterns of cortical reorganization. A further study using resting-state fMRI utilized a dose-matched control. Cortical motor network plasticity was investigated in 31 in-patients who had sustained a subcortical stroke, randomized to either conventional therapy or conventional therapy with motor imagery training (Wang et al., 2019). Participants were between three- and twelve-months post-stroke. Standard treatment was administered to all patients for three hours/day, five days/week for four weeks. In addition, experimental group participants engaged in 30 minutes of verbally-guided motor imagery practice on training days, comparable to the training provided in the Sun et al. (2013) study. Control group participants received stroke-related health education information for an equivalent amount of time. Post-intervention scores on the FM-UE indicated significant improvements in both groups, with the improvement in the experimental group significantly greater than the control. Statistical analysis of fMRI data revealed a significant bilateral M1increase in resting-state functional connectivity as an effect of time with both groups. There was a significant increase in the experimental group in post-intervention functional connectivity of the ipsilesional primary motor cortex (M1) with the ipsilesional precentral and postcentral gyri, middle cingulate gyrus and supramarginal gyrus, and a significant decrease in the control, but there was no significant correlation between functional connectivity change and FM-UE improvement. Graph-theory analysis yielded a significant post-intervention clustering coefficient increase in the experimental group that was not found in the control, indicating a possible motor imagery-induced increase in local neuronal communication efficiency. These results appear to suggest that motor imagery training is associated with improved brain network reorganization. A study with a larger sample size and long-term follow-up would be needed to substantiate results.

A number of systematic reviews concluded that mental practice using motor imagery is an effective adjunct to active treatment (Barclay-Goddard et al., 2011; López et al., 2019; Machado et al., 2019; Nilsen et al., 2010; Park et al., 2018; Song et al., 2019). Caveats included a need for consensus regarding effective protocols and dosage, determining who will benefit, assessing stability of improvements and translation to ADLs. Two reviews were less positive, citing high heterogeneity in methodological quality and protocols, as well as a need for larger, sufficiently-powered studies to ascertain effects (Braun et al., 2013; Guerra et al., 2017). In a critical review, Malouin, Jackson and Richards (2013) identified factors impacting the effectiveness of motor imagery, including adherence to protocols, interactions between overt and covert practice, selection of outcome measures, participant selection, heterogeneous groups, and implementation procedures, and proposed a stepwise framework for progressively introducing motor imagery into clinical practice to mitigate some of the concerns and encourage successful integration. Likewise, Harris and Hebert (2015) highlighted the inconsistencies in motor imagery delivery and reporting, rendering comparisons across populations and studies problematic. To promote discussion on optimum usage, the authors drew on the PETTLEP (Physical, Environment, Task, Timing, Learning, Emotion, and Perspective) approach to motor imagery from sport psychology (Holmes & Collins, 2001). For instance, Harris and Hebert (2015) noted that none of the studies reviewed adapted the pace of motor imagery to individual physical performance abilities of participants. Furthermore, many of the studies did not update imagery tasks as learning occurred, but rather relied on a standardized approach that was identical for all participants. The authors recommended utilization of a standardized checklist based on the PETTLEP approach to promote greater detail, consistency, and transparency with respect to the elements of motor imagery interventions.

The current study seeks to examine the differential effects of dose-matched active training with training plus two different motor imagery conditions. The externally cued condition, TIMP+cMI, utilizes a beat set to the same participant preferred pace used in active training. This external cue is intended to provide an attentional focus and temporal framework to guide motor imagery practice while inducing subconscious beat entrainment. In contrast, the motor imagery condition without external cueing, TIMP+MI, allows the participant to practice motor imagery without any temporal constraint or other form of external input. Based on the above research findings (e.g. Page, Levine & Leonard, 2007; J. Park et al., 2015; J. H. Park, 2015), it is anticipated that there will be greater reductions in impairment and improvements in functional capacity using motor imagery in conjunction with active practice. It is also anticipated that use of an auditory entrainment cue set to the participant's preferred pace will yield superior results to motor imagery without an external cue.

It is worth noting that there are conflicting reports regarding the impact of stroke on motor imagery ability. Sirigu and colleagues (1996) reported deficits in individuals with parietal cortex lesions in representations of hand movements. While nine healthy controls exhibited excellent congruence between maximum speeds for imagining and executing a continuous thumb-finger opposition sequence, times estimated by patients with unilateral parietal lobe lesions (n = 4) were either systematically too fast or slow, or inconsistent. Ability to generate accurate mental representations of affected hand movements was compromised in the patients with parietal lobe damage, as demonstrated by inability to modulate imagery timing estimates in a visuo-manual pointing task involving targets of variable width. The motor imagery representation impairment for the patients with parietal lesions appeared to be selective for distal extremities, as comparable duration estimate discrepancies were not demonstrated for imagined and executed movements of more proximal limb joints. In contrast, internal representations remained robust in a group of four chronically hemiplegic patients with intact premotor and parietal areas - areas which are associated with internal action representation processes (Johnson et al., 2002). A systematic review into the effects of brain lesion site on explicit motor imagery ability found the greatest negative impact associated with parietal lobe damage; however, associations between frontal lobe damage (possibly excluding the posterior region) and basal ganglia lesions (notably the putamen) and motor imagery impairment were also found (McInnes et al., 2016). Furthermore, a study investigating the effects of post-stroke somatosensory deficits on mental chronometry and spatial aspects of motor imagery found that presence of severe somatosensory disturbances affected chronometry but not spatial aspects, with movement execution times typically underestimated (Liepert et al., 2016). Together these findings underscore the need to consider the effects of pathophysiologic constraints on motor imagery ability, which may be compromised in some post-stroke individuals. There were, for example, four participants in the TIMP+cMI condition and two in the TIMP+MI condition who reported MCA infarcts that could have affected the parietal lobe. While administration of the Kinesthetic and Visual Imagery Questionnaire (KVIQ) (Malouin et al., 2007) had been planned to ascertain motor imagery ability, this had to be discontinued after the first participant's initial baseline to reduce the assessment time frame.

To conclude, a number of studies have been undertaken examining the efficacy of motor imagery in neurorehabilitation; however, to date study samples and approaches have been heterogeneous (Santoro et al., 2019), yielding mixed results. Further research investigating specific aspects and doses of motor imagery in conjunction with active practice is required to elucidate its effects.

Chapter 3
Methodology

3 Materials and Methods

The purpose of this study is to investigate the effectiveness of TIMP interventions, with or without motor imagery, in facilitating improvements on motor outcomes for individuals with upper extremity limitations at the chronic post-stroke stage. While previous research has been undertaken using music-based interventions in post-stroke rehabilitation, no studies have been conducted systematically contrasting the use of TIMP with motor imagery conditions. In particular, no studies have incorporated rhythmic auditory entrainment as a sensory-enhanced, cued motor imagery condition. This study attempts to address this gap in the literature. Statistical measures provide an opportunity to distil differential effects between groups and over time of TIMP administered alone, TIMP administered with cued motor imagery (TIMP+cMI), and TIMP administered with motor imagery, but without external sensory enhancement (TIMP+MI).

3.1 Hypotheses

This study investigates if TIMP interventions, facilitated by a qualified Neurologic Music Therapist, will lead to improved motor outcomes for persons with chronic post-stroke upper extremity hemiparesis relative to baseline performances. It seeks to answer the following research questions:

- Does active TIMP alone lead to greater improvements on motor outcomes than when it is combined with motor imagery?
- Does active TIMP combined with cued motor imagery (TIMP+cMI) lead to greater improvements on motor outcomes than TIMP alone or TIMP combined with uncued motor imagery?
- Does active TIMP combined with motor imagery without external cues (TIMP+MI) lead to greater improvements on motor outcomes than TIMP alone or TIMP+cMI?

It furthermore explores the following secondary research questions:

- Does participation in TIMP, with or without motor imagery, lead to improvements in cognition?

- Does participation in TIMP, with or without motor imagery, lead to improvements in affect?

In order to test the research hypotheses statistically, the Null Hypotheses are as follows:

- HO1: There will be no statistically significant differences between baseline and post-test motor scores, as measured by the Fugl-Meyer- Upper Extremity (FM-UE), Wolf Motor Function Test (WMFT), Motor Activity Log (MAL), and Trunk Impairment Scale (TIS).

- HO2: There will be no statistically significant differences between baseline and post-test scores for cognition, as measured by the Digit Span Test and Trail Making Test Part B.

- HO3: There will be no statistically significant differences between baseline and post-test scores for affect, as measured by the General Self-Efficacy Scale (GSE), Multiple Affect Adjective Checklist (MAACL), and Self-Assessment Manikin (SAM).

- HO4: There will be no statistically significant differences between TIMP, TIMP+cMI, or TIMP+MI on pre- and post-test motor, cognitive and affective scores.

3.2 Participants

Thirty-one persons provided informed consent; however, one individual had to withdraw after the initial assessment due to unforeseen scheduling issues. Thirty community-dwelling volunteers (14 females, ages 33-76, mean 55.93) participated in and completed this study (see Figure 1). All had had a unilateral stroke >6 months prior to enrollment (average time post-stroke 66.9 months, 14.41 SD). Inclusion criteria were hemiparesis, with at least minimal volitional movement of the affected limb; age ranging from 30-79 years; adequate language comprehension and neurocognitive function sufficient to understand and follow simple instructions. Participants were excluded if they were currently enrolled in an upper extremity (UE) rehabilitation program or study, had a comorbid neurological disorder (e.g. multiple sclerosis, Parkinson's disease), or had had injections for spasticity < 3 months before training.

This project was approved by the Social Sciences, Humanities and Education Research Ethics Board of the University of Toronto, and by the University Health Network Research Ethics Board. Permission for posting information about the study was also granted by the Mount Sinai Research Ethics Board. Volunteers provided written informed consent, prior to participation, in accordance with the Declaration of Helsinki. The population of the Greater Toronto Region, from which volunteers were recruited, is highly multicultural, and the study sample was reflective of this diversity. Participants were recruited through posters and by word of mouth. The study was also registered at ClinicalTrials.gov (ID# NCT03246217).

Demographic data collected included age, gender, hand dominance, years of education, music background, months since stroke onset, type of stroke, side and location of lesion (see Table 1). A score on the Montreal Cognitive Assessment (MoCA), which provides rapid screening for mild cognitive impairment, was also obtained, although some participants with aphasia were not able to complete portions of the test. Demographic data were similar for the three groups (see Table 1). A Kruskal-Wallis H test was conducted to determine if there were between-group differences in prior music training: TIMP *Mdn* = 1 (no prior training); TIMP + cMI *Mdn* = 1 (no prior training); TIMP + MI *Mdn* = 2 (limited, informal background), but the differences were not statistically significant, $H(2) = 5.10$, $p = .078$.

Figure 1

Consort Diagram for Participant Screening and Enrollment

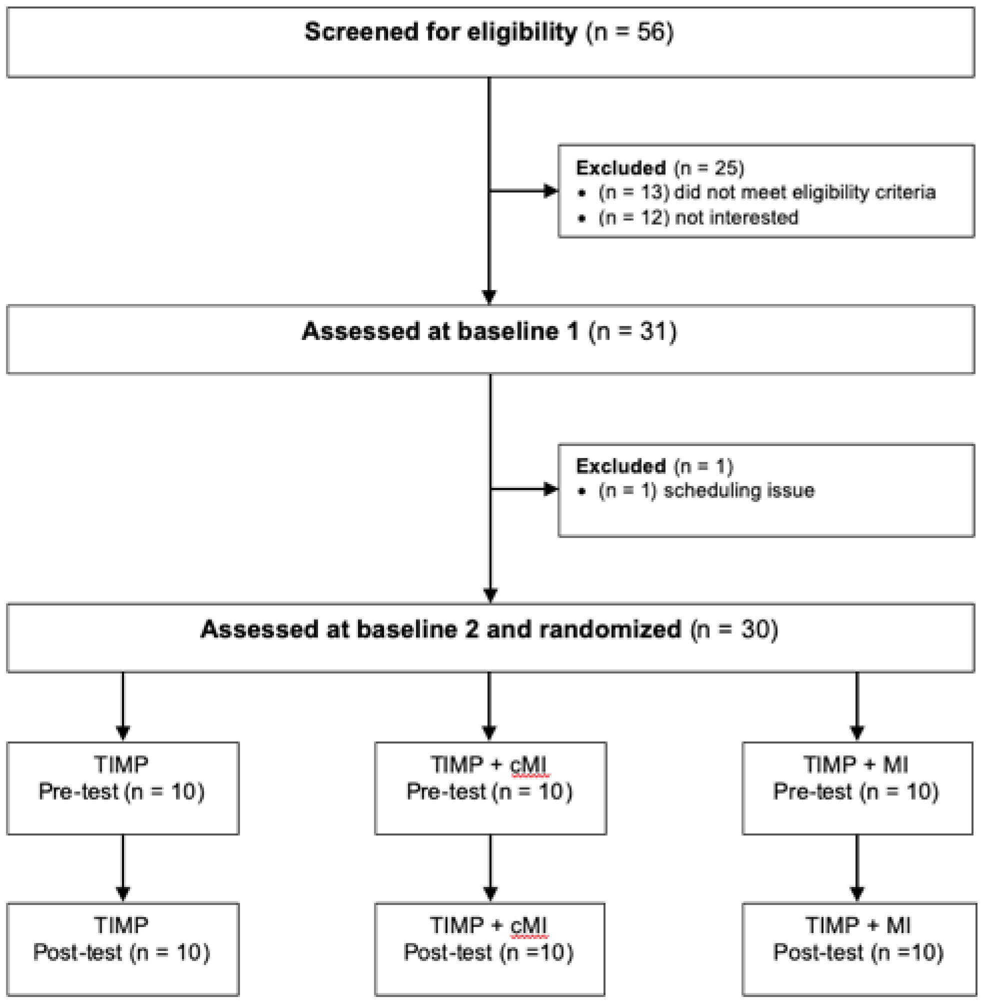


Table 1:

Demographic Characteristics

	Therapeutic Instrumental Music Performance (n=10)	Therapeutic Instrumental Music Performance + cued Motor Imagery (n=10)	Therapeutic Instrumental Music Performance + Motor Imagery (n=10)
Age, y[a] Range = 33 – 76 years	54.7 (10.76)	55.5 (15.01)	57.6 (11.14)
Males/Females	M: 5, F: 5	M: 5, F: 5	M: 6, F: 4
Years of education[a]	15.4 (3.24)	16 (1.83)	17.4 (2.68)
MoCA Score[a]	26.8 (3.74)	26.8 (2.90)	26.8 (3.01)
Music Training[b]	1: 6, 2: 2, 3: 2	1: 6, 2: 2, 3: 2	1: 1, 2: 5, 3: 4
Hand dominance, right/left	RH: 8, LH: 2	RH: 10	RH: 9, LH: 1
Dominant side affected, yes/no	Yes: 3, No: 7	Yes: 3, No, 7	Yes 6, No: 4
Months since stroke onset[a] Range = 9 - 188 months	71.7 (69.13)	50.7 (45.53)	78.3 (67.46)
Type of stroke, ischemic/hemorrhagic	H: 3, I: 7	H: 3, I: 7	H: 5, I: 5
Side of lesion, right/left	R: 7, L: 3	R: 7, L: 3	R: 3, L: 7

Location of lesion[c]	frontal lobe: 3 brainstem: 2 MCA: 4 basal ganglia: 1	frontal lobe: 2 brainstem: 0 MCA: 4 basal ganglia: 2 left thalamus, left occipital, right cerebellum: 1 lacunar stroke in right corona radiata: 1	frontal lobe: 2 brainstem: 4 MCA: 2 basal ganglia: 1 M1, PMC, IFG: 1

Note: MoCA (Montreal Cognitive Assessment); MCA (middle cerebral artery); M1 (primary motor cortex); PMC (premotor cortex); IFG (inferior frontal gyrus)

[a]Data represented as mean (SD). [b]Musical Background: 1 = No prior training; 2 = Limited, informal background; 3 = Some formal training (>1yr). [c]Location of lesion data was supplied by participants from their records/recollections.

3.3 Study Design and Procedures

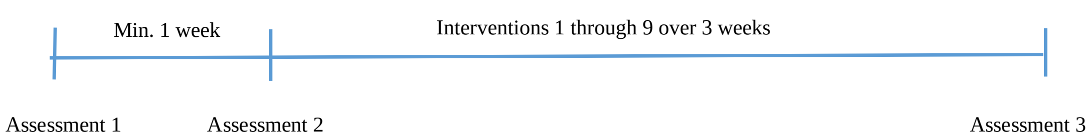
This was a three-armed randomized controlled trial with blinded assessment of outcome. Participants were randomly assigned to one of three intervention groups. Randomization procedures were carried out by a blinded independent allocator drawing a group number from an opaque box. Each group number was written on one of three identically-sized and folded pieces of paper and placed in the opaque box, which the independent allocator shook prior to removing one folded piece of paper with a group number. Participants were randomly allocated using blocked randomization, to ensure equal numbers were assigned to each group. Sessions were conducted over a 20-month period until a target sample size of 10 participants per arm was reached. The blinded independent allocator informed the participant's trainer of the group assignment, and provided the trainer with a unique identifying code for the participant. This identifying code was also provided to the independent assessors, who critically were not provided with group allocation information. The independent assessors and the investigator remained blinded therefore to treatment allocation. The investigator left the premises during training to remain blinded to condition, and was informed by the trainer via text messaging when the training had concluded. Participants were instructed not to disclose to the investigator or the assessor their group assignment or any details pertaining to their training sessions. In addition, at the conclusion of the trial, data entry was carried out by research assistants independent to the study, to ensure the investigator remained blinded to group assignment.

A power analysis indicated the following target sample size: The Fugl-Meyer – Upper Extremity (FM-UE) has a standardized response mean (SRM) of 1.42 (1.19, 1.80, 95% CI), and the Wolf Motor Function Test – Functional Ability Scale (WMFT – FAS) has a SRM of 1.3 (1.03, 1.67, 95% CI) (Hsieh et al., 2009). At a P value of 0.05 and 80% power, eight participants would be required per arm to detect a standardized difference for the FM-UE, and nine for the WMFT – FAS.

All participants were assessed at two baselines, separated by a minimum of one week. Training sessions were scheduled three times a week for three weeks, and were facilitated by a qualified Neurologic Music Therapist. Group 1 participants received nine individual 45-minute sessions of Therapeutic Instrumental Music Performance training (TIMP). Group 2 participants received nine individual 45-minute sessions, which included 30-minutes of TIMP followed by 15-minutes of sensory-enhanced motor imagery. Sensory-enhanced motor imagery involved listening to a metronome cue while engaging in motor imagery (cMI). The metronome cue was set to the participant's preferred pace for each previously practiced activity. Group 3 participants received nine individual sessions, including 30-minutes of TIMP followed by 15-minutes of motor imagery (MI) without sensory enhancement. The first training session followed the second baseline assessment, and the final training session preceded the final assessment. A 15-minute break was scheduled in-between assessment and training if the participant chose to take it.

Participation Timeline:

- Assessment 1 baseline
- Assessment 2 baseline, one week later, followed by intervention one.
- Interventions two through eight, three times a week for three weeks
- Intervention nine, followed by final assessment



TIMP is a standardized Neurologic Music Therapy (NMT) technique (Thaut & Hoemberg, 2014) in which selection of instruments, spatial configurations, and therapeutic sequences for playing are tailored to individual client needs, and designed to facilitate retraining of functional movement patterns, involving both proximal and distal control. The protocol for this study is provided in Appendix B. Examples of movements practiced included shoulder abduction/adduction, elbow flexion/extension, pronation/supination, selective finger dexterity, and upper trunk rotation. Each training session combined different types of exercises, which the trainer selected from the detailed protocol in Appendix C, depending on the impairment level and functional needs of each participant. Trainers adjusted spatial and temporal parameters, as well as number of repetitions, to meet individual evolving requirements. A tap metronome was used to ascertain the participant's preferred tempo, and the beat was subdivided for slow tempi to provide a consistent rhythmic template, allowing the participant to gauge movement trajectories in accordance with the beat and spatial constraints. A variety of instruments, acoustic and electronic, were used in training. Acoustic instruments included several different types of percussion instruments, such as hand tambourine, cylindrical shaker, cabasa, castanet, bongo drum and bodhran, as well as autoharp and ukulele. Electronic digital instruments included a Yamaha CP40 Stage Piano, Yamaha DTX Drums (see Plate 1), and a sonification arm training apparatus (SONATA) – an electronic digital touch tablet with illuminated squares (either small or large) arranged in rows and columns which emitted specific tuned pitches upon contact. The therapist trainer also provided vocal and/or instrumental facilitation for each exercise. Participants assigned to a motor imagery condition spent the last 15 minutes reviewing previously practiced exercises through motor imagery. The trainer modelled each activity, using a metronome set to the participant's preferred tempo for a specific task in the cMI condition, and no external cue in the MI condition. After each demonstration, the participants in TIMP + cMI engaged in MI for that particular exercise while continuing to listen to the metronome cue, while participants in the TIMP + MI condition engaged in MI without external input.

3.4 Assessments

As stroke is a complex condition, a variety of assessment tools are needed to assess and reflect therapeutic outcomes. To that end, measures of cognition and affect were selected to supplement primary motor outcome measures. The Kinesthetic and Visual Imagery Questionnaire (KVIQ) (Malouin et al., 2007), which assesses imagery ability, was initially included, but had to be omitted due to time constraints. The Borg Rating of Perceived Pain was completed by participants at the beginning and end of each training session to obtain a measure of any changes in perceived pain.

3.4.1 Motor Assessment Tools

Arm motor impairment was assessed using the motor performance portion of the Fugl Meyer assessment – upper extremity (FM-UE) (Fugl-Meyer et al., 1975); arm motor function was assessed by means of the Wolf Motor Function Test (WMFT) (Wolf et al., 1989), while perceived arm motor function was assessed with the Motor Activity Log (MAL) (Taub, McCulluch, et al., 2011). As improvements in arm function have been linked to decreases in compensatory trunk recruitment (Michaelsen et al., 2006), upper trunk impairment was also assessed using the upper trunk portion of the Trunk Impairment Scale (TIS) (Verheyden et al., 2004).

Developed specifically for the stroke population, the FM-UE is based on the observations of Twitchell (1951) and Brunnstrom (1966) of sequential stages of motor recovery following a stroke (Crow & Harmeling-van der Wel, 2008). It is the most commonly used post-stroke motor assessment (Santisteban et al., 2016), and has been shown to have strong psychometric properties (Gladstone et al., 2002), including high test-retest reliability (r=0.995-0.996) and interrater reliability (r=0.98-0.995) (Duncan et al., 1983). The upper extremity motor portion covers four areas, assessing shoulder/elbow/forearm, wrist, hand/finger, and coordination/speed, with a maximum score of 66.

The WMFT consists of 17 tasks arranged in order of complexity, and proceeding from proximal to distal joint recruitment (Wolf et al., 2001). Fifteen of these items are evaluated using a functional ability scale ranging from zero to five, with a maximum score of 75. Six of the 15 items are based on joint-segment movements, while the remaining nine require integrative functional movement (Wolf et al., 2001). Two of the tasks are strength-based measures: one evaluates maximum weight that can be lifted to a box with weights placed in a cuff around the forearm, while the other evaluates grip strength using a hand-held dynamometer (Taub, Morris, et al., 2011). The WMFT has been evaluated as having excellent psychometric properties and clinical utility (Morris et al., 2001; Murphy et al., 2015).

The Motor Activity Log (MAL) was selected to provide participants' perspectives on amount and quality of functional upper extremity use. It consists of 30 activities which participants rate on a 6-point scale (0 = unable to use affected extremity for task) according to how much and how well they are able to perform a particular movement. It has also been shown to be a reliable and valid measure of real-world use (Uswatte et al., 2006).

Motor impairment of the trunk was assessed using the upper trunk items of the Trunk Impairment Scale (TIS), with a maximum of 11 points. Analysis of clinimetric parameters support the use of this scale in clinical and research contexts (Verheyden et al., 2004).

3.4.2 Cognitive Assessment Tools

Two cognitive measures, the Trail Making Test - Part B (TMT) (Lezak et al., 2004) and the forward condition of the Digit Span Test (DST) (Wechsler, 1997) were selected. The TMT assesses psychomotor speed, mental flexibility and executive functioning; it consists of numbers and letters in circles which the participant connects as quickly as possible, alternating between numbers and letters in ascending order. Results are reported in seconds, with lower scores indicative of less impairment. It demonstrates good construct validity for assessment of attentional abilities (O'Donnell et al., 1994). The DST measures short-term memory capacity (Egeland, 2015). A score is assigned based on the longest span of numbers the participant is able to repeat from memory in sequential order, with a maximum score of 16.

3.4.3 Affective Assessment Tools

Measures of affect were obtained using the General Self-Efficacy Scale (GSE) (Scholz et al., 2002) and the state form of the Multiple Affect Adjective Check List-Revised (MAACL) (Lubin & Zuckerman, 1999). The GSE is a 10-item, self-report measure based on a scale ranging from 10-40, with higher scores indicating a greater sense of self-efficacy. The MAACL is comprised of seven scales, including two composite scales. Separate scales for anxiety, depression, and hostility are combined into one composite scale for negative affect, dysphoria. The positive affect scale (PA) (representing calm, happy affect) and the sensation seeking (SS) scale (representing positive affect that is more extraverted, aroused) are also combined into a single composite positive affect scale, PASS. In addition, the Self-Assessment Mannikin (SAM), a pictorial assessment tool, was completed by participants prior to and at the conclusion of each intervention session, to obtain a measure of affective response to training. Each of the three dimensions - valence, arousal, and dominance – is depicted with five pictures; a five-point rating scale was used to calculate the results for each dimension. The tool can be completed quickly, is non-verbal, and correlates well with ratings obtained from lengthier, verbal scales of affective responding (Bradley & Lang, 1994).

3.5 Data Analysis:

The original plan was to enter the data into a mixed ANOVA, with group assignment as between-subjects factor and pre versus post time-points as within-subjects factor. However, as the data did not meet assumptions required for parametric analyses, non-parametric equivalents were used instead. Differences between pre-tests 1 and 2, as well as differences between pre-test 2 and post-test were assessed using the Wilcoxon signed-rank test or the Sign test. The Kruskal-Wallis H Test was used to assess between-group differences. In addition, correlation analyses were run using Kendall's tau-b to ascertain possible associations between and within primary and secondary outcome measures, as well as the direction of any associations. These analyses were run using pooled group data to compare change scores. The 0.05 level of probability was established as statistically significant. All data were analyzed using Statistical Package for Social Sciences (SPSS) software, version 26.

Chapter 4
Results

4 Results of Motor, Cognitive, and Affective Measures

Non-parametric tests were used in all analyses. Significance was assessed at the .05* level. Pooled baseline measures for each of the assessments, as shown in Table 2, yielded non-significant results.

Table 2

Baseline Measures with Pooled Group of 30 Participants

	Pre-test 1	**Pre-test 2**	***P* value**
Fugl-Meyer Upper Extremity (FM-UE)	31.80 (14.67)	31.73 (14.76)	.727
Wolf Motor Function Test – Functional Ability Scale (WMFT-FAS)	33.07 (16.96)	32.97 (15.58)	.634
Wolf Motor Function Test – Weight	4.30 (4.74)	4.23 (4.57)	.479
Wolf Motor Function Test – Grip Strength	8.2 (9.24)	8.78 (9.85)	.328
Trunk Impairment Scale (TIS)[a]	9.70 (1.44)	10.13 (1.07)	.061
Digit Span Test (DST)	9.9 (3.06)	10.2 (3.43)	.402
Trail Making Test (TMT) Part B[a]	109.87 (48.86)	99.03 (48.22)	.066
General Self-Efficacy (GSE)	32.17 (4.46)	32.70 (4.76)	.193
Multiple Affect Adjective Checklist (MAACL) - Anxiety (A)	1.03 (2.08)	1.033 (1.45)	.888
MAACL Depression (D)	1.33 (2.15)	.90 (1.54)	.456
MAACL Hostility (H)	.53 (1.20)	.59 (1.05)	.662
MAACL Dysphoria (A, D, H)	2.90 (4.71)	2.50 (3.01)	.920
MAACL Positive Affect (PA)	7.60 (6.51)	8.47 (6.47)	.252
MAACL Sensation Seeking (SS)	5.067 (1.64)	5.20 (1.85)	.846
MAACL PASS (PA and SS)	12.67 (7.50)	13.67 (7.78)	.154

Note: Wilcoxon signed-rank test, Means (Standard Deviation), 2-sided asymptotic probability.

[a]Sign test

4.1 Fugl-Meyer Assessment – Upper Extremity

The Fugl-Meyer assessment - Upper Extremity (FM-UE) was administered to obtain a measure of upper extremity impairment. Data were analyzed using a Wilcoxon signed rank test. Medians for pooled group pre-test 1and 2 were identical (29.50). The pre-test 2, post-test means (SD) and probability values for each group are reported in Table 3. There was a statistically significant difference between pre-test 2 and post-test for each group: TIMP pre-test 2 (*Mdn* = 29.50), post-test (*Mdn* = 35.00), difference (*Mdn* = 8.50), $z = 2.81$, $p = .005$*, $r = .63$ (ten participants had a positive difference); TIMP + cMI pre-test 2 (*Mdn* = 28.00), post-test (*Mdn* = 31.00), difference (*Mdn* = 4.00), $z = 2.68$, $p = .007$*, $r = .63$ (nine participants had a positive change, one remained the same); TIMP + MI pre-test 2 (*Mdn* = 37.50), post-test (*Mdn* = 46.00), difference (*Mdn* = 5.00), $z = 2.71$, $p = .007$*, $r = .61$ (nine participants had a positive difference, one participant with a ceiling effect had a negative change of one point). Figure 2 shows group medians, individual data points, and difference scores. Figure 3 shows difference scores for subsections.

To determine if there were between-group differences, the Kruskal-Wallis H test was run based on percent change between pre-test 2 and post-test. Distributions of percent change scores were not similar for all groups, as assessed by visual inspection of a boxplot (Figure 2). The mean ranks of percent change scores were statistically significantly different between intervention groups, $H(2) = 6.731$, $p = .035$*. Pairwise comparisons were performed with a Bonferroni correction for multiple comparisons. Post hoc analyses revealed statistically larger differences in percent change scores between TIMP (mean rank = 21.05) and TIMP + cMI (mean rank = 11.00), $p = .032$*, $r = .57$. There was no statistically significant between-group difference involving TIMP + MI (mean rank = 14.45).

Table 3.

Fugl-Meyer – Upper Extremity (FM-UE) Pre-test 2 – Post-test by Group

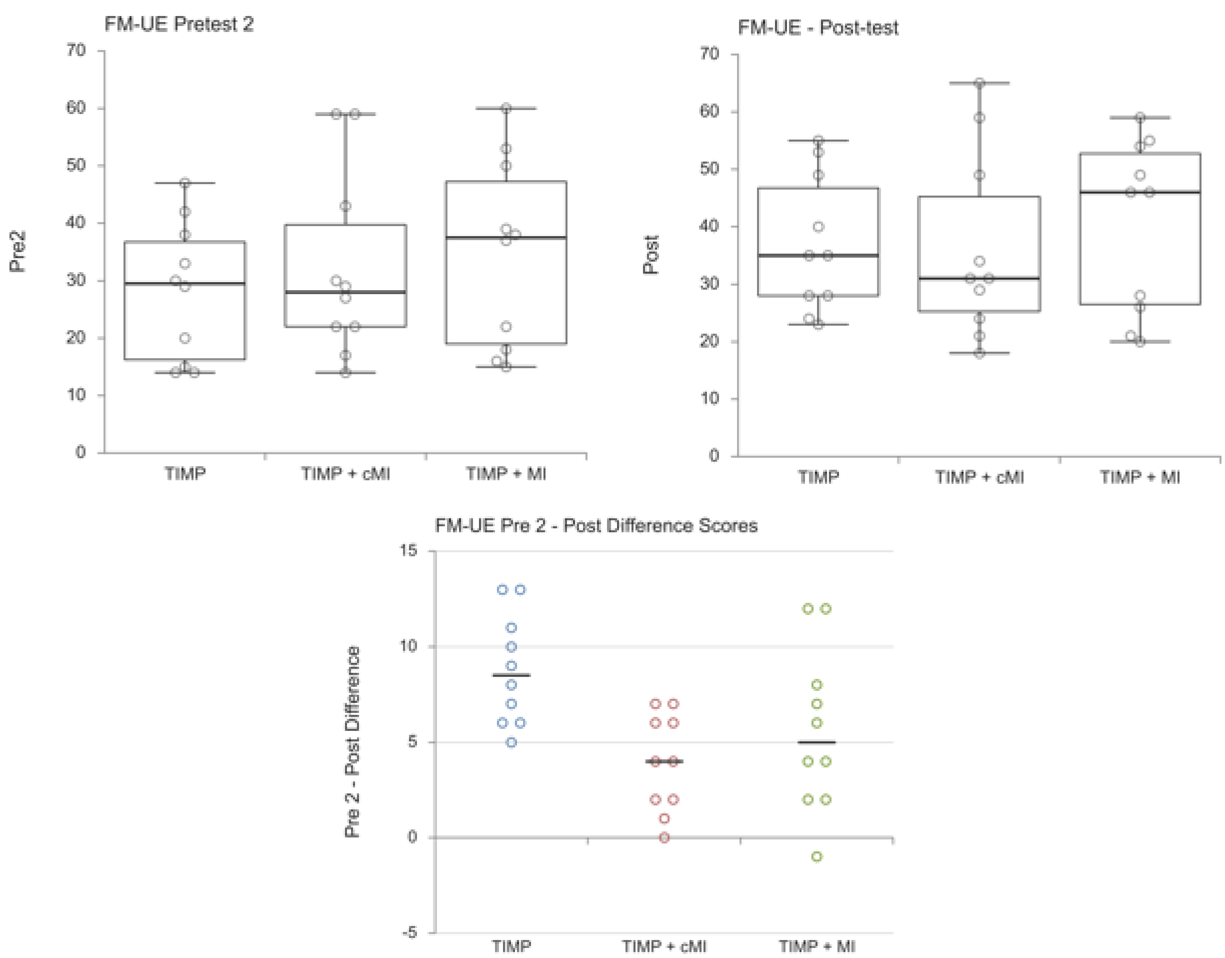
	TIMP	TIMP + cMI	TIMP + MI
Pre-test 2	28.20 (12.07)	32.20 (16.21)	34.80 (16.40)
Post-test	37.00 (11.87)	36.10 (16.11)	40.40 (15.04)
Probability (2-sided asymptotic)	.005**	.007**	.007**

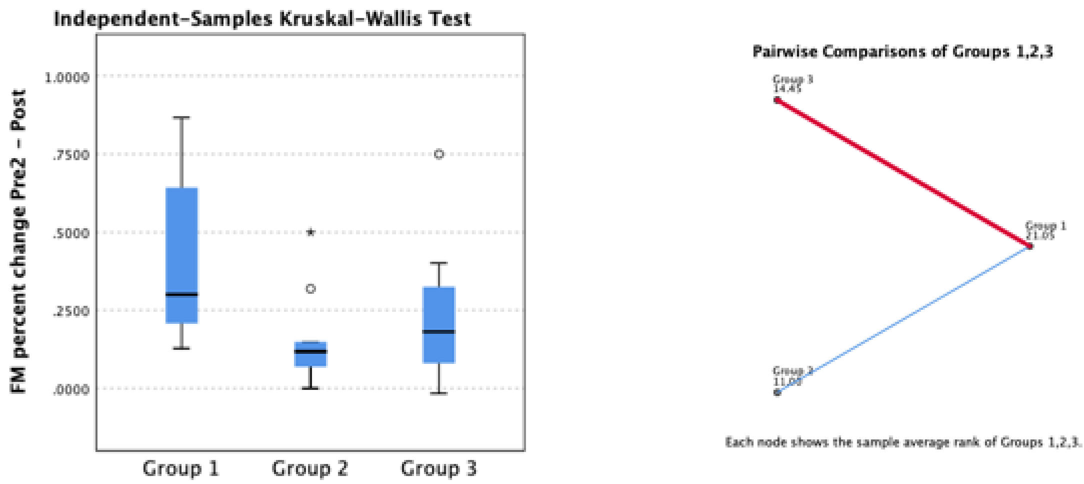
Note: Means, Standard Deviations (SD)

***p* < .01.

Figure 2.

Fugl-Meyer Upper Extremity (FM-UE) Individual Data Points and Percent Changes

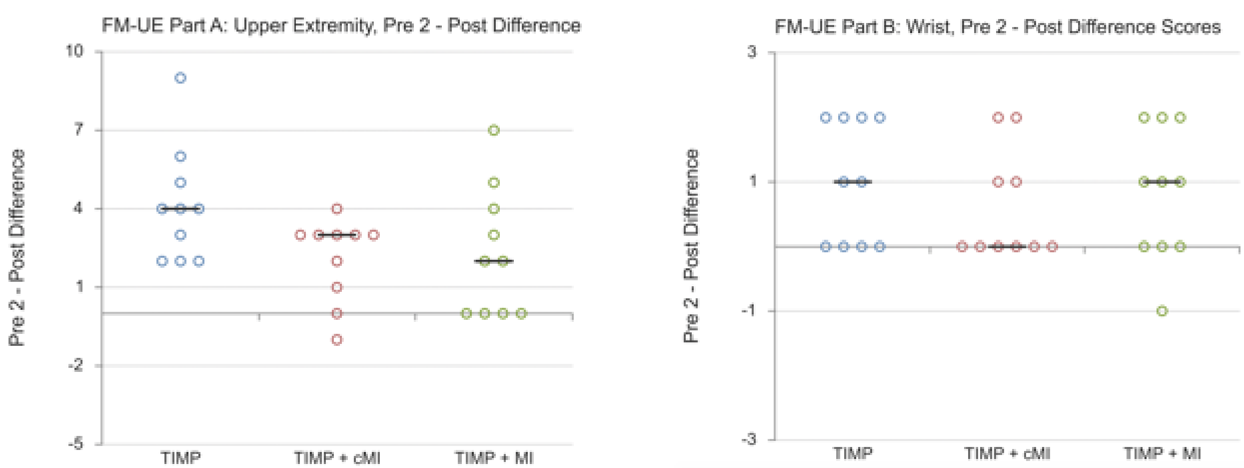


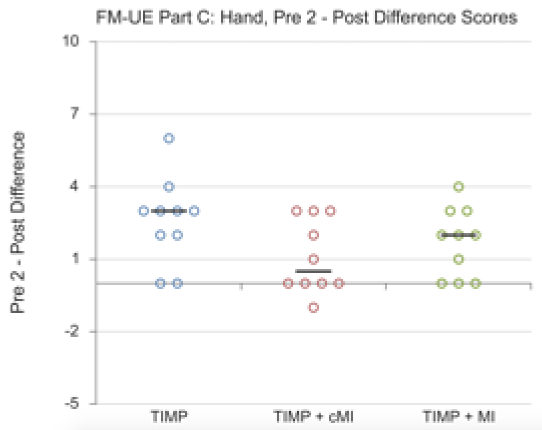


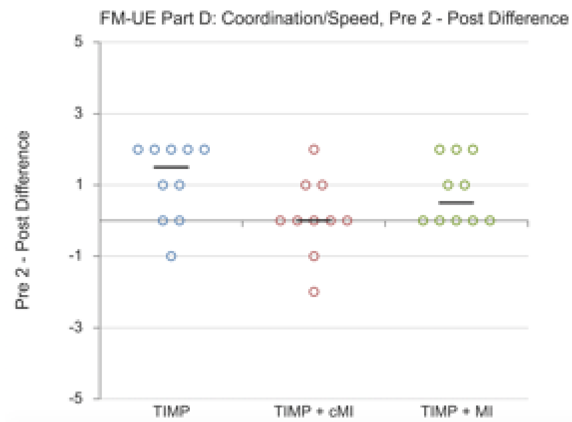
Note: Medians (top); pre-test 2–post-test difference scores (middle); percent change comparisons for Group 1 (TIMP), Group 2 (TIMP + cMI), and Group 3 (TIMP + MI) (bottom).

Figure 3.

Difference Scores for Fugl-Meyer Upper Extremity (FM-UE) Sections A - D







4.2 Wolf Motor Function Test

Upper extremity functional ability was assessed using the Wolf Motor Function Test – Functional Ability Scale (WMFT-FAS). Data were analyzed using a Wilcoxon signed rank test. The median for pooled pre-test 1 was 27.50, and for pooled pre-test 2 it was 28.00. Pre-test 2, post-test means (SD) and probability values are reported in Table 4a. There was a statistically significant difference between pre-test 2 and post-test for each group: TIMP pre-test 2 (*Mdn* = 22.50), post-test (*Mdn* = 23.50), difference (*Mdn* = 2.50), $z = 2.26$, $p = .024$*, $r = .53$ (eight positive differences, one negative difference, and one unchanged); TIMP + cMI pre-test 2 (*Mdn* = 28.00), post-test (*Mdn* = 33.00), difference (*Mdn* = 4.50), $z = 2.66$, $p = .008$*, $r = .60$ (nine positive differences and one negative); TIMP + MI pre-test 2 (*Mdn* = 35.00), post-test (*Mdn* = 42.50), difference (*Mdn* = 6.50), $z = 2.67$, $p = .008$*, $r = .63$ (nine positive differences, one unchanged). Figure 4a shows group medians, individual data points, and difference scores. A Kruskal-Wallis H test was run to assess independent group differences based on percent change between pre-test 2 and post-test. Distributions of percent change scores did not significantly differ, as assessed by visual inspection of a boxplot (Figure 4a). Median percent change scores were not statistically significantly different between groups, $H(2) = 1.27$, $p = .531$.

Table 4a

Wolf Motor Function Test – Functional Ability Scale (WMFT – FAS) Pre-test 2 – Post-test

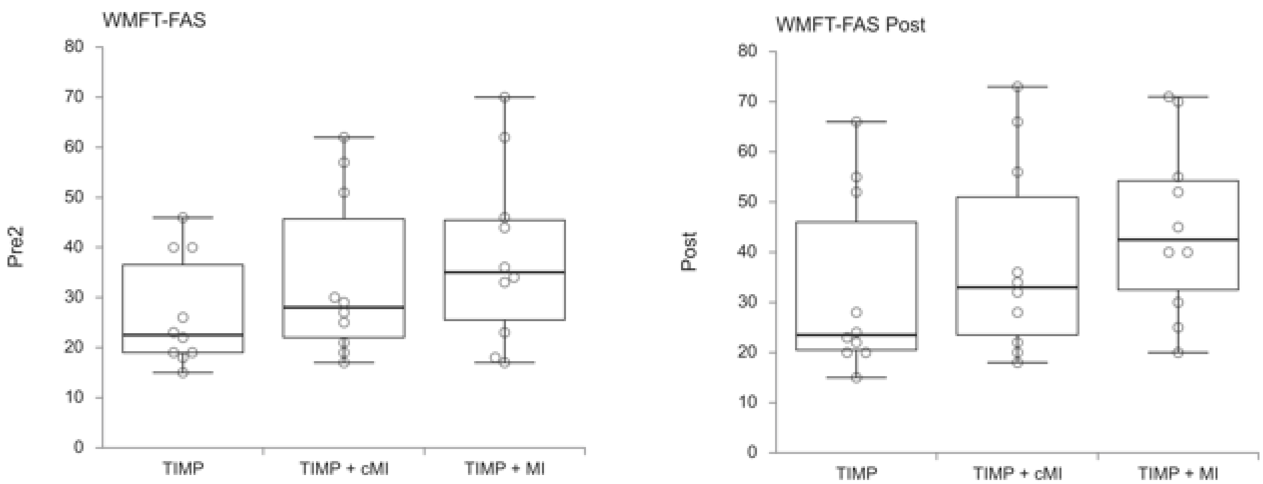
	TIMP	TIMP + cMI	TIMP + MI
Pre-test 2	26.8 (11.02)	33.8 (16.52)	38.3 (17.67)
Post-test	32.5 (18.01)	38.5 (19.63)	44.8 (17.48)
Probability (2-sided asymptotic)	.024*	.008**	.008**

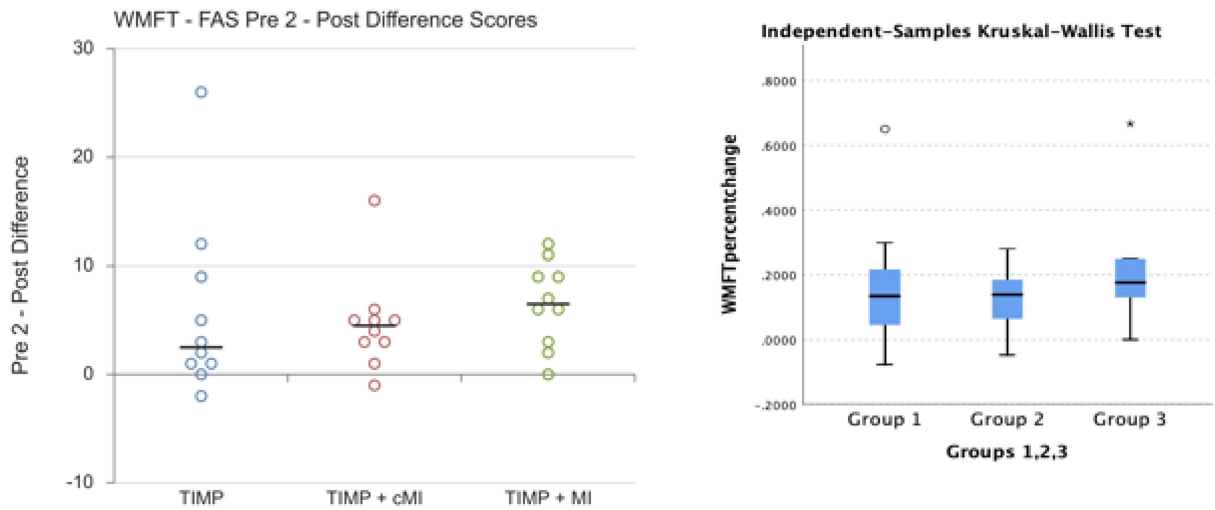
Note: Means, Standard Deviations (SD)

* $p < .05$. ** $p < .01$.

Figure 4a

Wolf Motor Function Test – Functional Ability Scale (WMFT – FAS) Pre-test 2, Post-test





Note: Individual data points, medians (top row); difference scores (bottom left); percent change comparisons (bottom right)

The Wilcoxon signed rank test yielded non-significant results between pre-test 2 and post-test for the WMFT – Weight and Grip Strength. WMFT - Weight scores were based on the maximum weight the participant was able to lift to a box with weights placed in a cuff around the forearm. Results were as follows: TIMP pre-test 2 (*Mdn* =.00), post-test (*Mdn* =.00), z = .45, p = .655; TIMP + cMI pre-test 2 (*Mdn* = 3.00), post-test (*Mdn* = 4.00), z = 1.34, p = .180; TIMP + MI pre-test 2 (*Mdn* = 6.00.), post-test (*Mdn* = 6.00), z = .38, p = .705. Grip Strength was based on the mean of three trials using a hand-held dynamometer. Results were as follows: TIMP pre-test 2 (*Mdn* = 4.15), post-test (*Mdn* = 4.74), z = .28, p = .779; TIMP + cMI pre-test 2 (*Mdn* = 4.90), post-test (*Mdn* = 4.05), z = .77, p = .441; TIMP + MI pre-test 2 (*Mdn* = 10.30), post-test (*Mdn* = 10.50), z = .53, p = .594. Figure 4b shows difference scores with median differences for WMFT – Weight and Grip Strength. Percent change could not be calculated for weight or grip strength as a number of participants had scores of zero. A Kruskal-Wallis H test indicated a non-significant difference for weight based on post-test scores, $H(2)$ = 3.33, p = .189. There was a significant difference across groups for grip strength, $H(2)$ = 6.55, p = .038. Pairwise comparisons were performed with Bonferroni correction for multiple comparisons. Post hoc analysis revealed statistically significant differences in post-test mean rank scores between TIMP (11.50) and TIMP + MI (21.15), $p = .014$, $r = .55$. There was no statistically significant between-group difference involving TIMP + cMI (mean rank = 13.85), although the difference between TIMP + cMI and TIMP + MI approached significance, $p = .063$.

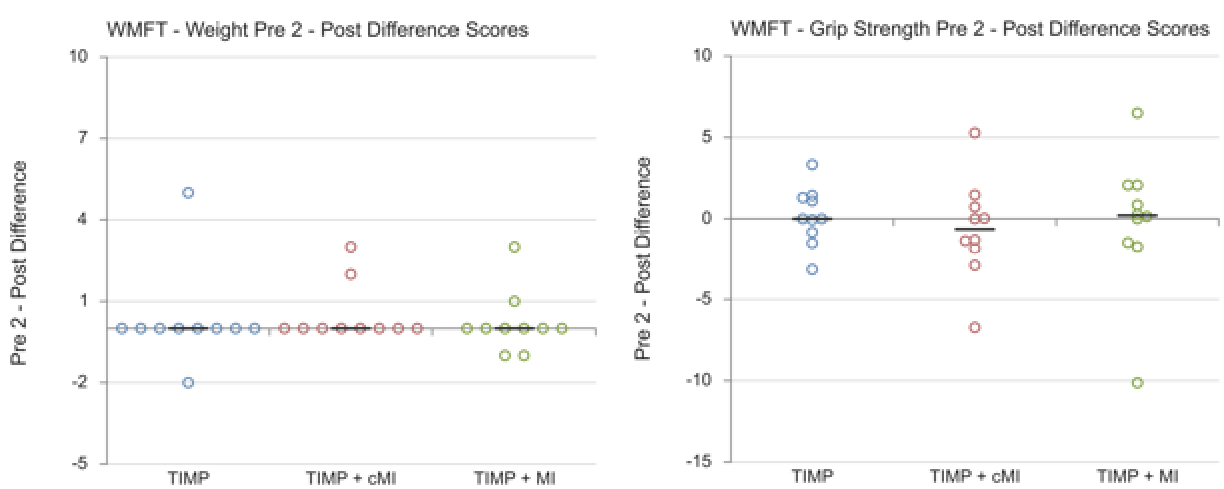
Table 4b

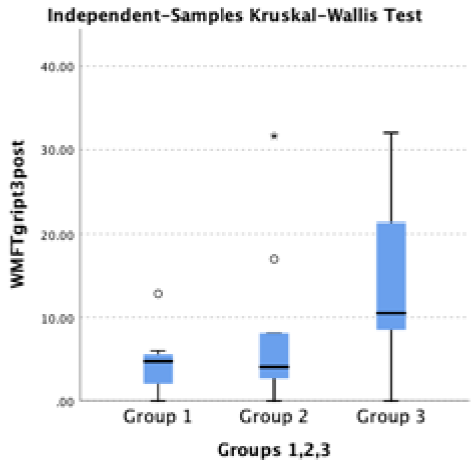
Wolf Motor Function Test Weight and Grip Strength Pre-test 2–Post-test by Group, Means (SD)

	TIMP	TIMP + cMI	TIMP + MI
Pre-test 2 - Weight	2.10 (3.32)	4.80 (5.57)	5.80 (4.13)
Post-test - Weight	2.40 (4.06)	5.30 (5.68)	6.00 (4.32)
Probability (2-sided asymptotic) -Weight	.655	.180	.705
Pre-test 2 - Grip	4.22 (3.94)	8.44 (8.80)	13.66 (13.05)
Post-test-Grip	4.38 (3.73)	7.78 (9.97)	13.52 (9.73)
Probability (2-sided asymptotic) - Grip	.779	.441	.594

Figure 4b

Wolf Motor Function Test Weight and Grip Strength Difference Scores





Note: Difference scores with median differences (top row); post-test grip strength across groups (bottom row).

4.3 Motor Activity Log

The Motor Activity Log (MAL) was completed by participants on two occasions - prior to the first intervention, and again prior to the final intervention - to obtain a subjective measure of participants' use of the affected extremity in activities of daily living. The Amount Scale measures how much the UE is used for an activity, and the How Well scale assesses the quality of this movement. This scale was completed by participants on their own; completion was at times inconsistent in terms of number of items scored. Results for the Amount Scale were computed based on the total number of items each participant completed. There was insufficient data to compute a score for the How Well scale. Based on data for the Amount Scale, there was a statistically significant difference in perceived amount of use for participants in TIMP, $z = 2.17$, $p = .030$*, $r = 0.54$, as well as for participants in TIMP + MI, $z = 2.68$, $p = .007$*, $r = 0.63$, and a non-significant difference for participants in TIMP + cMI, $z = .42$, $p = .677$, $r = 0.10$. For participants in TIMP, there was a median increase of .20 from the median of the first time point (.25) to post intervention (.40). Seven participants had a positive change in their scores, two remained the same, and one had a negative change. Similarly, for participants in TIMP + MI, there was a median increase of .20 from the first median (.85) to the final median (1.00). Nine participants reported a positive difference, and one person reported no change. For participants in

TIMP + cMI, there was a median difference of .04 from the first time point (.25) to post intervention (.20). Five participants in Group 2 reported a positive difference, four reported a negative difference, and one person reported no change. Figure 5 shows independent data points, medians, and difference scores. An independent-samples Kruskal-Wallis test was run to determine if there were differences between post-tests for the three groups. There were no statistically significant differences, $H(2) = 2.45$, $p = .294$.

Table 5

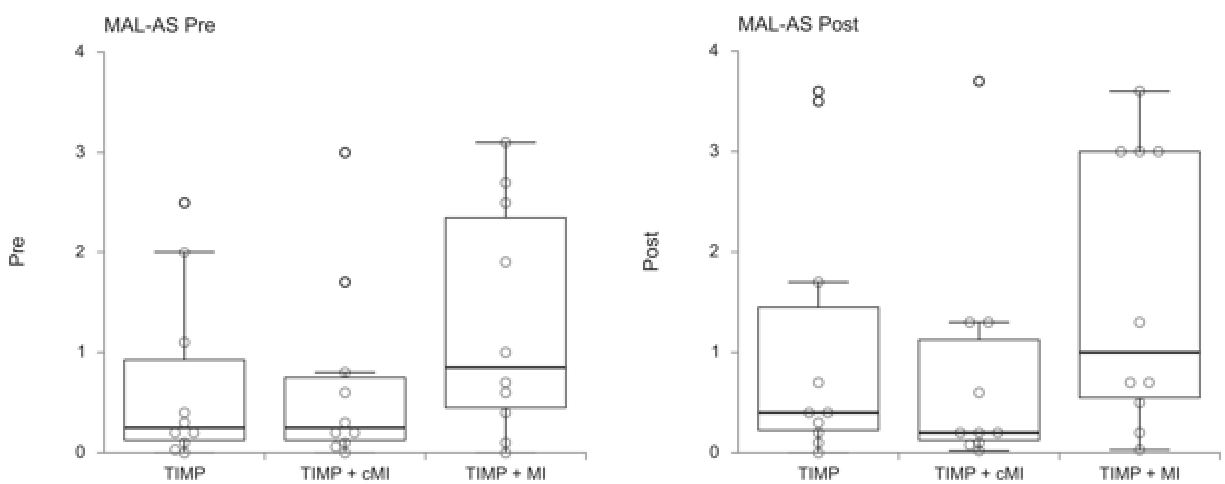
Motor Activity Log - Amount Scale (MAL-AS) Pre-test 2 – Post-test by Group, Means (SD)

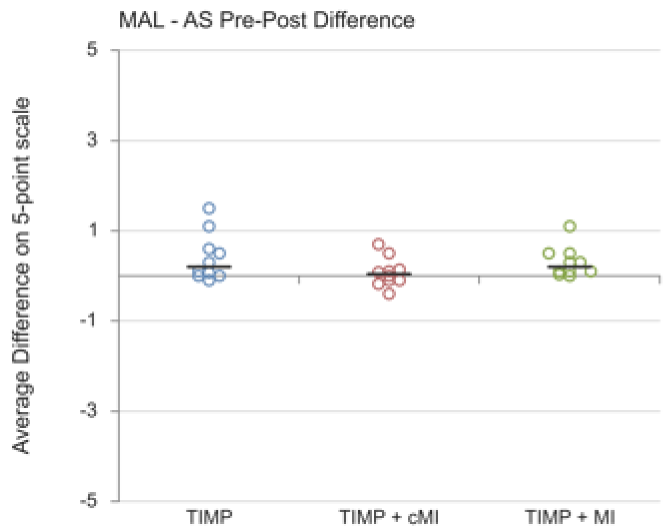
	TIMP	TIMP + cMI	TIMP + MI
Pre-test	.683 (.89)	.696 (.96)	1.300 (1.15)
Post-test	1.090 (1.38)	.770 (1.14)	1.603 (1.38)
Probability (2-sided asymptotic)	.030*	.677	.007**

* $p < .05$. ** $p < .01$.

Figure 5

Motor Activity Log – Amount Scale (MAL-AS) Pre-test 2, Post-test





Note: Individual data points, medians, and difference scores.

4.4 Trunk Impairment Scale

The upper trunk portion of the Trunk Impairment Scale (TIS) provided a measure of participants' upper trunk control. The distribution of differences was not symmetrically shaped, and the related-samples sign test was used instead to determine differences between pooled pre-tests. There was no statistically significant change between pooled pr-etest 1 median (10.00) and the pooled pre-test 2 median at ceiling (11.00), $z = 1.87$, $p = .057$, $r = 0.35$. There was also no significant difference from pre-test 2 to post-test on the related-samples sign test for any of the three groups (Table 5): TIMP pre-test (*Mdn* = 11.00), post-test (*Mdn* = 11.00), $z = 1.16$, $p = .250$; TIMP + cMI pre-test (*Mdn* = 11.00), post-test (*Mdn* = 11.00), $z = .00$, $p = 1.00$; TIMP + MI pre-test 2 (*Mdn* = 9.50), post-test (*Mdn* = 10.50), $z = .50$, $p = .625$. Figure 6 shows medians for each group, with a maximum score of 11. There was no statistically significant difference between groups as assessed by an independent-samples Kruskal-Wallis test, $H(2) = 1.19$, $p = .551$.

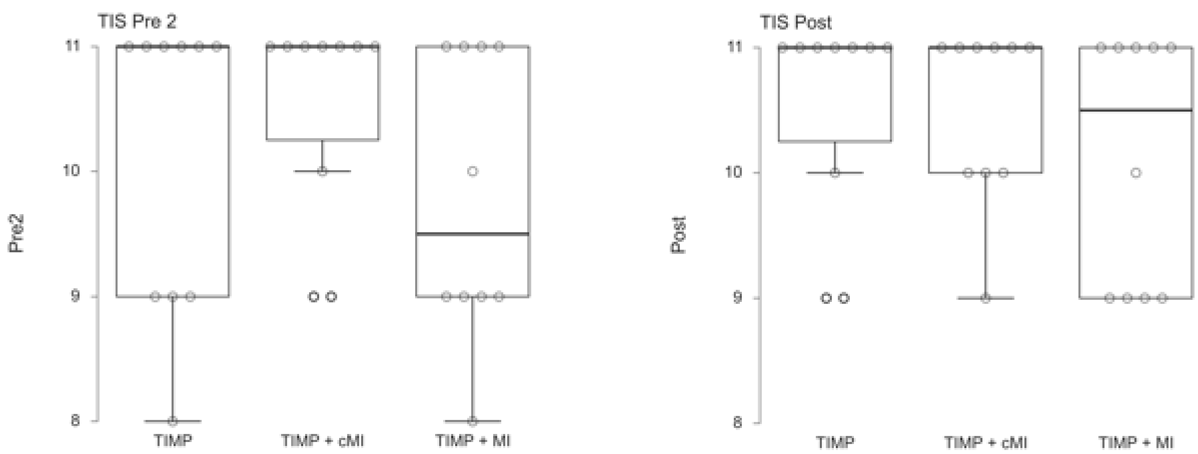
Table 6

Trunk Impairment Scale (TIS) Pre-test 2 – Post-test by Group, Means (SD)

	TIMP	TIMP + cMI	TIMP + MI
Pre-test 2	10.10 (1.20)	10.50 (.85)	9.80 (1.14)
Post-test	10.50 (.85)	10.50 (.71)	10.10 (.99)
Probability (2-sided asymptotic)	.250	1.000	.625

Figure 6

Trunk Impairment Scale (TIS) Pre-test 2, Post-test with Medians



4.5 Digit Span Test

The Digit Span Test (DST) was administered to understand the effects of interventions on Working Memory (WM). A related-samples Wilcoxon signed-rank test found no significant difference between pooled group pre-test 1 (*Mdn* = 10.00), and pooled group pre-test 2 (*Mdn* = 10.00), *z* = .84, *p* = .402. There was also no significant difference between pre-test 2 and post-test for any of the three groups: TIMP pre-test 2 (*Mdn* = 10.00), post-test (*Mdn* = 12.00), *z* = .74, *p* = .459; TIMP + cMI pre-test 2 (*Mdn* = 10.00), post-test (*Mdn* = 10.50), *z* = .17, *p* = .865; TIMP + MI pre-test 2 (*Mdn* = 11.50), post-test (*Mdn* = 10.00), *z* = .43, *p* = .669. Figure 7 displays individual scores with medians. A Kruskal-Wallis H test of median post-test scores across groups yielded a non-significant difference, $H(2) = .83$, $p = .662$.

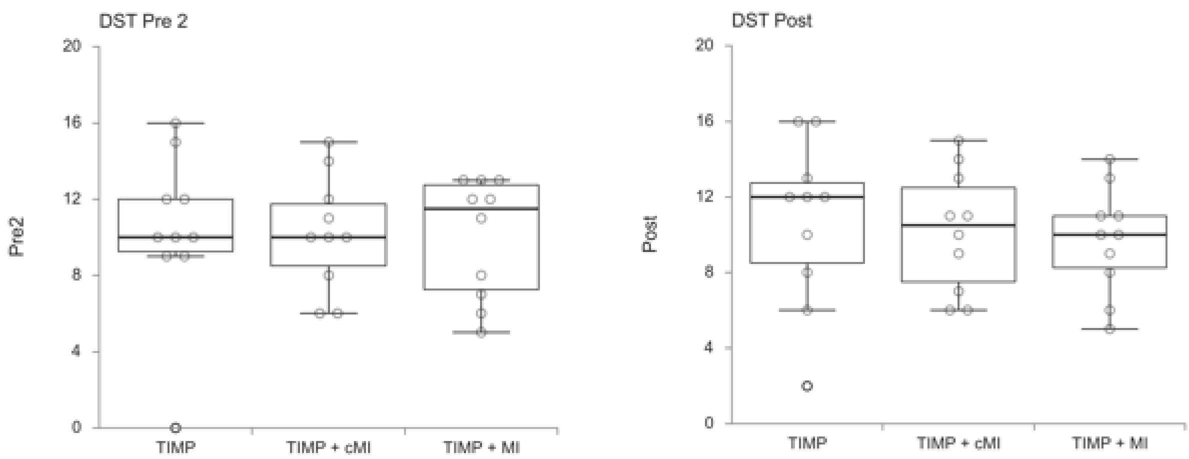
Table 7

Digit Span Test (DST) Pre-test 2 – Post-test by Group, Means (SD)

	TIMP	**TIMP + cMI**	**TIMP + MI**
Pre-test 2	10.30 (4.35)	10.20 (3.01)	10.00 (3.16)
Post-test	10.70 (4.37)	10.20 (3.23)	9.70 (2.83)
Probability (2-sided asymptotic)	.459	.865	.669

Figure 7

Digit Span Test (DST) Pre-test 2 – Post-test with Medians



4.6 Trail Making Test

The Trail Making Test - Part B (TMT) was administered to assess effects of interventions on Executive Functioning (EF). The distribution of differences was not symmetrically shaped, and the related-samples sign test was used instead for analyses. There was a non-significant difference between pooled group medians for pre-test 1 (94.50) and pre-test 2 (84.50), median difference (3.00), $z = 1.84$, $p = .064$. TIMP participants had no statistically significant decrease in time taken to complete the TMT from pre-test 2 (*Mdn* = 84.50) to post-test (*Mdn* = 77.50), median difference (.50), $z = .00$, $p = 1.00$. Five participants took less time, four took longer, and one participant took the same amount of time. Similarly, there was a non-significant decrease in time taken for participants in TIMP + cMI: pre-test 2 (*Mdn* = 88.50), post-test (*Mdn* = 72.00), median difference (3.00), $z = 1.51$, $p = .125$. Six participants took less time, three stayed the same, and one took longer. However, there was a statistically significant decrease in time for TIMP + MI participants from pre-test 2 (*Mdn* = 87.50) to post-test (*Mdn* = 71.00), median difference (11.00) $z = 2.00$, $p = .039$*, $r = .47$. Eight participants in this group completed the test in less time, one took longer, and one stayed the same. Figure 8 displays medians and pre-test 2 – post-test differences. There was no statistically significant difference between the three groups as assessed by an independent-samples Kruskal-Wallis test of percent change between pre-test 2 and post-test, $H(2) = 2.621$, $p = .270$.

Table 8

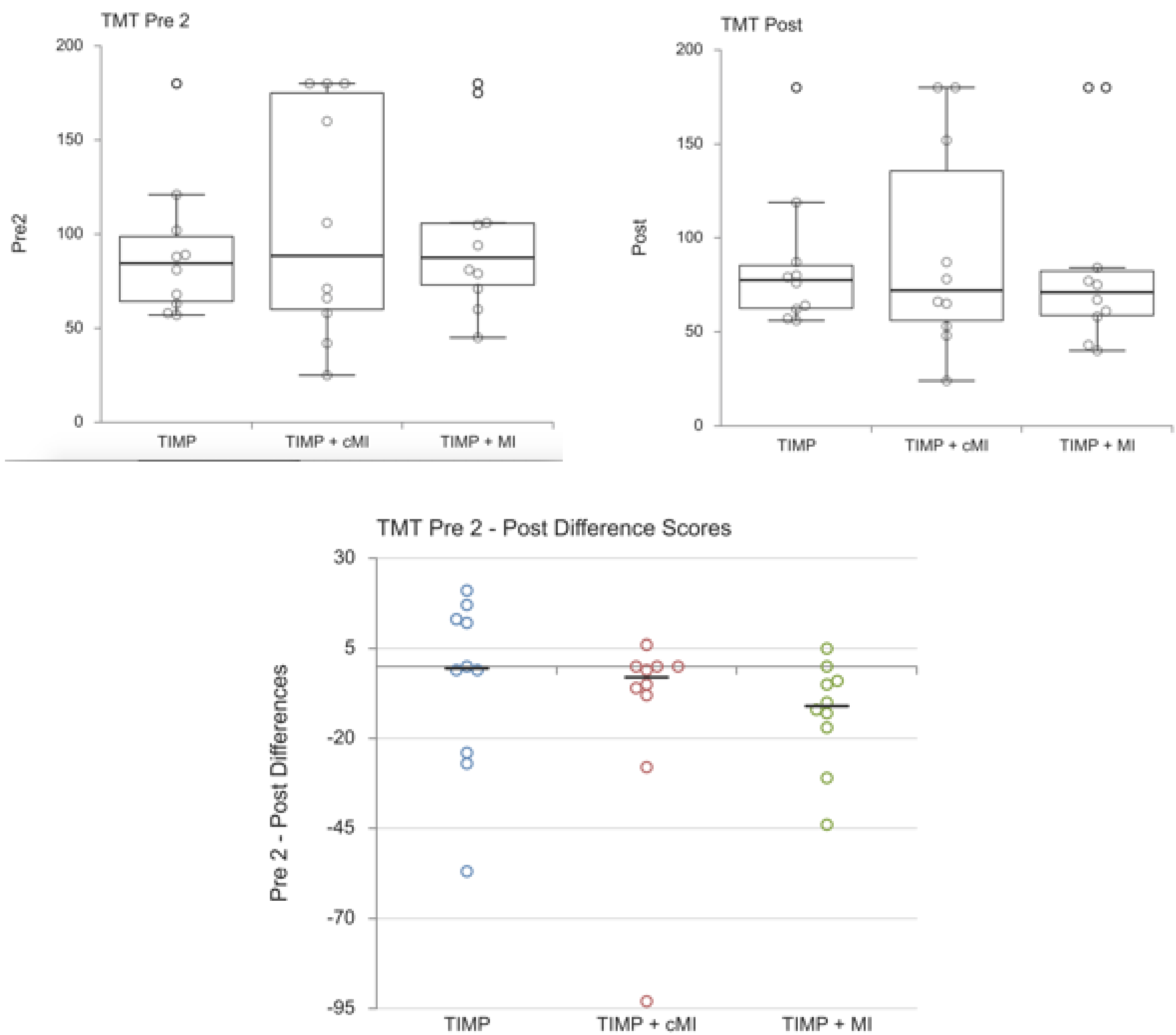
Trail Making Test (TMT) - Part B Pre-test 2 – Post-test by Group, Means (SD)

	TIMP	**TIMP + cMI**	**TIMP + MI**
Pre-test 2	90.70 (37.43)	106.80 (62.47)	99.60 (45.20)
Post-test	86.00 (37.88)	93.30 (56.55)	86.50 (51.22)
Probability (2-sided asymptotic)	1.000	.125	.039*

* $p < .05$.

Figure 8

Trail Making Test (TMT) Part B - Pre-test 2, Post-test



Note: Individual data points, medians, difference scores

4.7 General Self-Efficacy Scale

The General Self-Efficacy scale (GSE) provided a measure of participants' perceived sense of self-efficacy. Results of a Wilcoxon signed-rank test indicated a non-significant difference between medians for pooled group pre-tests 1 (*Mdn* = 32.00) and 2 (*Mdn* = 34.00), $z = 1.30$, $p =$

.193. There was a nonsignificant difference in medians from pre-test 2 to post-test for each of the groups: TIMP pre-test 2 (34.00), post-test (34.00), median difference (.50), z = 1.28, p = .202; TIMP + cMI pre-test 2 (35.00), post-test (35.00), median difference (1.50), z = 1.65, p = .098; TIMP + MI pre-test 2 ((30.00), post-test (30.50), median difference (0), z =.00, p = 1.00. Figure 9 displays individual data with medians. There was no statistically significant difference between the three groups as assessed by an independent-samples Kruskal-Wallis test of percent change between pre-test 2 and post-test, $H(2)$ = 1.244, p = .537.

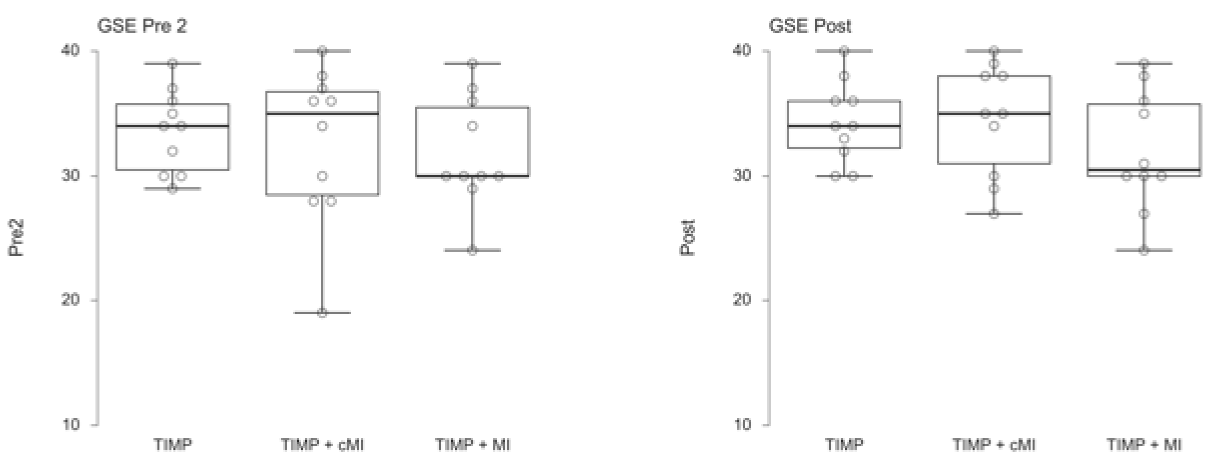
Table 9

General Self-Efficacy (GSE) Scale Pre-test 2 – Post-test by Group, Means (SD)

	TIMP	**TIMP + cMI**	**TIMP + MI**
Pre-test 2	33.60 (3.31)	32.60 (6.35)	31.90 (4.51)
Post-test	34.30 (3.27)	34.50 (4.50)	32.00 (4.85)
Probability (2-sided asymptotic)	.202	.098	1.000

Figure 9

General Self-Efficacy Scale (GSE) Pre-test 2, Post-test with Medians



4.8 Multiple Affect Adjective Checklist

The state Multiple Affect Adjective Checklist – Revised (MAACL-R) was administered to assess current affective state at three timepoints.

4.8.1 Positive Affect

For the Positive Affect and Sensation Seeking (PASS) composite score, there was a non-significant difference between pooled group pre-test 1 (*Mdn* = 12.00) and pre-test 2 (*Mdn* = 12.50), $z = 1.43$, $p = .154$. TIMP participants had a non-significant increase from pre-test 2 (*Mdn* = 8.50) to post-test (*Mdn* = 12.00), $z = 1.62$, $p = .105$. Six participants reported a positive change, two participants remained the same, and two had a negative change. There was a statistically significant change for TIMP + cMI participants from pre-test 2 (*Mdn* = 16.00) to post-test (*Mdn* = 24.50), $z = 2.00$, $p = .045$*, $r = 0.45$, with seven participants scoring a positive difference, and three a negative difference. There was a non-significant change from pre-test 2 (*Mdn* =13.50) to post-test (*Mdn* = 9.50) for participants in TIMP + MI, $z = 1.13$, $p = .261$, with four reporting a positive difference and six a negative difference. Figure 10a indicates individual data points, medians, and difference scores. A Kruskal-Wallis test found a significant between-group difference at post-test, $H(2) = 6.44$, $p = .040$*. Pairwise comparisons were performed with a Bonferroni correction for multiple comparisons. Adjusted *p*-values are presented. Post hoc analysis revealed statistically significant differences in mean rank scores between TIMP + cMI (20.80) and TIMP + MI (10.90), $p = .035$*. There were no statistically significant differences involving TIMP (mean rank = 14.80).

Table 10a

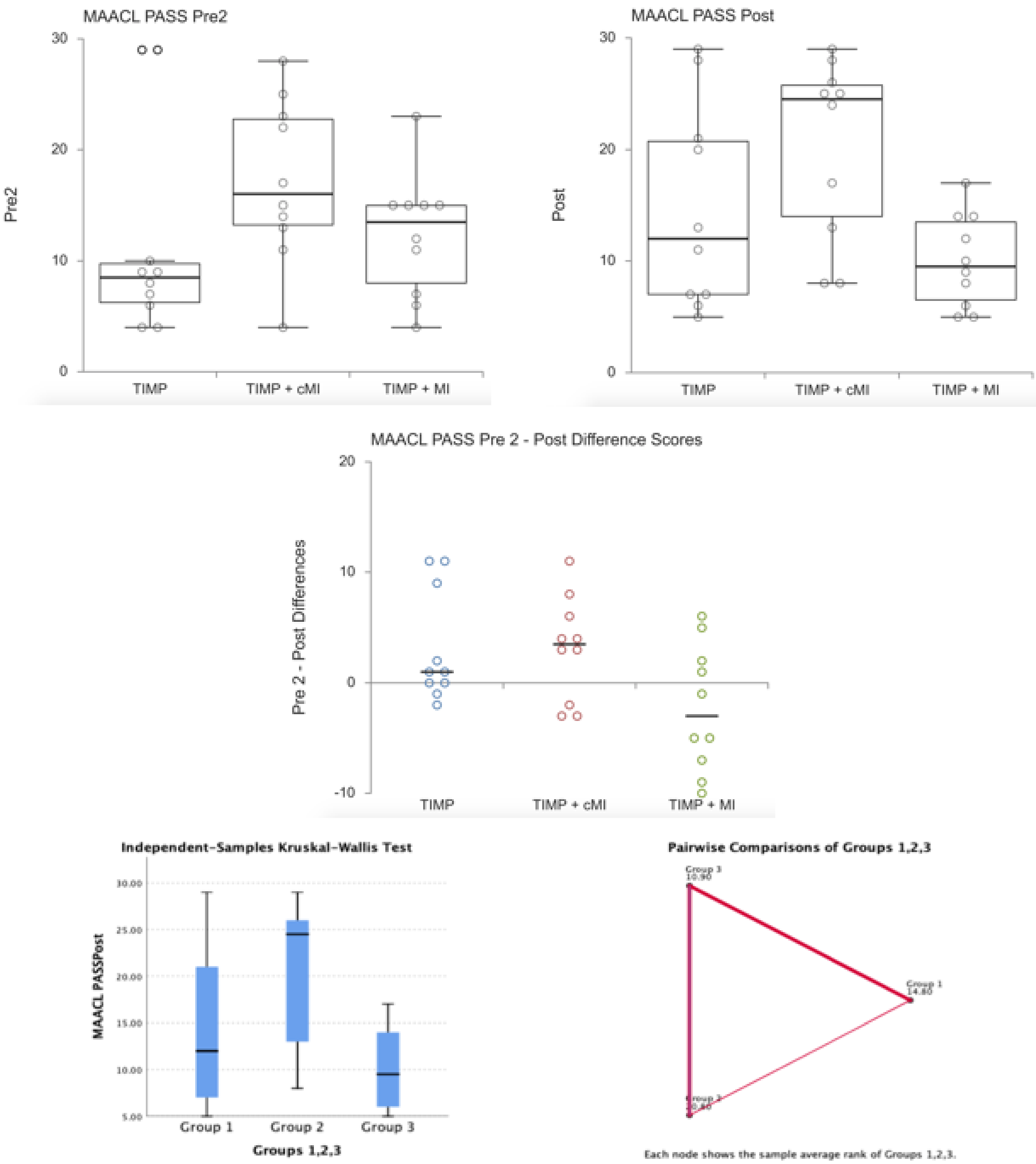
Multiple Affect Adjective Checklist (MAACL) – (PASS), Means (SD)

	TIMP	TIMP + cMI	TIMP + MI
Pre-test 2	11.50 (9.44)	17.20 (7.30)	12.30 (5.59)
Post-test	14.70 (9.15)	20.30 (8.11)	10.00 (4.16)
Probability (2-sided asymptotic)	.105	.045*	.261

* $p < .05$.

Figure 10a

Multiple Affect Adjective Checklist (MAACL) (PASS) Pre-test 2, Post-test



Note: Individual data points and medians (top); difference scores (middle); comparisons for Group 1 TIMP, Group 2 TIMP + cMI, and Group 3 TIMP + MI (bottom row).

For Positive Affect alone, there were no significant median differences between pooled group pre-test 1 (6.50) and 2 (7.50), $z = 1.15$, $p = .252$. For TIMP, there was a non-significant change from pre-test 2 (*Mdn* = 5.00) to post-test (*Mdn* = 8.00), $z = 1.12$, $p = .261$, with five persons reporting a positive change, three a negative change, and two no change. For TIMP + cMI, there was a non-significant improvement from pre-test 2 (*Mdn* = 10.50) to post-test (*Mdn* = 18.00), $z = 1.644$, $p = .102$, with seven positive changes, and three negative. For TIMP + MI, there was a non-significant decrease between pre-test 2 (*Mdn* =7.00) and post-test (*Mdn* =4.50), $z = 1.187$, $p = .235$, with three people reporting a positive change, six a negative, and one no change. Figure 10b shows individual data points, medians, and difference scores. A Kruskal-Wallis test was run to determine if there were differences in post-test scores between groups. Median post-test scores were significantly different between groups, $H(2) = 6.73$, $p = .035$*. Pairwise comparisons were performed with a Bonferroni correction for multiple comparisons. Adjusted *p*-values are presented. Post hoc analysis revealed statistically significant differences between TIMP + cMI (mean rank = 21.00) and TIMP + MI (mean rank = 10.95), $p = .031$*. There were no statistically significant differences involving TIMP (mean rank = 14.55).

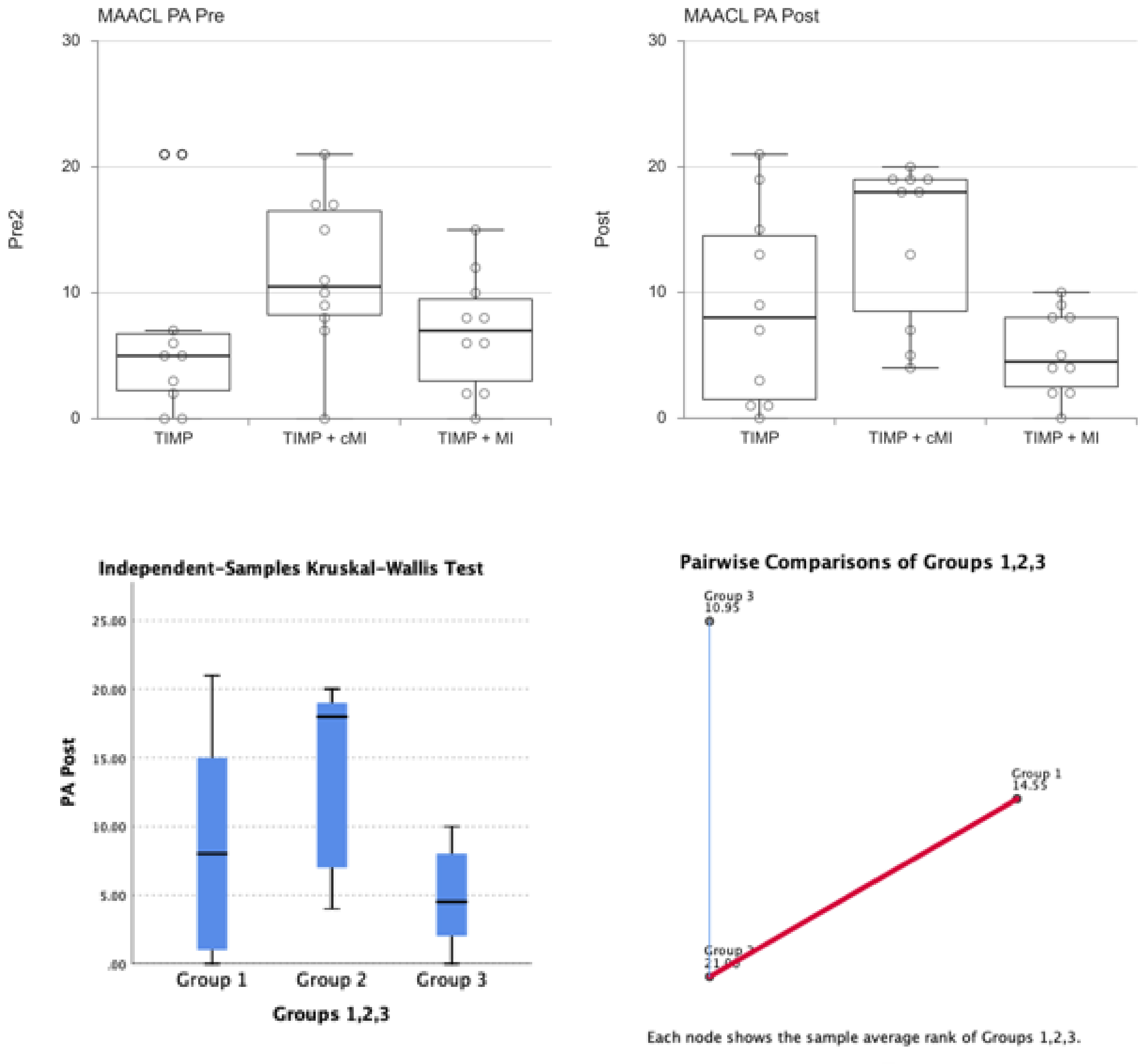
Table 10b

Multiple Affect Adjective Checklist (MAACL) – Positive Affect (PA) by Group, Means (SD)

	TIMP	**TIMP + cMI**	**TIMP + MI**
Pre-test 2	7.00 (7.75)	11.50 (6.11)	6.90 (4.72)
Post-test	8.90 (7.78)	14.20 (6.44)	5.20 (3.39)
Probability (2-sided asymptotic)	.261	.102	.235

Figure 10b

Multiple Affect Adjective Checklist (MAACL) -Positive Affect (PA) Pre-test 2, Post-test



Note: Individual data points and medians (top);

comparisons for Group 1 TIMP, Group 2 TIMP + cMI, and Group 3 TIMP + MI (bottom).

For Sensation Seeking, there was a non-significant change between pooled group pre-tests 1 (*Mdn* = 4.50) and 2 (*Mdn* = 5.00), $z = .194$, $p = .846$. For TIMP, there was a statistically significant change from pre-test 2 (*Mdn* =4.00) to post-test (*Mdn* =5.50), $z = 2.03$, $p = .042$*, $r = 0.64$, with five participants reporting positive differences, and five no change. For TIMP + cMI, there was a non-significant change from pre-test 2 (5.50) to post-test (*Mdn* =6.00), $z = .91$, $p = .364$, with six positive differences, three negative differences, and one unchanged. There was a non-significant change for TIMP + MI participants from pre-test 2 (*Mdn* =5.00) to post-test (*Mdn* =5.00), $z = .987$, $p = .323$, with five negative differences, three positive differences, and two unchanged. Figure 10c shows individual data points with medians and difference scores. There was a non-significant percent change between groups as assessed by a Kruskal-Wallis test, $H(2) = 1.93$, $p = .380$.

Table 10c

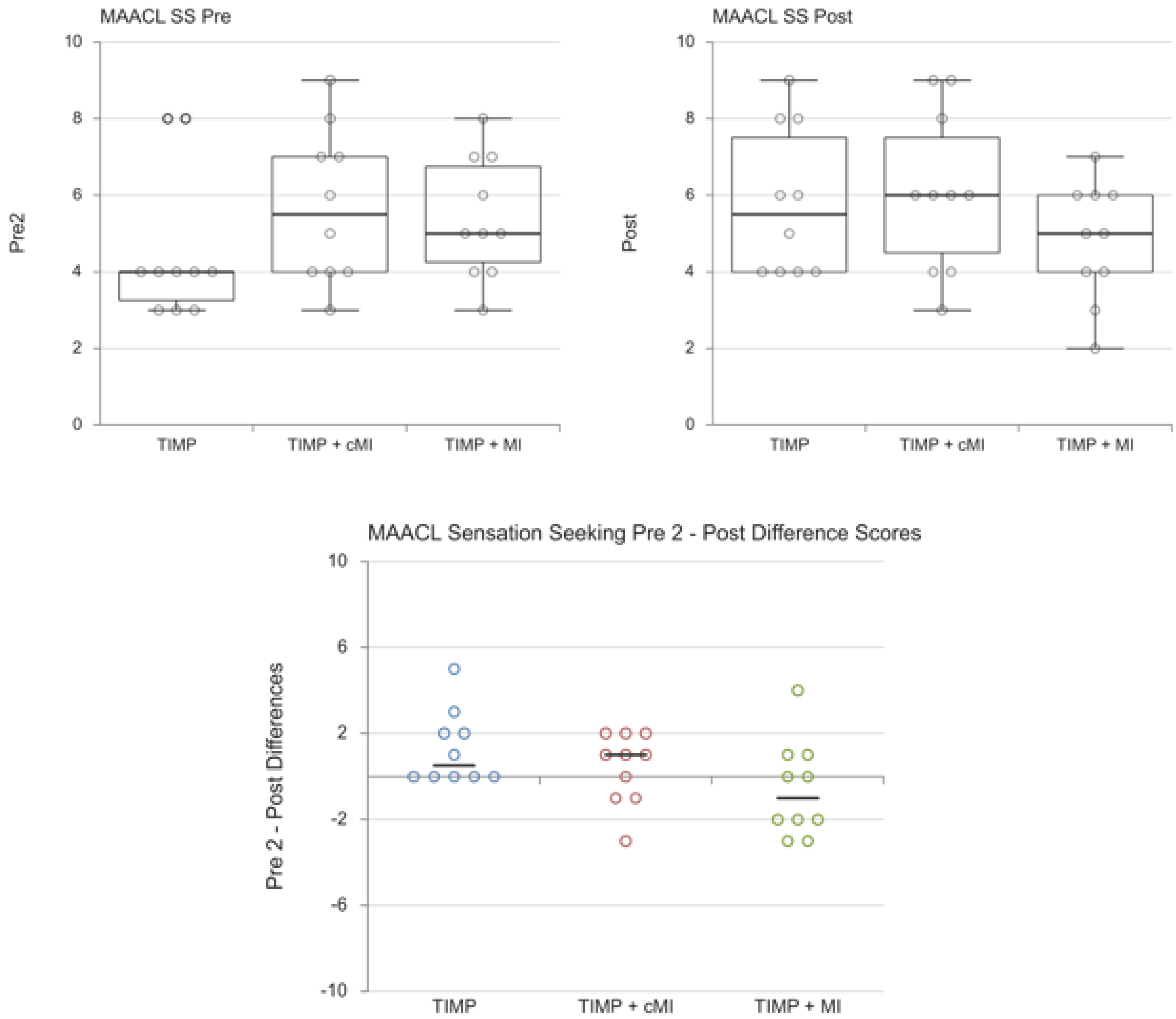
Multiple Affect Adjective Checklist (MAACL) – Sensation Seeking (SS) by Group, Means (SD)

	TIMP	**TIMP + cMI**	**TIMP + MI**
Pre-test 2	4.50 (1.90)	5.70 (2.00)	5.40 (1.58)
Post-test	5.80 (1.93)	6.10 (2.08)	4.80 (1.55)
Probability (2-sided asymptotic)	.042*	.364	.323

* $p < .05$.

Figure 10c

Multiple Affect Adjective Checklist (MAACL) Sensation Seeking (SS) Pre-test 2, Post-test



Note: Individual data points, medians, difference scores.

4.8.2 Negative Affect

There was a non-significant change between pooled group pre-test 1 (*Mdn* = 1.00) and pre-test 2 (*Mdn* = 1.50) for the composite Dysphoria (Anxiety, Depression, and Hostility), $z = .101$, $p = .920$. TIMP participants reported a non-significant change from pre-test 2 (*Mdn* = 1.00) to post-test (*Mdn* = 2.00), $z = 1.45$, $p = .147$, with five indicating an increase in negative affect, three remaining the same, and two reporting a decrease. For participants in TIMP + cMI, there was a significant decrease in negative affect from pre-test 2 (*Mdn* = 2.50) to post-test (*Mdn* = 1.00), $z = 2.04$, $p = .041$*, $r = .55$, with six participants reporting a decrease in negative affect, three remaining the same, and one an increase. There was a non-significant decrease for participants in TIMP + MI from pre-test 2 (*Mdn* = 1.50) to post-test (*Mdn* = 1.00), $z = .687$, $p = .492$, with four persons reporting a decrease in negative affect, one an increase, and five reporting no change. Figure 10d shows medians and individual data points. Median post-test scores were not statistically significantly different between groups, as assessed by a Kruskal-Wallis test, $H(2) = 2.341$, $p = .310$.

Table 10d

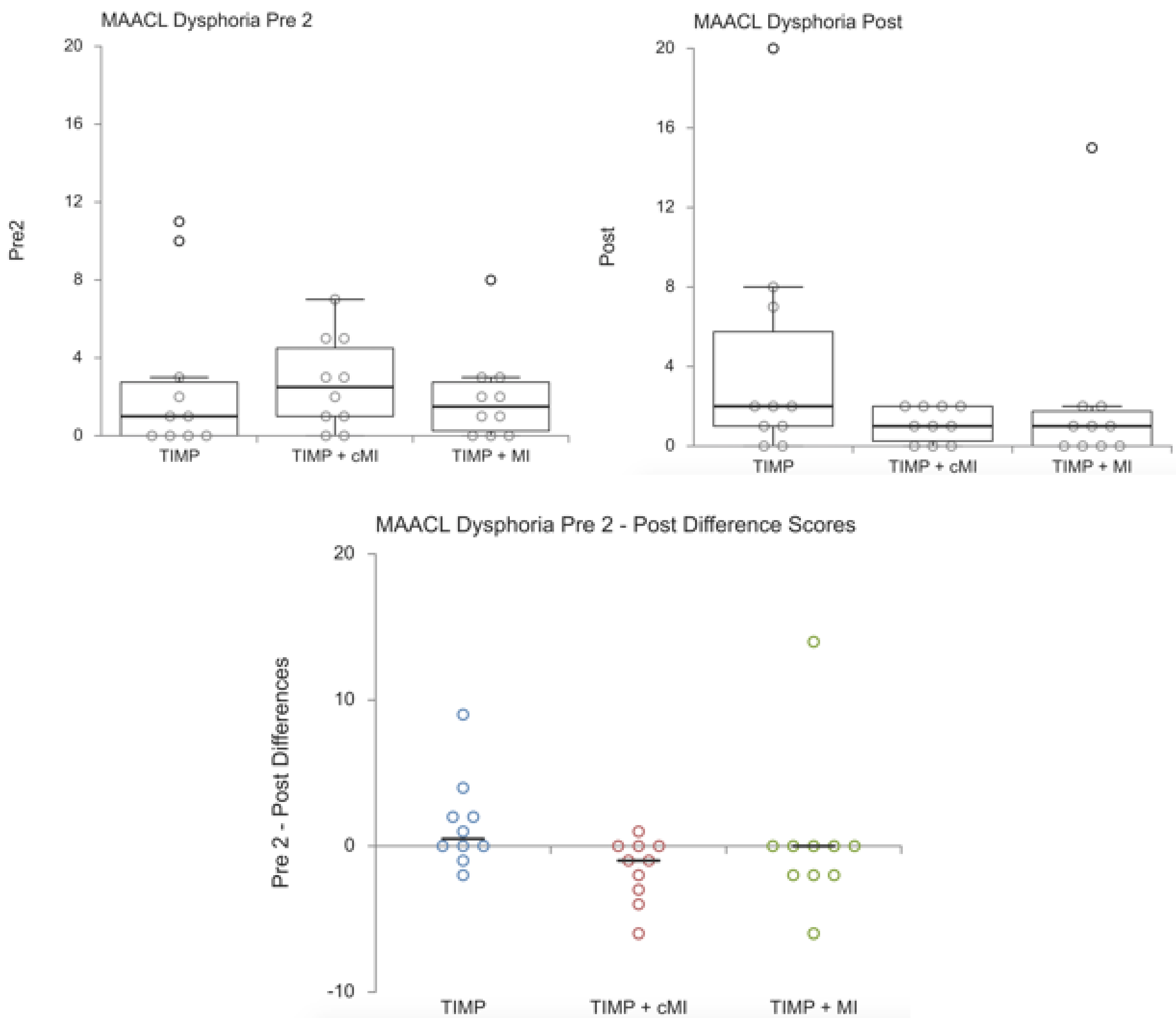
Multiple Affect Adjective Checklist (MAACL) – Dysphoria (DYS) by Group, Means (SD)

	TIMP	**TIMP + cMI**	**TIMP + MI**
Pre-test 2	2.80 (4.18)	2.70 (2.36)	2.00 (2.40)
Post-test	4.30 (6.17)	1.10 (.88)	2.20 (4.57)
Probability (2-sided asymptotic)	.147	.041*	.492

* $p < .05$.

Figure 10d

Multiple Affect Adjective Checklist (MAACL) Dysphoria (DYS) Pre-test 2, Post-test



Note: Individual data points, medians, difference scores.

Pooled group pre-test 1median (.00) for anxiety did not differ statistically from pre-test 2 (.50). There was a statistically significant decrease for TIMP + cMI participants from pre-test 2 (*Mdn* = 1.00) to post-test (*Mdn* = .00), z = 2.04, p = .041*, r = 0.65. Five participants reported a reduction in anxiety, while five remained the same. There was no statistically significant change for TIMP participants from pre-test 2 (*Mdn* = .50) to post-test (*Mdn* = 1.00), z = .96, p = .336, where five persons remained the same, three had an increase and two a decrease in negative affect. Likewise, for participants in TIMP + MI, there was a non-significant change from pre-test 2 (*Mdn* = .00) to post-test (*Mdn* = .00), z = .27, p = .785, with seven persons reporting no change, two reporting a positive difference, and one a negative difference. Figure 10e shows individual data points with medians and difference scores. Median post-test scores were not statistically significantly different between groups, as assessed by a Kruskal-Wallis test, $H(2)$ = 2.767, p = .251.

Table 10e

Multiple Affect Adjective Checklist (MAACL) – Anxiety (A) Pre-test 2 – Post-test by Group

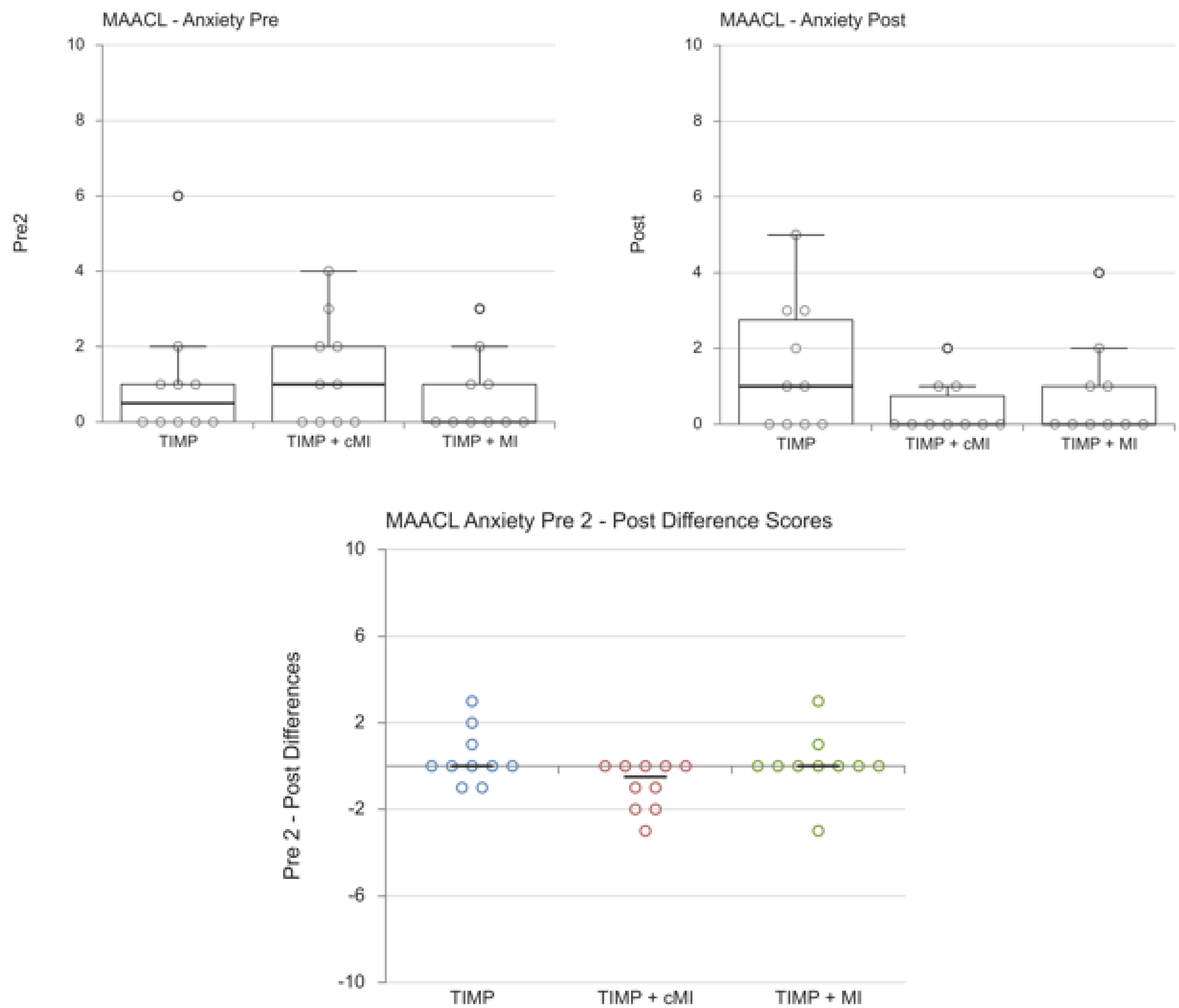
	TIMP	**TIMP + cMI**	**TIMP + MI**
Pre-test 2	1.10 (1.85)	1.30 (1.42)	.70 (1.06)
Post-test	1.50 (1.72)	.40 (.70)	.80 (1.32)
Probability (2-sided asymptotic)	.336	.041*	.785

Note: Means and standard deviations (SD)

* $p < .05$.

Figure 10e

Multiple Affect Adjective Checklist (MAACL) – Anxiety (A) Pre-test 2, Post-test



Note: Individual data points, medians, difference scores.

There was no significant change in Depression between pooled group pre-test1 (*Mdn* = .00) and pre-test 2 (*Mdn* = .00), *z* = .745, *p* = .456. There was no statistical change for participants in TIMP from pre-test 2 (*Mdn* = .00) to post-test (*Mdn* = .50), *z* =1.46, *p* = .144. Similarly, there were no significant changes for the two motor imagery groups: TIMP + cMI pre-test 2 *Mdn* = .00, post-test *Mdn* = .00, *z* = 1.22, *p* = .223; TIMP + MI pre-test 2 *Mdn* = .00, post-test *Mdn* = .00, *z* = .00, *p* = 1.00. Individual data points and medians are shown in Figure 10f. Median post-test scores were not statistically significantly different between groups, as assessed by a Kruskal-Wallis test, $H(2) = 2.54$, $p = .280$.

Table 10f

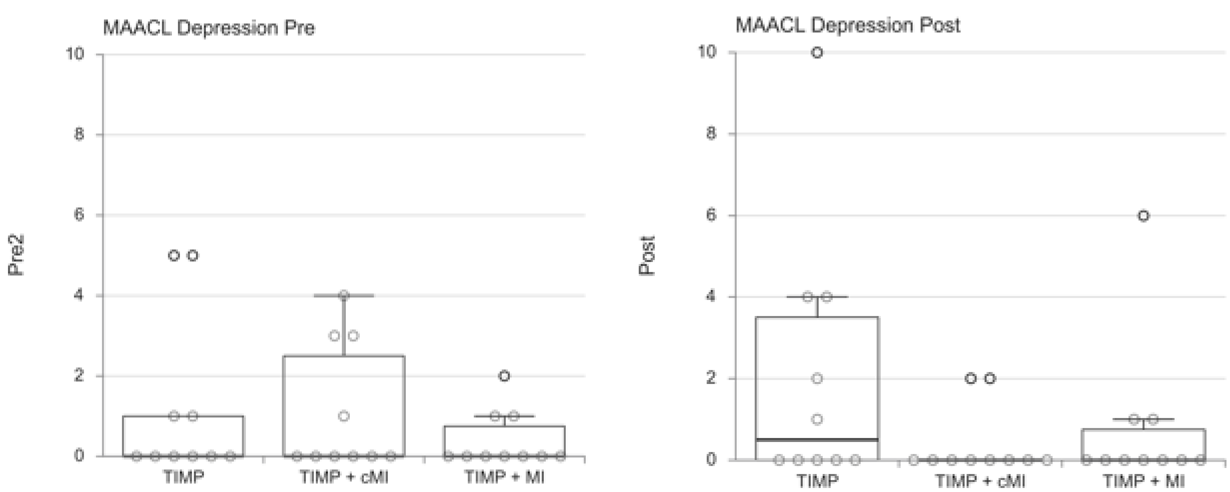
Multiple Affect Adjective Checklist (MAACL) – Depression (D) Pre-test 2 – Post-test by Group

	TIMP	TIMP + cMI	TIMP + MI
Pre-test 2	1.20 (2.04)	1.10 (1.60)	.40 (.70)
Post-test	2.10 (3.21)	.40 (.84)	.80 (1.87)
Probability (2-sided asymptotic)	.144	.223	1.000

Note: Means and standard deviations (SD)

Figure 10f

Multiple Affect Adjective Checklist (MAACL) -Depression (D) Pre-test 2, Post-test



Note: Individual data points and medians.

Ratings for hostility showed no statistical change between pooled group pre-test 1 (*Mdn* = .00) and pre-test 2 (*Mdn* = .00), $z = .438$, $p = .662$. TIMP participants had no statistical change from pre-test 2 (*Mdn* =.00) to post-test (*Mdn* = .00), $z = .00$, $p = 1.00$. For TIMP + cMI, there was no statistical change from pre-test 2 (*Mdn* =.00) to post-test (*Mdn* = .00), $z = .00$, $p = 1.0$. Similarly, TIMP + MI participants had a non-significant change from pre-test 2 (*Mdn* =.00) to post-test

(*Mdn* = .00), $z = .677$, $p = .498$. Figure 10g shows individual data points and medians. Median post-test scores were not statistically significantly different between groups, as assessed by a Kruskal-Wallis test, $H(2) = .322$, $p = .851$.

Table 10g

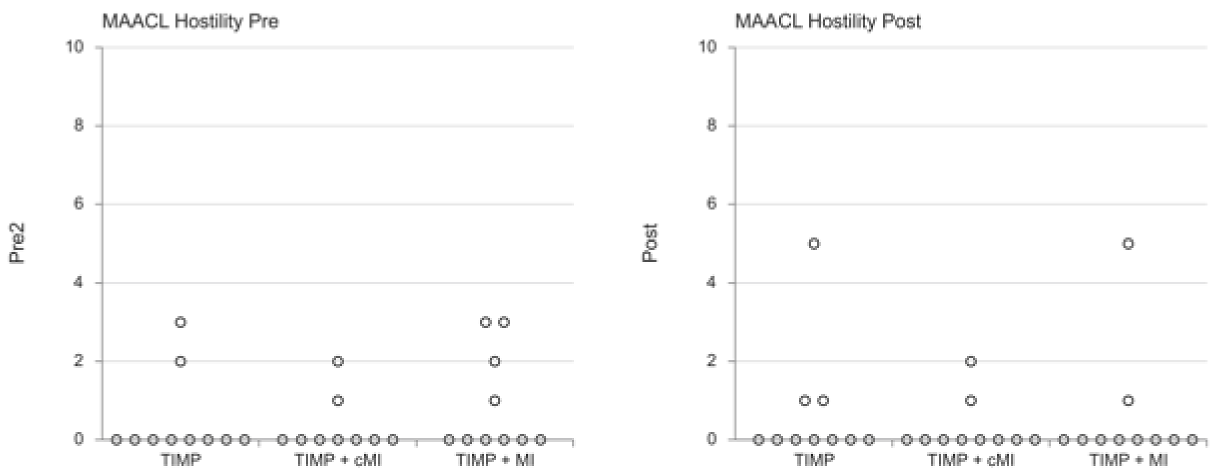
Multiple Affect Adjective Checklist (MAACL) – Hostility (H) Pre-test 2 – Post-test by Group

	TIMP	TIMP + cMI	TIMP + MI
Pre-test 2	.50 (1.08)	.33 (.71)	.90 (1.29)
Post-test	.70 (1.57)	.30 (.67)	.60 (1.58)
Probability (2-sided asymptotic)	1.000	1.000	.498

Note: Means and standard deviations (SD)

Figure 10g

Multiple Affect Adjective Checklist (MAACL) - Hostility (H) Pre-test 2 – Post-test



Note: Individual data points and medians.

4.9 Self-Assessment Manikin

The Self-Assessment Manikin (SAM) provided a subjective measure of changes in valence, arousal, and dominance before and after the nine intervention sessions. There was a statistically significant improvement in valence for participants in TIMP and TIMP + cMI: TIMP pre-test

(*Mdn* =30.50), post-test (*Mdn* = 37.50), z = 2.53, p = .011*, r = .90, with eight positive differences and two unchanged; TIMP + cMI pre-test (*Mdn* = 33.50), post-test (*Mdn* = 35.00), z = 2.12, p = .034*, r = 0.80, with six positive differences, three unchanged, and one negative. There was a non-significant change for participants in TIMP + MI: pre-test (*Mdn* =36.50), post-test (*Mdn* =36.50), z = .93, p = .351, r = 0.35, with five positive changes, three unchanged, and two negative changes. Figure 11a shows individual data points, medians, and difference scores. There was a non-statistically significant percent change between groups as determined by a Kruskal-Wallis test, $H(2)$ = 5.481, p = .065.

Table 11a

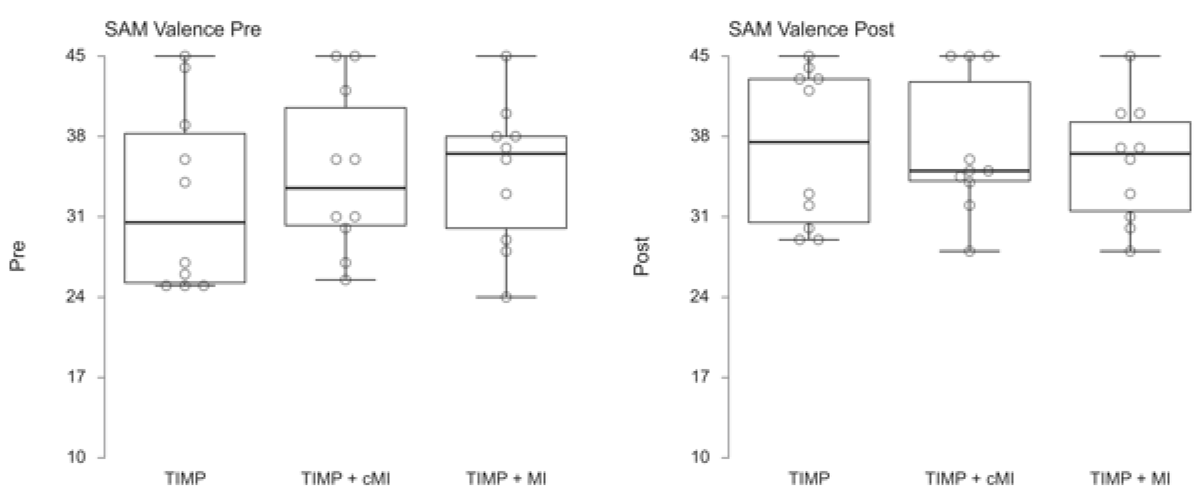
Self-Assessment Manikin (SAM) – Valence by Pre-test 2 – Post-test by Group, Means (SD)

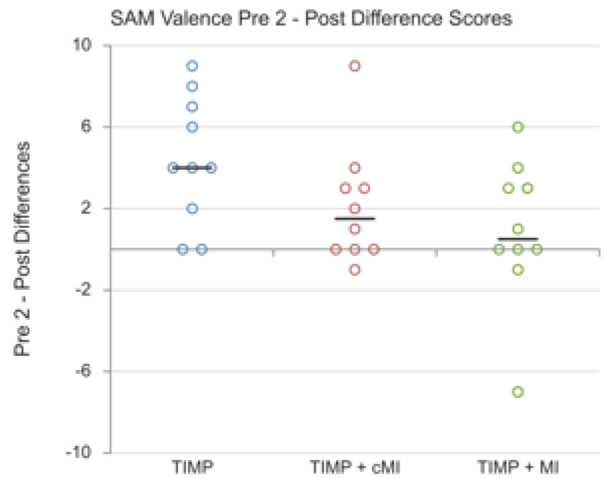
	TIMP	**TIMP + cMI**	**TIMP + MI**
Pre-test	32.60 (8.07)	34.85 (7.17)	34.80 (6.30)
Post-test	37.00 (6.90)	36.95 (5.98)	35.70 (5.25)
Probability (2-sided asymptotic)	.011*	.034*	.351

* p < .05.

Figure 11a

*Self-Assessment Manikin (*SAM) Valence Pre-test 2 – Post-test





Note: Individual data points, medians, difference scores.

There was a statistically significant change in arousal for participants in TIMP + cMI from pre-test (*Mdn* = 38.00) to post-test (*Mdn* = 41.00), $z = 2.11$, $p = .035$*, $r = 0.74$, with seven positive changes, two unchanged, and one negative difference. TIMP and TIMP + MI results were non-significant: TIMP pre-test (Mdn =26.50), post-test (*Mdn* =26.00), $z = -1.08$, $p = .282$, $r = -0.34$, with seven negative differences, and three positive differences; TIMP + MI pre-test (*Mdn* = 30.00), post-test (*Mdn* = 30.50), $z =.357$, $p = .721$, $r = 0.12$, where there were six positive changes, three negative, and one unchanged. There was a non-statistically significant percent change between groups as determined by a Kruskal-Wallis test, $H(2) = 4.480$, $p = .106$.

Table 11b

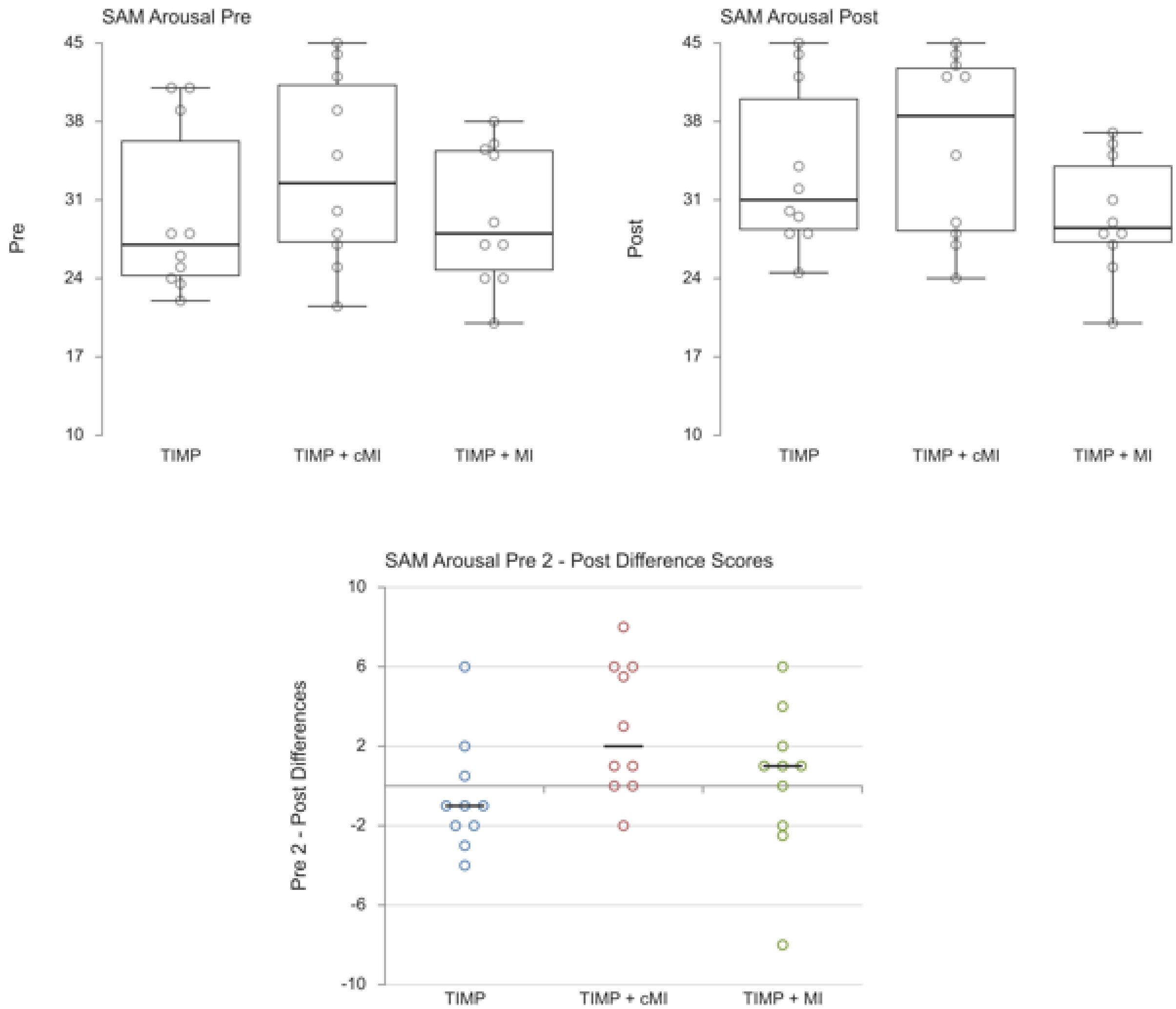
Self-Assessment Manikin (SAM) – Arousal Pre-test 2 – Post-test by Group, Means (SD)

	TIMP	**TIMP + cMI**	**TIMP + MI**
Pre-test	26.90 (8.60)	37.45 (6.76)	31.60 (6.17)
Post-test	26.35 (6.92)	40.30 (4.03)	31.85 (6.84)
Probability (2-sided asymptotic)	.282	.035*	.721

* $p < .05$.

Figure 11b

Self-Assessment Manikin (SAM) Arousal Pre-test 2 – Post-test



Note: Individual data points, medians, difference scores.

There was a statistically significant change in dominance for participants in TIMP and TIMP + cMI: TIMP pre-test (*Mdn* =27.00), post-test (*Mdn* = 31.00), z = 2.70, p = .007*, r = 0.90, with nine participants reporting a positive difference, and one remaining unchanged; TIMP + cMI pre-test (*Mdn* =32.50), post-test (*Mdn* =38.50), z =2.20, p = .028*, r = 0.73, with seven positive changes, two negative changes, and one remaining unchanged. There was a non-significant change for TIMP + MI: pre-test (*Mdn* =28.00), post-test (*Mdn* =28.50), z = .341, p = .733, r = 0.13, with five participants reporting a positive difference, three remaining the same, and two reporting a negative difference. A Kruskal-Wallis H test was run to determine if there were differences between groups. Differences in percent change scores were statistically significant, $H(2)$ = 7.359, p = .025. Pairwise comparisons were performed with a Bonferroni correction for multiple comparisons, with adjusted p-values presented. Post hoc analysis revealed statistically significant differences between the median percent change for TIMP (.14) and TIMP + MI (.02), p = .020, but there was no statistically significant difference between TIMP + cMI (*Mdn* = .06) and any other group.

Table 11c

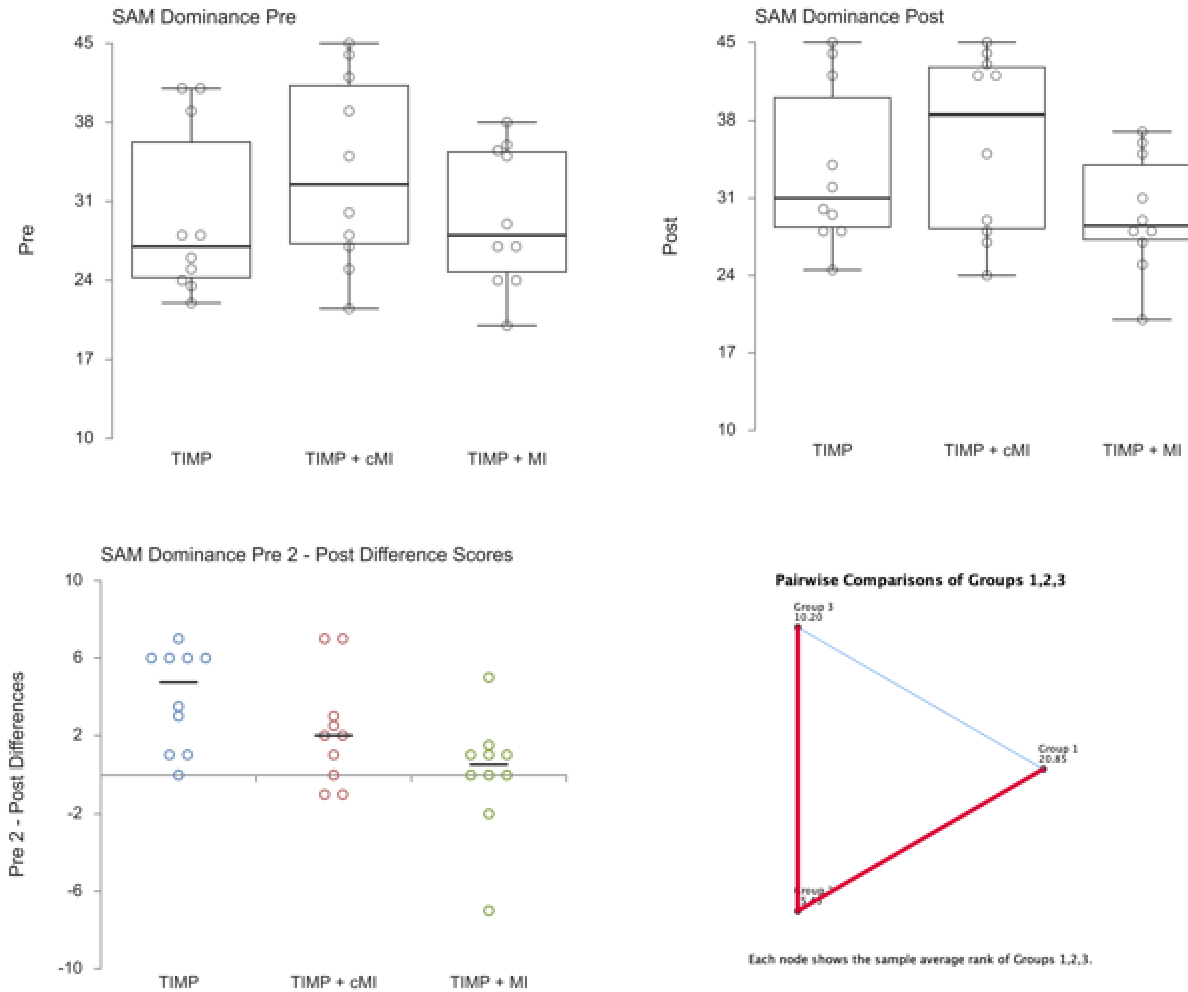
Self-Assessment Manikin (SAM) – Dominance Pre-test 2 – Post-test by Group, Means (SD)

	TIMP	TIMP + cMI	TIMP + MI
Pre-test	29.75 (7.55)	33.65 (8.49)	29.55 (6.18)
Post-test	33.70 (7.35)	35.90 (8.20)	29.60 (5.30)
Probability (2-sided asymptotic)	.007*	.028*	.733

* p < .05. **p < .01.

Figure 11c

Self-Assessment Manikin (SAM) Dominance Pre-test 2, Post-test



Note: Individual data points, medians, difference scores, pairwise comparisons.

4.10 Borg Rating of Perceived Pain

Participants completed the Borg Rating of Perceived Pain prior to and following each training session, to track any changes in level of perceived pain. There was a non-significant change from pooled group pre-test (*Mdn* = 2.50) to post-test (*Mdn* = 3.00), $z = 1.17$, $p = .241$. Median post-test scores were not statistically significantly different between groups, as assessed by a Kruskal-Wallis test, $H(2) = 3.912$, $p = .141$.

4.11 Non-parametric Correlation Analyses

As data did not meet assumptions for parametric tests, non-parametric analyses were conducted instead. Kendall's tau-b correlations were run using pooled group data to compare change scores between primary and secondary outcome measures, and within primary and secondary measures. Results are provided in the tables below:

Table 12a

Correlation Analyses Within Primary and Secondary Measures

Paired Difference Scores	**Kendall's tau-b**	***P* value**
FM-UE Part A, Part B	$\tau = .208$	$p = .174$
FM-UE Part A, Part C	$\tau = .149$	$p = .310$
FM-UE, Part A, Part D	$\boldsymbol{\tau = .329}$	$\boldsymbol{p = .029}$*****
FM-UE Part B, Part C	$\tau = -.071$	$p = .650$
FM-UE Part B, Part D	$\tau = .156$	$p = .333$
FM-UE Part C, Part D	$\tau = .072$	$p = .640$
FM-UE, WMFT-FAS	$\tau = .187$	$p = .170$
FM-UE, MAL-AS	$\boldsymbol{\tau = .233}$	$\boldsymbol{p = .084}$

WMFT-FAS, MAL-AS	***τ* = .388**	***p* = .004****
PASS, SAM-V	*τ* = .022	*p* = .870
SAM-V, SAM-A	*τ* = .066	*p* = .635
SAM-V, SAM-D	***τ* = .390**	***p* = .005****
SAM-A, SAM-D	*τ* = .122	*p* = .374

*$p < .05$. **$p < .01$.

Table 12b

Correlation Analyses Between Primary and Secondary Outcome Measures

Paired Difference Scores	**Kendall's tau-b**	***P* value**
FM-UE, TMT	*τ* = .061	*p* = .652
WMFT-FAS, TMT	*τ* = -.178	*p* = .183
FM-UE, PASS	*τ* = -.022	*p* = .871
WMFT-FAS, PASS	*τ* = -.094	*p* = .483
FM-UE, DYS	***τ* = .292**	***p* = .038***
WMFT-FAS, DYS	*τ* = -.085	*p* = .542
TMT, PASS	*τ* = .105	*p* = .430
TMT, DYS	*τ* = -.023	*p* = .868
FM-UE, SAM-V	*τ* = -.003	*p* = .985
FM-UE, SAM - A	***τ* = -.264**	***p* = .053**
FM-UE, SAM-D	*τ* = .122	*p* = .374

WMFT-FAS, SAM-V	$\tau = -.088$	$p = .524$
WMFT-FAS, SAM-A	$\tau = .088$	$p = .516$
WMFT-FAS, SAM-D	$\tau = -.045$	$p = .745$
FM-UE, GSE	$\tau = .089$	$p = .531$
WMFT-FAS, GSE	$\tau = -.057$	$p = .686$

$^{*}p < .05$.

Chapter 5
Discussion

5 Review of Results

This study assessed the effects of TIMP, TIMP + cMI, and TIMP + MI on upper-extremity motor, cognitive, and affective outcome measures in a sample of 30 chronic, post-stroke participants. Groups were equal in number, each having 10 participants. Demographic characteristics were comparable between groups (Table 1). A multiple baseline design was used, with two baseline measures obtained a minimum of one week apart. Results indicated participants had stable levels of impairment, with non-significant differences between pre-tests 1 and 2 (Table 2).

5.1 Primary Outcome Measures

All three groups made significant baseline to post-test gains on the two primary outcome measures – FM-UE and WMFT-FAS. There was also a significant between-group difference on the FM-UE between TIMP and TIMP + cMI, with the former yielding stronger results. There were no significant between-group differences on the WMFT-FAS. In addition, a significant effect of time was obtained on the MAL-AS for TIMP and TIMP + MI; however, there were no significant between-group differences. Results appear to support the efficacy of a TIMP-based approach to upper extremity rehabilitation for individuals at the chronic stage following a stroke. Teasell and colleagues (2012) suggest that given evidence supporting efficacy of rehabilitation at the chronic post-stroke stage, it is time to rethink chronic post-stroke management approaches, where there are few if any resources, stating that not doing so may compromise individuals' abilities to attain maximal functional recovery and regain independent living skills.

5.1.1 Impairment-based Measures

Two motor impairment-based measures were used: the Fugl-Meyer Upper Extremity (FM-UE) and the Trunk Impairment Scale (TIS). Each of these assessments will be reviewed in turn.

5.1.1.1 Fugl-Meyer – Upper Extremity

Modelled on Brunnström's sequential recovery stages (1966), the FM-UE is constructed on the assumption that motor recovery proceeds stepwise. Beginning with the re-emergence of reflexes, there is an initial reliance on synergistic movement, which gradually decreases as voluntary movement with reduced abnormal synergy returns, finally progressing to normal voluntary motor function and reflex activity (Fugl-Meyer et al., 1975). Wrist and hand recovery, viewed as being somewhat independent of arm recovery, are tested in separate sections. A retrospective analysis conducted to investigate the hierarchical properties of the FM-UE supported the phylogenetic construct on which the FM-UE stage- and subsection-wise hierarchy is based (Crow & Harmeling-van der Wel, 2008). However, Woodbury and colleagues (2013; 2007) challenged the notion of a hierarchical structure underpinning the FM-UE, proposing instead a linear rather than stage-wise difficulty order, and using this as a basis for matching task difficulty in rehabilitation to evolving upper extremity abilities (Woodbury et al., 2016). The detailed protocol for the current study (Appendix C), though not specifically organized according to stages, contains many music-based tasks modelled on activities in the FM-UE assessment tool.

What rehabilitative gains, indexed against the 66-point FM-UE scale, need to be made to constitute a clinically meaningful change? Researchers estimated the FM-UE clinically important difference (CID) range for persons with minimal to moderate chronic post-stroke impairment to be 4.25 to 7.25 (Page et al., 2012). The median pre-test 2–post-test increase was 8.5 for TIMP, 4 for TIMP + cMI, and 5 for TIMP + MI. However, contrary to the sample used in the Page et al. (2012) study, group medians indicate that many participants had levels of impairment in the low rather than high-moderate range. The TIMP baseline 2 median was 29.50 (range 14-47), the TIMP + cMI median was 28.00 (range 14-59), and the TIMP + MI median was 37.50 (range 15-60). The data used for the Page et al. (2012) estimate was a secondary analysis of data derived from the Everest RCT, which included participants with FM-UE scores of 28-50 (Harvey & Winstein, 2009). In the current TIMP study, 13 out of 30 participants had baseline scores < 28, while four had scores > 50, and may have experienced ceiling effects. Hence, only 13 participants in this study fell within the minimal to moderate impairment range used by Page and colleagues (2012) in determining a CID. Despite these differences, rehabilitative gains in the current TIMP study were still largely within the identified CID range.

Different frameworks have been proposed for stratifying post-stroke individuals using the FM-UE. One study classified severe impairment as a score of 0 to 27, moderate impairment as 28 to 57, and mild impairment as 58 to the maximum of 66 (Pang et al., 2006), while another study stratified based on <50 as more severe (moderate) and ≥50 as less severe (mild) arm impairment

(Michaelsen et al., 2006).[3] The target number of participants for this study was 30, a target that was reached; however, it was unknown at the outset how many participants would actually enroll, and no statistical minimizing procedure (Altman & Bland, 2005), such as severity of motor impairment, was used in randomization. As a result, although groups were not entirely heterogeneous in terms of demographics, they were in terms of impairment levels. Using the framework proposed by Michaelsen et al. (2006), all participants in the TIMP group had severe/moderate impairment (three FM-UE <20). In TIMP + cMI, eight had severe/moderate (two FM-UE<20) and two mild impairment, while in TIMP + MI, seven had severe/moderate (three FM-UE<20) and three mild impairment. Initial medians for TIMP and TIMP + cMI were comparable, yet means were not, and standard deviations were wide. As a result, percent change scores were used where possible in comparing groups. For the FM-UE, the percent change score for TIMP was significantly greater than TIMP + cMI, despite the TIMP group having a low initial median and the lowest initial mean. This appears to indicate the active practice condition was more effective in remediating impairment than active practice combined with external cueing during motor imagery. Percent change differences between active practice and active practice including motor imagery without external cues, in contrast, were not significant, suggesting the combination of TIMP + MI may lead to results comparable to those attained in the active practice alone condition.

Traditionally it has been thought that individuals with low FM-UE scores exhibit proximal rather than distal movements, whereas those with milder impairment demonstrate both (Woodbury et al., 2013). The upper extremity portion of the FM-UE (Part A), which focuses on proximal movements, has a total of 36 out of 66 points, while the wrist portion (Part B) has a total of 10, the hand portion (Part C) 14, and coordination/speed (Part D) a maximum of 6 points. At first glance it appeared that the TIMP group may have had more room for improvement, given that the first section has more than half the total number of points, and no one in this group had mild impairment.[4] Raghavan and colleagues (2016) found that participants who had more

[3]It should be noted that in the Michaelsen et al. (2006) study there were no participants with severe impairment, which the researchers categorized as FM-UE <20.

[4]Potential gains in Part A were somewhat limited by ceiling effects for two participants with mild impairment in each of TIMP + cMI and TIMP+MI, which may have impacted median differences for these two groups.

functional impairment (classified according to degrees of active wrist extension, in this case <15°) made greater gains on the FM-UE post-treatment and at follow-up than participants with less functional impairment (>30° active wrist extension). However, closer inspection in this study revealed that the median increase for the TIMP group in each of the FM-UE sub-sections was consistently higher than for the other two groups (with the exception of Part B, where there was a median gain of one point in each of TIMP and TIMP + MI). This seems to indicate that for participants in the TIMP group gains in each section were co-occurring, rather than proceeding in a proximal to distal pattern.

The traditionally-held notion of a proximal to distal recovery gradient has been challenged (Beebe & Lang, 2008; Lang & Beebe, 2007; Woodbury et al., 2013; Woodbury et al., 2007). Beebe and Lang (2008) tested selected movements spanning proximal to distal musculature in a group of patients early post-stroke, and found all segments to be similarly affected. In addition, the researchers found that hand function loss was not confined to effects on distal segments, but instead depended on many upper extremity segments for positioning and orienting, with variance in hand function best predicted by active shoulder range of motion. Results from a cross-sectional sample of chronic post-stroke participants similarly indicated that movement control loss covaried across proximal, middle, and distal segments, with each impacting hand function (Lang & Beebe, 2007). These results were not in accordance, however, with findings of a statistically significant difference between partially spared shoulder adduction and abduction muscles and the on average most severely affected wrist and finger flexors (Colebatch & Gandevia, 1989). In the present study, despite apparent proximal and distal gains in the more highly-impaired TIMP group, neither pooled group nor TIMP group change score comparisons yielded statistically significant associations between Part A – Shoulder/ Arm, Part B – Wrist, or Part C – Hand subsections.

There was, however, a significantly positive association between Part A and Part D (Coordination/Speed) pooled group change scores (Table 13b). This possibly implies a relationship between improved kinematics and reduced UE impairment. Senesac and colleagues(2010) speculated that improvements on the FM-UE scale may be an indicator of underlying smoothing of sub-movements, which previous experimental results have shown may characterize the process of post-stroke motor recovery (Dipietro et al., 2009). Thaut and colleagues (2002) found rhythmic auditory cueing significantly reduced spatiotemporal variability during hemiparetic reaching, with effects evident within the initial two to three trial repetitions. Rhythmic auditory entrainment, used in each of the therapeutic exercises for the TIMP study, may have facilitated an underlying improvement in kinematics, leading to the positive Shoulder/Arm, Coordination/Speed association.

Researchers conducting a critical review of the FM-UE's measurement properties noted that the hand portion is subject to ceiling effects (Gladstone et al., 2002). Five of the seven hand assessments involve different types of grasp, resulting in underrepresentation of fine motor control, considered indicative of good motor recovery. Indeed, a number of participants in the TIMP study expressed interest in finger individuation exercises on the keyboard, requests which were accommodated, although the FM-UE is not sensitive to these fine motor changes. One participant with the least impairment in the TIMP group, three participants in TIMP + cMI, and two in TIMP + MI achieved the maximum score of 14 on the Part C (Hand) subsection at both pre and post-test. Gains these participants may have made in fine motor control can therefore not be determined from FM-UE assessment results given the limitations of the tool in assessing these aspects of motor control.

According to Dipietro and colleagues (2007), the process of augmenting or "tuning", rather than eliminating, abnormal synergies may underlie progress in motor recovery. Apart from two individuals for whom ceiling effects may have played a role (one in TIMP + cMI and one in TIMP + MI) who did not appear to make any gains, the remaining participants had some improvement in their FM-UE scores. Provisions for exercising within synergies were made in this protocol, as well as exercises with mixed or little to no synergy, according to individual need. Despite overall higher levels of impairment, all participants in the TIMP group had gains that were five points or greater on the FM-UE scale, placing them within the range of achieving a CID (Page et al., 2012). It is possible that by building on individual capacities, working within synergistic constraints when required, impairment reduction was promoted, facilitating the stepwise progression originally conceived of in Brunnström's model (1966) and in the design of the FM-UE scale (1975).

5.1.1.2 Trunk Impairment Scale

Outcomes on the upper trunk portion of the Trunk Impairment Scale (TIS) revealed that half of the participants were already performing at ceiling on both pre- and post-tests: six participants in each of TIMP and TIMP + cMI, and three in TIMP + MI. There were non-significant changes between pre-test 2 and post-test in all of the groups. Two of the activities in the detailed protocol were upper trunk exercises, which trainers may or may not have included in sessions depending on individual needs. Participants were instructed during training not to use compensatory trunk movement to facilitate reaching tasks. This was particularly critical for those with more severe impairment, who were positioned directly in front of a table and instructed to keep their backs against the chair while practicing forward reaching movements. While verbal coaching was provided, no physical restraints were used. The effects of compensatory movement suppression through trunk restraint on post-stroke hemiparetic reaching ability were investigated in two trials (Michaelsen & Levin, 2004; Michaelsen et al., 2001). Results indicated that use of a harness to prevent abnormal trunk recruitment facilitated inter-joint elbow and shoulder coordination through increased ROM and improved temporal relations between the two joints. A follow-up RCT in which participants were stratified according to impairment level found that chronic post-stroke participants with moderate-to-severe arm hemiparesis, whose compensatory trunk movements were restrained during reach-to-grasp task training, demonstrated improved impairment and function relative to control group participants (Michaelsen et al., 2006). Specifically, they exhibited decreased trunk movement and significantly increased elbow extension at post-test and one-month follow-up, while control group participants' compensatory trunk movements increased and elbow extensions decreased at both timepoints. In contrast to experimental group participants with severe/moderate impairment, those with mild impairment demonstrated no beneficial effects from training with a trunk restraint. The research highlights the importance of minimizing compensatory movement for individuals with more severe hemiparesis to maximize training-induced impairment reduction.

5.1.2 Function-based Measures

The Motor Activity Log – Amount of Use (MAL-AU) scale, a self-report measure, and the Wolf Motor Function Test – Functional Ability Scale (WMFT-FAS) comprised the two, motor function-based measures.

5.1.2.1 Motor Activity Log – Amount of Use

Though there were no significant between-group differences on the MAL-AU, there were significant improvements between pre and post intervention assessments for the TIMP and TIMP

+ MI groups. Many of the participants in this study, however, had severe to moderate levels of impairment, and use of the affected arm/hand for ADLs remained minimal (Figure 5). An earlier study investigating the effects of modBATRAC found that when participants were stratified according to baseline FM-UE (less impaired >35), the participants with milder impairment indicated greater gains in amount of use on the MAL-AU, whereas those with more severe impairment did not indicate positive changes (Richards et al., 2008). The researchers surmised that participants with milder impairment had greater capacity to integrate functional gains into their ADLs. Van der Lee and colleagues (2004; 1999) arbitrarily established the MCID on the MAL as 0.5 points (10% of the scale range). Applying the same stratification criteria as Richards and colleagues (2008) to pooled group participants in this study, those with milder impairment ($n = 12$) had a statistically significant median pre-post perceived gain of 0.50 on the MAL-AU, $z = 2.75$, $p = .006$, $r = 0.56$. In contrast, the remaining 18 participants with greater levels of impairment (FM-UE ≤35) had a non-significant median gain of .05. This would appear to corroborate the previous observation of less impaired participants having greater ability for translating clinical gains into ADLs. Wolf and colleagues (2010) noted that scores of three or more out of the maximum of five denote independent use of the affected extremity. Only two of the thirty participants in the TIMP study had mean scores ≥3 prior to training. Post training, the mean scores for these two individuals (one in TIMP +cMI and one in TIMP + MI) increased; in addition, two individuals in the TIMP group and three in the TIMP + MI group had post training mean scores ≥3, representing a 16.7% increase in the number of individuals indicating independent functional use of their affected extremity post-training. While the amount of use of the affected extremity remained restricted for many participants, there was a statistically significant, positive association between MAL-AU and WMFT-FAS change scores. Furthermore, there was a positive association trending towards significance between change scores on the MAL-AU and FM-UE, suggesting a relationship between perceived improved functional capacity and reduction in overall impairment.

5.1.2.2 Wolf Motor Function Test – Functional Ability Scale

The WMFT was developed as a tool for quantifying motor function to provide a basis for linking treatment planning with functional outcome measures (Wolf et al., 2001). The WMFT-FAS is comprised of 15 tasks based on functional activities, and two strength-based measures. Tasks in the WMFT-FAS are sequenced in order of complexity, moving from proximal to distal joint recruitment, with the first six activities focusing on joint-segment movements involving gross motor control, and the remaining nine involving integrative functional activities requiring progressively greater interjoint coordination (Wolf et al., 2001; Wolf et al., 1989). Quality of movement for functional ability tasks is rated on a scale of zero to five, with five representing normal movement.

According to Lin and colleagues (2009), mean change scores on the WMFT-FAS of 0.2 to 0.4 may be indicative of a CID. The mean change scores for the TIMP group (M = 0.38), TIMP + cMI (M = 0.31), and TIMP + MI (M = 0.43) were all within the CID range. Each of the groups had statistically significant positive changes, and there were no between-group differences. Changes in functional ability, however, appeared to be unevenly spread amongst participants within groups. There was, for instance, a 7-point increase in SD between pre-test 2 and post-test for the TIMP group. Closer examination revealed that the three individuals who at pre-test 2 scored in the top 25% (range of 40–46) made the largest gains (M = 1.04), while the remaining seven participants (range of 15-26) had a mean change of 0.10 points. In TIMP + cMI changes were somewhat more evenly distributed, with the three individuals initially in the top 25% (range of 51-62) obtaining a mean increase of 0.56, and participants in the lower three quartiles (range of 17-30) scoring a CID mean increase of 0.21. In TIMP + MI gains were, however, evenly distributed, with the four participants who had the highest initial scores (range of 44-70) obtaining a mean change of 0.43 (including the individual performing near ceiling who had no change), and the six participants with the lowest initial scores (range of 17-36) also obtaining a 0.43 mean increase. The TIMP + MI condition appears, therefore, to have facilitated consolidation of motor representations in participants irrespective of level of disability. In the TIMP condition, additional active practice time continued to foster gains in participants who at the outset had more functional ability; however, additional active practice time without motor imagery consolidation did not appear to effect functional improvements for those with more severe restrictions. In TIMP + cMI, individuals who had lower initial scores had gains that were stronger than those in TIMP, but these improvements were still modest relative to those made by comparable participants in TIMP + MI. For comparison purposes, participants in the early entry group of the EXCITE Stroke Trial, with two weeks of CIT training, had pre-treatment WMFT-FAS least square means of 2.38, and post-treatment means of 2.67, while participants in the delayed entry group (one year later) had a pre-training least-squares means measure of 2.70 and post training measure of 2.78 (Wolf et al., 2010).

As the potential for functional improvement is likely greater in individuals who can demonstrate some dexterity, a certain amount of voluntary wrist and finger extension is often required in UE clinical trials (Kwakkel et al., 2004). The WMFT-FAS was originally developed for persons with some distal post-stroke movement capacity undergoing forced use intervention (Wolf et al., 1989). Studies involving CIT require a specified degree of active voluntary wrist and finger extension in order to participate (Taub et al., 1993; Winstein et al., 2003; Wolf et al., 2001; Wolf et al., 2005). To ensure high ecological validity, voluntary distal movement was not an inclusion criterion for the TIMP study, yet the group with the least overall disability, TIMP + MI, also had the greatest gains on the WMFT-FAS measure. Hsieh and colleagues (2009) found the WMFT-FAS to be responsive to changes over time; however, researchers also found it had significant floor effects, affecting 26.4% of participants (J. H. Lin et al., 2009). Given that more than half of the tasks involve some dexterity and several participants in the TIMP study did not have distal movement, there may have been underlying changes not captured by the WMFT-FAS. It is noteworthy, for instance, that the same participants in the TIMP group who demonstrated only slight differences on the WMFT-FAS all had CID gains on the FM-UE, suggesting that reductions in impairment for persons with higher levels of disability had not yet translated into measurable functional gains. It remains to be determined whether a longer training period would facilitate this transfer. There was a positive correlation between the MAL-AS and the WMFT-FAS pooled group change scores, suggesting a relationship between improvements on these functional measures, although the positive association favoured participants with greater initial functional capacity levels.

For the WMFT-Weight and Grip Strength measures there were non-significant changes in each of the groups. The limited time frame and higher levels of disability for many of the participants may have contributed to these outcomes. Lin et al. (2009) did not include weight and grip components in determining the CID for the WMFT-FAS. Luft et al. (2004), reporting a mean weight change of 0.23 kg in the experimental BATRAC group after six weeks of training, suggest that severe impairment on the WMFT-Weight corresponds to 0 kg and moderate impairment corresponds to 1-2 kg (2.2-4.4 lbs.). The median for the TIMP group remained unchanged at .00 lb. from pre-test to post, while the median for TIMP + cMI rose by one point to

4.00 and the TIMP + MI median remained unchanged at 6.00. There was no strength training component included in the TIMP study protocol, and this appears to be reflected in results. Since a number of participants had scores of zero, percent change scores could not be calculated for between-group comparisons. The significant difference in post-test mean rank scores between TIMP and TIMP + MI is therefore more reflective of differences in group composition, with participants in the TIMP group having higher levels of disability.

5.2 Secondary Outcome Measures

In keeping with the biopsychosocial model of disability (World Health Organization, 2002), effects of motor and MI interventions on cognition and affect were investigated as secondary outcomes. A review of these results, as well as motor imagery conditions, follows.

5.2.1 Cognitive Outcomes

The forward Digit Span Test (DST) was administered to assess effects of interventions on short-term memory capacity. Results yielded non-significant between-group and timepoint changes. Using the MST protocol, researchers found small, non-significant post-treatment improvements on the DST (Grau-Sánchez et al., 2018; Ripollés et al., 2015). In contrast, Fujioka et al. (2018), also using a MST protocol, found a slight, non-significant decline in the Alpha span test, which targets working memory, after five weeks of intervention, as well as no significant post-treatment changes in the memory and thinking domain of the Stroke Impact Scale (SIS). Wolf et al. (2008), using the same self-report SIS subscale in the EXCITE trial to assess effects of CIT, found that only participants stratified to the group with higher motor functioning ability had significant improvements at 24-month follow-up but not post-training, while Van Delden et al. (2013), in a comparison of modCIT, modBATRAC and dose-matched control, found no significant differences in memory/thinking on the SIS at either post-test or follow-up.

Researchers found evidence of subliminal entrainment that dynamically replicated changing periodic structures during experimentally-manipulated rhythmic sensorimotor synchronization tasks, suggesting the presence of physiological auditory-motor entrainment mechanisms that did not involve conscious learning processes (Thaut et al., 1999; Thaut, Miller, et al., 1998; Thaut, Tian, et al., 1998). Training in the TIMP study involved auditory-motor coupling to an isochronous beat at a tempo within each participant’s preferred entrainment range, which may have contributed to physiological entrainment at subliminal levels. Using a synchronization-continuation paradigm, Serrien and colleagues (2008) discovered that unpaced relative to paced performance increased involvement of mesial-central regions, including the SMA. Furthermore, a delay interval inserted between pacing and continuation tasks was found to activate the prefrontal-parietal-temporal network, associated with working memory, during the continuation phase (Jantzen et al., 2007). The researchers suggested this may reflect working memory recruitment during the delay period, providing explicit mnemonic support in the absence of external cueing, which may otherwise drive implicit motor system representations of the temporal interval. In the MST protocol, exercises are modelled for participants, but rhythmic facilitation is not provided throughout (Schneider et al., 2007), a procedure which may increase working memory requirements, and may have contributed to the slight improvements on the DST assessments noted in some MST experiments (Grau-Sánchez et al., 2018; Ripollés et al., 2015). In addition, Chen and colleagues (2008) observed greater activation of working memory regions in musicians presented with progressively more complex rhythms, reflecting increased reliance on top-down processing in the more challenging synchronization tasks. In contrast, in the TIMP study a readily discernible, predictable beat was used for entrainment purposes that did not require top-down processing, which may have reduced the need to recruit additional neural resources subserving working memory networks.

The Trail Making Test–Part B (TMT) was selected to evaluate effects of interventions on mental flexibility and executive functioning. There was a significant Pre2–Post decrease in time for TIMP + MI, with eight participants showing improvements, although effects were not seen in the two participants with the greatest levels of impairment. Post-training times decreased for the TIMP + cMI group but did not reach significance, while the TIMP group showed no change. There were no significant between-group effects. These results would appear to suggest that motor imagery practice in conjunction with sensorimotor training may enhance cognitive flexibility.

Previous music-based studies have also found secondary effects on executive functioning. In the study conducted by Fujioka and colleagues (2018), the MST group had significant improvements on the TMT-Part B at the mid-training timepoint, while control group participants demonstrated post-training improvements. In another MST study (Ripollés et al., 2015), there were significant experimental-group improvements on TMT-Part A, a measure of cognitive processing speed, but not on Part B. Researchers who examined the cognitive effects of individualized piano instruction administered to older adults over a six month period found significant improvements on Parts A and B of the TMT, suggesting that such multimodal training may have positive effects on executive functioning (Bugos et al., 2007).

5.2.2 Affective Outcomes

Results obtained on the General Self-Efficacy Scale (GSE) were non-significant; however, there was a slight positive trend, and effect sizes for both TIMP and TIMP + cMI were in the small-medium range ($r = 0.37$). Interestingly, a Friedman test using pooled group data indicated a significant effect of time, $\chi^2(2) = 11.77$, $p = .003$. Post hoc analysis revealed a statistically significant increase from Pre-test 1 ($Mdn = 32.00$) to Post-test ($Mdn = 34.00$), $p = .007$, $r = .46$, showing a positive trend in perceived self-efficacy over the duration of participation. Pre- and post-test scores on the four-point scale tended to be confirmatory, in the “moderately true” to “exactly true” range. A sample of 367 Canadians had a mean GSE score of 3.12 (Scholz et al., 2002), whereas the means for this study sample were consistently higher (pre-test 1, M = 3.22; pre-test 2, M = 3.27; post-test, M = 3.36), indicating a generally strong sense of self-efficacy.

A systematic review found a positive association for persons with stroke between self-efficacy and ADLs and health-related quality of life, and a negative association between self-efficacy and depression (Korpershoek et al., 2011). The mean age (56 years) for participants in this study was younger than the mean age identified for participants in stroke rehabilitation studies (M = 64 years) (Gaynor et al., 2014), though temporal trends have shown increasing incidence of stroke at younger ages (Kissela et al., 2012). Wulf and colleagues (2012) noted that older adults may be negatively impacted by beliefs in reduced ability due to age, limiting their performance and learning. Participation in this study required independent transportation to a downtown location in a large urban centre, and while logistics may have been a deterrent for some, those who chose to participate demonstrated strong commitment throughout the training program. Tasks viewed as acquirable skills have been shown to strengthen self-efficacy and a sense of personal attainment, leading to heightened performance levels (Jourden et al., 1991). Trainers selected and shaped exercises from the protocol according to individual needs, building on existing capacities and providing participants with sufficient challenge, while cultivating and maintaining a sense of personal accomplishment.

The state form of the Multiple Affect Adjective Checklist – Revised (MAACL-R) was used to obtain current measures of well-being (positive affect and sensation seeking) and dysphoria (anxiety, depression, and hostility). The positive affect (PA) scale assesses passive aspects of well-being, while the sensation seeking (SS) scale evaluates active, energetic aspects. PA and SS together comprise a composite well-being scale - PASS. Gains were significant for TIMP + cMI on PASS, and for TIMP on SS. Both of these groups had either non-significant or significant gains on each of the well-being scales. The TIMP + MI group, in contrast, had non-significant pre2–post decreases on the well-being scales. Furthermore, there were significant post-test differences between TIMP + cMI and TIMP + MI on PASS and PA, although a Kruskal-Wallis test conducted on between-group percent change scores for PASS yielded no significant differences, $H(2) = 3.19$, $p = .203$. Pooled PASS data showed seventeen participants indicating improvement in combined positive affect scores, two reporting no change, and eleven indicating a decrease in positive affect. It is difficult in the absence of a formal interview to determine reasons for the decrease that some indicated. The majority of these participants were in the TIMP + MI group, which had the greatest gains in functional motor improvement and cognitive flexibility. It is possible that some of the state affect ratings were associated with the realization that this was the end of their participation in the study, which they appeared to enjoy. For the majority of volunteers, this meant they would no longer be receiving any form of rehabilitation. Anecdotally, a number of individuals expressed regret that the training was over, stating they wished it had been longer.

On the Dysphoria (DYS) composite scale there was a significant pre2-post decrease in negative affect for the TIMP + cMI group. There were no effects of time for TIMP or TIMP + MI, nor any significant between-group differences. Similarly, the TIMP + cMI group had a significant decrease on the Anxiety (A) scale, while the other two groups had non-significant changes. Half of the participants, however, indicated no levels of anxiety at either time point. There were no significant changes on the Depression and Hostility scales for any of the three groups, or between-group differences. Again, many participants (more than half) indicated no levels of depression or hostility on these measures either pre- or post-intervention. The dysphoria scores were generally low, with all but four participants having composite scores of four or less both pre- and post-training. Pooled data indicated that twelve participants had a pre2-post decrease in dysphoria, while eleven remained the same, and seven had a slight increase. Depression is negatively associated with functional outcomes (Kutlubaev & Hackett, 2014), and although over time the proportional frequency of depression in the post-stroke population reduces from 31% to 23% at five years after a stroke (Hackett & Pickles, 2014), the prevalence of those experiencing depressive symptoms remains higher than amongst the general population (Lanctôt et al., 2019). Interventions that have the potential to mitigate depressive symptoms may contribute to a more positive sense of well-being and promote rehabilitative gains.

The Self-Assessment Manikin (SAM) was used to assess the emotional dimensions of valence, dominance, and arousal before and after training sessions. There was a statistically significant pre- to post-training change in Valence and Dominance for the TIMP and TIMP +cMI groups. Pooled group data of change scores for these dimensions yielded a statistically significant positive correlation, suggesting an association between increases in feelings of pleasure and perceptions of autonomy and control over their situations. Percent change medians for the dominance dimension were significantly higher for TIMP than for TIMP + MI, possibly reflecting the effects of the active practice condition for participants in the TIMP group immediately preceding post-test completion. TIMP + cMI was the only group that had a significant increase on the Arousal dimension. Pooled group data, however, indicated a slightly negative association between this dimension and change scores on the FM-UE, that approached but did not reach significance. A number of participants viewed the graphic representations of arousal as calmness versus stress, and it may be that the lower scores reflected this interpretation. The TIMP group had the greatest gains on the FM-UE, and generally indicated a decrease in arousal post-intervention. Similarly, the TIMP + MI group had the second highest gains on the FM-UE and the highest on the WMFT-FAS, and generally rated either a decrease or marginal increase in arousal. It is possible that a calmer, alert affect may have facilitated motor learning more than high energy levels. It is also possible that the external cueing in TIMP + cMI may have presented additional cognitive processing challenges which could have contributed to a heightened arousal response.

Grau-Sánchez et al. (2018), in a MST study involving participants at the subacute stage, found a positive correlation between a higher capacity to enjoy participating in music activities, which appeared to enhance intrinsic motivation, and improvement on assessment of motor function. Fujioka and colleagues (2018) found earlier improvements for the MST group on measures of well-being from the Stroke Impact Scale (SIS) that coincided with improved results on the TMT assessment of executive functioning. Using a multi-faceted approach that included therapeutic goals of promoting emotional awareness and expression, Raghavan et al. (2015) obtained significant improvements on the World Health Organization (Five) well-being index at post-treatment and follow-up, and improvements in ADLs and participation, measured using the SIS, at one-year follow-up. The current study focused on upper-extremity motor rehabilitation, yet positive post-treatment improvements on cognitive and affective indices suggest that sensorimotor training with rhythmic auditory entrainment may yield benefits that encompass affective and cognitive as well as motor domains.

Pooled group data yielded no statistically significant associations between change scores on cognitive and affective measures. The TIMP + MI group, which had statistically significant improvements on the TMT of mental flexibility, reported no significant changes on measures of affective responding. However, TIMP + MI group valence scores were generally positive both pre- and post-intervention period, and negative affect ratings low. Maier et al. (2019), in a study examining effects of depression on post-stroke attentional processing, found that increasing levels of depression negatively impact top-down cognitive processing ability, affecting working memory and executive functioning, but bottom-up, unconscious attentional processes are spared. Antidepressants are the primary treatment modality for reducing depressive symptoms following a stroke (Lanctôt et al., 2019), yet there is an increased risk of adverse side effects (M.L. Hackett et al., 2008), and the effectiveness of pharmacotherapy in preventing depression or improving motor recovery has not been clearly established (Maree L. Hackett et al., 2008). Sensorimotor training, involving entrainment at subconscious levels, may enhance positive affective responding and mitigate negative effects of depressive symptoms on cognitive load as well as on motor learning, without incurring negative side effects.

5.2.3 Motor Imagery Conditions

Contrary to expectations, the TIMP + MI group consistently outperformed the TIMP + cMI group on motor outcomes, with the exception of the Trunk Impairment Scale (TIS). Although both groups made significant gains on the two primary motor outcome measures, the FM-UE and the WMFT-FAS, gains in the TIMP + MI group were superior. Various factors could have impacted these differences. For one, while both groups were heterogeneous, the TIMP + MI group had higher initial means and medians, and it is possible that on the WMFT-FAS, for example, the participants in this group had greater capacity for improvement. However, the fact that improvements were greater for both impairment and function suggests that there may have been other contributing factors. Originally, the planned pre- and post-test assessments included the Kinesthetic and Visual Imagery Questionnaire (KVIQ) (Malouin et al., 2007), but use of this questionnaire had to be discontinued to shorten the timeframe for test administration. As a result, there was no assessment that evaluated motor imagery ability; there may have been a difference between the two groups in this regard. A third possibility has to do with the nature of the motor imagery interventions, which differed in one critical aspect: participants in the cMI condition listened to a metronome beat set at their preferred tempo for each exercise, while MI participants engaged in motor imagery without external auditory input. The difference in outcomes may therefore lie in the simulation conditions.

Both motor imagery conditions began with a demonstration of the task by the therapist. This was done for each of the exercises practiced previously in the session, with time allotted for motor imagery rehearsal after each demonstration (Appendix B). For participants in the TIMP + cMI condition, the demonstration included using a metronome set to the participant's preferred tempo for executing that particular activity. After the therapist had modelled a particular exercise, participants engaged in motor imagery practice, TIMP + cMI with rhythmic input, and TIMP + MI with no external input. In the emulation theory of motor imagery (Grush, 2004a), efferent motor centres of the brain drive a body emulator, which includes the musculoskeletal system and relevant sensors. This emulator generates likely proprioceptive and kinesthetic signals that can be compared to the efferent copy. There can be no external input providing sensory feedback correction during this process. Instead, the emulator is a flexible system that evolves according to its own internal dynamic. In the TIMP + MI condition, the emulator was allowed this flexibility without external sensory input. In TIMP + cMI, the provision of an auditory cue may have caused additional sensory integration challenges in synchronizing an external beat with internally-generated motor imagery, reducing the flexibility and responsiveness of the emulator, and hindering the fluid formation of motor representations. In addition, imagery for actions where representations are not yet fully developed has been shown to take longer than execution of the associated action. In an experiment designed to evaluate the effects of low and high task precision requirements on motor imagery, the high precision motor imagery condition took significantly longer than overt action of the same task (Glover & Baran, 2017). In TIMP + cMI, the external auditory cue was provided at the preferred tempo for the participant's action execution, but not necessarily action emulation. The elaboration and formation of a novel motor representation requiring conscious online control may have necessitated a longer timeframe than the one provided by the external cue. Interestingly, the pre2 and post-test means for the TIMP +cMI group on the TMT were the highest of the three groups, indicating longer processing times and greater challenges with cognitive flexibility, which may have impacted their ability to integrate an external cue. Finally, it is possible, given that each of the exercises was actively practiced to a beat, that participants in TIMP + MI internally generated an isochronous pulse during motor imagery review, fostering simulated audiomotor coupling in motor regions of the brain. Research has shown that during the continuation phase of a synchronization task, in the absence of external reference cues, activity in the putamen, involved in beat prediction, as well as the SMA and premotor cortex, increases in both musicians and non-musicians (Grahn & Rowe, 2013).

5.3 General Discussion

Ascertaining the relationship between quality of movement and functional performance is critical in advancing post-stroke rehabilitation programs (Levin et al., 2019). A systematic review identified CIT as the only motor skill learning technique with sufficient scientific evidence (n > 500) to support its implementation in stroke rehabilitation, in order to effect impairment and disability-related changes (Hatem et al., 2016). However, trials involving CIT have been restricted to participants with limited arm impairment and preservation of some distal movement (Langhorne et al., 2011; Langhorne, Coupar, et al., 2009). Furthermore, research findings suggest that functional gains following CIT may be achieved through compensatory strategies rather than a return to premorbid movement patterns (Kitago et al., 2013; Kwakkel et al., 2015; Massie et al., 2009). Krakauer and colleagues (2012) note the need for rehabilitative treatments that are effective in reducing impairment at all stages following a stroke. Primary impairments are paresis, slowness of movement, and incoordination, impairments which may be attributed to decreased motor unit recruitment, firing rates, and synchronization (Carr & Shepherd, 2010). Results from the present study suggest that TIMP-based interventions serve to reduce motor impairment as well as improve functional performance. A possible mechanism underlying these changes is rhythmic auditory entrainment, used consistently during each of the training sessions.

5.3.1 Rhythmic Auditory Cueing – More than a Mechanism for Planning Movements?

Sensorimotor learning involves acquiring new mappings of sensory and motor variables, with ensuing transformations leading to development of internal models of the body in its environment. These mappings and internal models change as the system adapts to internal and external factors, seeking more energetically-efficient solutions to given constraints (Wolpert et al., 2011). A ‘cue’ refers to sensory information which provides a sensory estimate – an online estimate that must be reliable for the system to perform optimally (Ernst & Bülthoff, 2004). Rhythmic auditory entrainment to an isochronous beat provides such a reliable cue, which may be used for clinical purposes in regaining and retraining motor control. The rhythmic cue allows the brain to plan a movement within a fixed time constraint, adjusting velocity and acceleration parameters in accordance with the rhythmic template, to maximize efficiency and optimize performance. Prior knowledge of the rhythmic period facilitates this mapping, allowing for greater control of the effector’s movement in space, and modulating muscle activation patterns (Thaut, 2013). Each exercise in the TIMP protocol was conducted using a rhythmic cue set at the participant’s preferred tempo, with the beat for slower preferred tempi subdivided to provide the individual with more consistent online guidance, reduce movement variability (Patel et al., 2005), and facilitate audiomotor coupling (McAuley et al., 2012). In addition to conscious entrainment-evoked planning processes, evidence of subconscious sensorimotor entrainment (Thaut, Miller, et al., 1998), even in persons with cerebellar pathology and no musical experience, suggests a direct, driving influence of unconscious auditory processing on motor structures (Molinari et al., 2003).

Experience can modify not only internal models and ensuing behavior, but also brain structure (Nudo, 2013). Sensory and motor cortices have the ability to dynamically reorganize in response both to sensory deprivation and to an increase in sensory input (Mulder, 2007). A key function of the brain is to anticipate future probabilities, with neuronal oscillators predicting the timing of occurrences (Buzsaki & Draguhn, 2004). An influence that is entirely predictable acts as a driving force, while remaining unpredictable external influences are part of process noise (Grush, 2004a). McCrea and Eng (2005) found increased neuromotor noise in persons with stroke, affecting both planning and execution stages of movement. Entrained neural oscillations have been shown to stabilize sensory representations, with attended stimuli having less variable response amplitudes than ignored stimuli. Entrainment may serve a mechanistic function underpinning selective attention to temporally predictable stimuli, entraining oscillations in high excitability phases in areas processing the attended stream, while attenuating entrainment of unattended stimuli (Calderone et al., 2014; Lakatos et al., 2019). In dynamic attending theory, which links attention with entrainment, anticipatory attending is enhanced by regular temporal contexts, improving subsequent performance (Jones, 1976, 2010). Study results have shown that neural oscillations from auditory stimuli drive auditory-motor entrainment, with greater neural synchronization occurring in the presence rather than the absence of an isochronous auditory stimulus (Crasta et al., 2018). Given the extensive connections between auditory and motor systems and rhythm processing in the brain (Thaut, 2003; Zatorre et al., 2007), it is conceivable that participants in the TIMP study, training to a predictable pulse at their preferred rate, induced entrainment of neural oscillations to the attended beat, facilitating a reduction in neuromotor noise and creating a substrate for improved quality of movement and performance.

Motor regions of the brain are engaged when listening to musical rhythms with and without subsequent action intention (J. L. Chen et al., 2008). This highlights the potential priming effects of auditory rhythm on the motor system. By preparing the motor system for action, subsequent response quality is enhanced (Thaut, 2013). Crasta and colleagues (2018) examined the influence of auditory priming on neural oscillations in auditory-motor entrainment, and found a robust effect, with less neural activity required when auditory priming preceded motor activity. Auditory priming was used in addition to visual demonstration when therapists modelled activities for participants in the TIMP study, and the effects of priming may have led to greater neural efficiency during subsequent practice. Gemperline et al. (1995) reported disorganized motor unit recruitment and inefficient rate modulation patterns in paretic arm muscles, contributing to an increased sense of weakness, more effortful movement, and fatigue. Auditory priming in advance of active practice may serve to promote neural efficiency and reduce the impact of negative stroke sequelae.

Predictive processes induced by a reliable auditory stimulus allow an emulator of the musculoskeletal system to place more weight on *a priori* estimates than on peripheral feedback (Grush, 2004a). In a reaching task, persons with stroke demonstrated heavier reliance than controls on feedback control, with velocity profiles indicating less direct, positively skewed, segmented movements (McCrea & Eng, 2005). While kinematic measures were not a part of the

TIMP study, previous research has shown that rhythmic auditory cueing significantly reduces trajectory and timing variability during forward reaching (Thaut et al., 2002), as less weight is placed on feedback control and more stable representations are formed.

Aspects of motor impairment, including lack of coordination and inability to fractionate movements, may be mitigated by provision of a predictable auditory cue. Electromyographic (EMG) patterns of two antagonist muscles taken while participants executed a gross motor task to an even auditory rhythm were significantly less variable than patterns in the uneven or no rhythm conditions (Safranek et al., 1982). Similarly, in a study involving elbow flexion and extension to a target pad, there was a statistically significant reduction in triceps EMG variation prior to target contact, as well as a significant increase in triceps activity duration and biceps/triceps co-contraction, suggesting rhythmic cueing can modify the variability, duration, and onset of EMG patterns in antagonist muscles (Thaut et al., 1991). Inadequate agonist recruitment rather than impaired antagonist inhibition has been found in patients who were unable to complete movement tasks (Gowland et al., 1992). A role for rhythmic auditory cueing is suggested in facilitating muscle activity by promoting more consistent motor unit recruitment (Thaut et al., 1991). In addition, abnormal synergies may emerge as the motor system attempts to coordinate movement by converting any existing degrees of freedom into a controllable system (Bernstein, 1967). This may be viewed as an adaptive response given the current neurophysiological state (Latash & Anson, 1996). Reducing the complexity of a movement may increase its predictability, rendering actions more energetically cost efficient. Dipietro and colleagues (2007) observed that the process of recovery appeared to be aided when existing abnormal synergies were “tuned” or augmented rather than eliminated. The TIMP protocol allowed participants to work within as well as out of synergy. There was a significantly positive association between the shoulder/arm and coordination/speed portions of the FM-UE, suggesting improvements in underlying kinematics. Thaut and colleagues (Thaut et al., 2002) found paretic elbow range of motion increased significantly in the rhythmic cueing condition of an experimental trial, with some residual synergistic shoulder movement. Gribble and Ostry (1999) reported predictive compensation for interaction torques in the central control signals sent to muscles in single- and multi-joint limb movement. Training to an anticipatory rhythmic template may facilitate such predictive adjustments.

5.3.2 Motor Learning Principles

Relatively few studies have focused on motor learning following a stroke (Krakauer, 2006), and there is an ongoing need to bridge motor learning mechanisms with clinical applications (M. Maier et al., 2019). With a view to synthesizing elements of effective post-stroke neurorehabilitation practice, Maier et al. (2019) reviewed existing literature and identified 15 principles of motor learning and recovery: repetitive practice, spaced practice, dose, task-specific practice, variable practice, increasing difficulty, multisensory stimulation, knowledge of results, knowledge of performance, modulating effector selection, action observation, goal-oriented practice, rhythmic cueing, motor imagery, and social interaction. Operationalization of these principles within the context of the TIMP study will be briefly reviewed, with the exception of rhythmic cueing and motor imagery, discussed separately:

- Amount of repetition is a critical factor in retraining motor skills (Bütefisch et al., 1995; Hoemberg, 2014). Repetition without learning new skills, however, will not induce neuroplastic changes (Plautz et al., 2000). In the TIMP study, each activity was practiced as a sequential movement, with number of repetitions tailored according to individual needs and time constraints. However, the practice also involved mapping movements to correspond to specific spatiotemporal constraints, which required greater skill and coordination and hence motor learning.

- Distributed practice has been consistently found to improve performance and learning (Krakauer, 2006). The TIMP study was designed to take place three times a week, with a rest day in-between each session. In practice, this was not always possible, and often participants came two days in a row, with a break before the third day. However, sessions were never scheduled three days in a row.

- Greater doses of therapy do not necessarily translate into superior upper extremity outcomes (Basso & Lang, 2017). Page (2003) found contact times of 30-45 minutes/ session of task-specific practice to be effective. In this study, MI groups had 30 minutes of active practice as well as 15 minutes of MI, and the TIMP group had 45 minutes of active practice; each group achieved significant gains on motor impairment and function outcomes with these amounts of time.

- Task-specific training refers to improving performance on functional tasks, by means of repetition and goal-setting, rather than focusing on reducing impairment (Hubbard et al., 2009). A systematic review found low quality evidence that repetitive task training improves arm and hand function post-stroke (French et al., 2016). In the TIMP study, a number of therapeutic exercises were modelled on ADL's, and isomorphic translations were mapped onto the playing of musical instruments.

- Goal-directed practice involves setting an achievable challenge; this principle was incorporated into BATRAC training sessions with the goal of synchronizing endpoint stops to the auditory cue (Whitall & Waller, 2013). In the TIMP study, participants listened to auditory cues with the goal of matching movements to the periodic rhythmic template.

- Variability of practice may facilitate applicability of learning to novel situations (Schmidt & Lee, 2011). Exercises for proximal and distal movements were included in the TIMP protocol and choice of exercises was tailored to the needs of the participant. Several different options were provided for most movements to give opportunities for practice variability.

- Shaping, which involves small, successive approximations towards a desired motor behavior, is a core foundational principle of CIT (Kwakkel et al., 2015; Taub et al., 1994). Increased task difficulty may be achieved in TIMP exercises by changing the positioning of instruments to increase joint angle requirements and/or varying the speed of the rhythmic auditory cue, providing the tempo remains within the individual's entrainment range.

- Multisensory training has greater ecological validity and may contribute to more effective learning (Shams & Seitz, 2008). The TIMP protocol involved incorporating visual and temporal constraints, as well as haptic feedback in the form of musical instruments and target endpoints.

- Knowledge of results is feedback regarding the outcome of a movement with respect to its environmental goal (Schmidt & Lee, 2011). In a proof of concept case series, four individuals with stroke had reduced movement reaching times in the rhythmic knowledge of results condition (Chen et al., 2016). Participants in the TIMP study also received knowledge of results feedback as they entrained to the period of a beat, with haptic feedback at endpoints of movements. The trainer provided initial hands-on guidance and support if needed, as well as verbal feedback at the conclusion of an exercise, such as pointing out that a movement had been accomplished with less shakiness, greater range of motion, or improvement of the movement pattern.

- Knowledge of performance refers to intrinsic knowledge about the quality of the movement pattern (Gentile, 1972). In the TIMP study the beat set to the participant's preferred tempo was subdivided to ensure consistent rhythmic input throughout the duration of a movement, providing a constant reference framework against which online kinematic adjustments could be made. The trainer provided hands-on support if required to assist with coordinating the movement to the rhythmic cue. Participants also relied on visual and proprioceptive feedback during the movement to make corrections.

- Encouraging increased paretic arm use in ADLs helps mitigate the effects of learned non-use (Taub et al., 2006). Though there was no retention assessment in the TIMP study, participants with milder levels of impairment had statistically significant median gains pre- to post-training on the MAL.

- Action observation may be effective in facilitating improved arm/hand function (Peng et al., 2019). Action observation was used in the TIMP trial in conjunction with rhythmic auditory cueing both in active practice and for demonstrating exercises prior to motor imagery.

- Enhancing perceived self-efficacy through positive social interactions has been shown to influence motor performance and learning (Wulf et al., 2012). In the TIMP study, ratings on the GSE trended upwards over the three timepoints, suggesting participants felt supported and also felt positively about their efforts.

As well as the principles outlined above, three additional aspects deserve to be highlighted: motivation, an intrinsic versus extrinsic focus, and generalization. Optimal learning and performance may be mediated by motivational factors operating through enhanced expectancies (Wulf & Lewthwaite, 2016). Grau-Sánchez and colleagues (2018) found a correlation between improvements on primary motor outcomes and participants' intrinsic motivation to engage in music-based activities with a strong sensorimotor component. All participants in the TIMP study who began the protocol completed the training, with positive levels of affect indicated on measures of affective responding. In contrast, in a large trial involving CIT, 8 participants assigned to receive treatment withdrew, while 11participants assigned to the control condition did not complete treatment (Wolf et al., 2006). Furthermore, researchers found an external focus of attention to be more beneficial for learning than an internal focus (Wulf et al., 1998). Participants in the TIMP study were encouraged to focus on the external auditory cues as well as the given spatial constraints during movement execution and instrumental music playing. Finally, for rehabilitation to be effective, there must be generalization to untrained tasks. Variable practice may aid transfer of learning to new contexts (Krakauer, 2006). However, practicing basic coordinated movements may also serve as building blocks for more complex actions (Senesac et al., 2010). Internal models for simpler tasks may combine to create models for more complex tasks, transferring learning from simpler to more complex motor behaviours (Gribble & Scott, 2002). Participants in the TIMP study practised basic volitional movements aimed at reducing impairment as well as movements targeting improved functional performance, and demonstrated significant gains on standardized assessments for each.

5.3.3 Motor Imagery Practice

Enhanced functional gains were obtained in the current study when 15 minutes of motor imagery review practice followed active TIMP training. A recent systematic review found the combination of MI with conventional rehabilitation to be effective in recovery of post-stroke functionality (López et al., 2019). However, Harris and Hebert (2015) noted the difficulty of determining what constitutes effective elements of motor imagery due to inconsistencies in delivery. The researchers employed the PETTLEP model (Physical, Environment, Task, Timing, Learning, Emotion, and Perspective), derived from sports psychology (Holmes & Collins, 2001), in their review of MI in UE rehabilitation, recommending use of this evidence-based checklist to improve delineation of MI interventions.

Based on Jeannerod's notion of functional equivalence (Jeannerod, 1994), PETTLEP posits psychophysiological congruence between covert and overt stages of motor behavior: close equivalence of action execution processes during MI is critical to optimize MI success. Following this model, first in terms of the physical component of PETTLEP, physiological arousal during imagery should match that required for action execution. In the TIMP study, MI was conducted with participants seated in the chair used in active training, but was not preceded with a relaxation phase, used to begin MI in some motor rehabilitation studies (e.g., Page et al., 20111: Page et al., 2007; J. Park et al., 2015) to more closely approximate an active training state. Second, relevant, multisensory content presentation is recommended as environmental stimuli. Both auditory and visual modalities were accessed in the therapist demonstration preceding MI practice. Research has shown that motor regions of the brain, including the mid-premotor cortex, SMA and cerebellum, are activated when listening to rhythms without subsequent action intention (J. L. Chen et al., 2008), while premotor-parietal and occipital cortical networks are recruited during action observation (Hardwick et al., 2018). However, provision of an external rhythmic template during cMI may have interfered with the flexibility needed in synthesizing efference copy with likely proprioceptive and kinesthetic signals in the process of emulation and formation of a representation (Grush, 2004a). Third, tasks that were demonstrated and rehearsed through MI were identical to those practiced in the immediately preceding active training session. Fourth, Harris and colleagues (2015) noted that matching timing of MI rehearsal to the timing of physical performance has received little attention in the literature. Verbal or prerecorded scripts may also confound generation of temporal representations, seen as critical in athletic performances (Holmes & Collins, 2001). In the TIMP+cMI condition, the therapist demonstrated the selected activity using the individual's preferred tempo for executing that particular activity. However, action representations that are still in the formative stage may require longer time periods than the cMI condition provided, resulting in poorer performance outcomes. Fifth, as learning evolves, motor imagery content needs to be updated to maintain functional equivalence (Holmes & Collins, 2001). While Harris and colleagues (2015) found that some studies adopted a standardized approach without updating content according to individual progress, therapists in the TIMP study selected and modelled actions the participant had actively practiced in the immediately preceding 30-minute session. Sixth, memory trace may be strengthened by emotionally motivating tasks (Harris & Hebert, 2015); enjoyment of the TIMP activities may have encouraged more active participation during MI review. Finally, the motor imagery perspective adopted in most rehabilitation studies involved first person, internal kinesthesis (Harris & Hebert, 2015). TIMP study participants were asked to engage in motor imagery rehearsal of the demonstrated exercise they had previously practised, and this would presumably have fostered an internal, first-person perspective. The externally driven, auditory modality would have dominated in the cMI condition, and this may have hindered multimodal processing. Sathian (2004) comments that multisensory emulators, in contrast to Grush's (2004a) proposal of amodal emulators, preserve the nature of individual sensory modalities, accounting for multisensory integration, coordinate transformation, and cross-modal recruitment during imagery. Flexibility to facilitate multisensory emulation was built into the MI condition, which may have led to stronger performance outcomes.

5.3.4 Study Limitations

This study had a number of limitations that may have impacted results. Due to time constraints, the number of participants had to be capped at 30, with only 10 participants per arm, hence it was a small clinical trial. In addition, as a result of slow initial recruitment and logistical issues, the number of training sessions had to be abbreviated. The original plan was to include 12 training sessions over four weeks, as a longer time frame with more sessions would have been preferable for participants at the chronic stage. However, this had to be reduced to nine training sessions over a three-week period. Furthermore, the facility where the study was conducted was also a music practice building, and rooms were not sound proof. There were occasions when driving rhythmic music from overhead practice studios interfered with rhythmic auditory entrainment during active practice and attention/focus during motor imagery components of training. Finally, there were no follow-up evaluations following the final post-training assessment to ascertain the stability of training effects. A minimum of one retention assessment, conducted three months after training completion, would have been preferable.

5.3.5 Future Directions

While results of the TIMP study are encouraging, the sample size of 30 participants was small, and there were no follow-up assessments to ascertain stability of effects. Several systematic reviews have indicated the need for high-quality RCTs with consistent comparators (D'Anci et al., 2019; Hatem et al., 2016; Pollock et al., 2014). Hatem and colleagues (2016) suggest that to have sufficient scientific evidence for a meta-analysis, >500 participants is needed. Progressive staging of pilot studies is required to build a better foundation for larger clinical trials (Dobkin, 2009). Krakauer and colleagues (2012) note the need for more mechanistic phase II studies prior to conducting phase III trials. The Stroke Recovery and Rehabilitation Roundtable (Kwakkel et al., 2017) recommends outcome measurement tools to be used, including kinetic and kinematic quantification to distil differences between compensation and restitution. These recommendations will facilitate meta-analyses and help build consensus for best practices moving forward.

5.3.6 Conclusion

The primary goal of stroke rehabilitation is to help each individual optimize their physical and psychological performance, in order to regain functional independence and be able to participate once again in community life (Kwakkel et al., 2004). While post-stroke recovery was once thought to plateau after six months, recent studies have indicated significant positive gains in motor, cognitive, and psychosocial domains at the chronic stage (Teasell et al., 2012). The current study investigated the efficacy of TIMP interventions, with and without motor imagery, on motor outcomes for persons with chronic, post-stroke hemiparesis. Although the participants in this study had a wide range of impairments and functional abilities, significant gains were made in a relatively short period of time, not only on primary motor outcome measures, but also in cognitive and affective domains. TIMP interventions therefore provide a comprehensive, holistic approach to rehabilitation, one that is in keeping with the ICF model (World Health Organization, 2002). In addition, the high retention rate, with participants expressing regret when the study was over, indicated strong levels of compliance and engagement. Across the globe there are millions of people living with post-stroke disability (Johnson et al., 2019), placing added strain on existing healthcare resources (Feigin & Vos, 2019). There is an ongoing need for provision of accessible, low-cost neurological rehabilitation services (Sihvonen et al., 2017). Results of the current study support implementation of a TIMP-based, Neurologic Music Therapy approach, in conjunction with motor imagery, as a viable and cost-effective means of addressing chronic, post-stroke rehabilitative goals.

Appendices

Appendix A: Definitions of Terms

Action simulation, Motor imagery:

- Action simulation – the internal representation of motor programs without involving overt action. Simulation theory predicts similarity in neural terms between overt action execution and covert action simulation representing future action, in which the motor system is also activated, even though overt action does not necessarily follow (Jeannerod, 2001)

- Motor imagery – the representation of a motor act is rehearsed internally within working memory without motor output (Decety & Grezes, 1999). This covert stage includes the action intention, action plan, and action consequences on the individual organism and on its environmental context (Jeannerod, 2001).

Disability adjusted life years (DALY):

- A composite measure of disease burden yielded by summing years of life lost (premature mortality) and years lived with disability (Kyu et al., 2018)

Degrees of freedom:

- Bernstein's concept of coordination and regulation (Bernstein, 1967) interpreted as "the number of available control variables (degrees of freedom) (Latash, 1993, p. 206)

Entrainment, Synchronization:

- Entrainment refers to alignment of oscillating system(s) to an external rhythm with primarily unidirectional interaction, whereas synchronization refers to bidirectional coupling of oscillators (Lakatos et al., 2019).

Feedforward, Feedback control:

- Feedforward control - predictive control based on advance planning that does not incorporate sensory feedback (Bastian, 2006)
- Feedback control – error-driven, reactive control that uses sensory input to make movement corrections (Wolpert et al., 2013)

Impairment, Disability, Functioning:

- Impairment – significant deviation or loss in body function or structure

- Disability – *International Classification of Functioning, Disability and Health* (ICF) umbrella term for impairments, activity limitations and participation restrictions

- Functioning – ICF umbrella term referring to all body functions, activities and participation (World Health Organization, 2002)

Internal models:

- Representations of the relationship between the body and the environment: inverse models specify the motor commands required to produce a behavioural goal; forward models predict behavioural outcomes through simulation, using efference copy, of the interaction of the motor system with its environment (Wolpert et al., 2013)

Motor control, Motor learning, Motor recovery:

- Motor control – the study of how movement is controlled by the central nervous system, which organizes coordination of the many individual muscles and joints, and by utilization of sensory information, both from the body and from the environment (Schmidt & Lee, 2011)

- Motor learning – relatively permanent changes in how movements are produced as a result of practice or experience (Schmidt & Lee, 2011)

- Motor recovery – involves the restitution or repair of structures or function, such that premorbid movement patterns reappear, using the same end effectors and joints for accomplishing tasks as would be used by individuals without disability (Levin et al., 2009)

Neuromotor noise:

- uncontrolled variability, or unpredictable noise, in the motor system (De Jong & Van Galen, 1997)

Neuroplasticity:

- ability of the nervous system to reorganize structure, function, connections in response to intrinsic or extrinsic stimuli (Cramer et al., 2011). In cognitive neuroscience, the term plasticity refers to experience or training-induced structural and functional changes in the brain that impact behavior (Herholz & Zatorre, 2012).

Paresis:

- Reduced ability to activate spinal motoneurons voluntarily (Beebe & Lang, 2008)

Priming:

- Prior experience with the same or related stimulus which changes subsequent speed, bias or accuracy of processing (Henson, 2003)

Self-efficacy:

- Belief in one’s capability to carry out a behavior (American Heart Association/American Stroke Association, 2016)

Sensorimotor transformations:

- Circuits of motor commands, causing muscular contraction to generate movement, and sensory inputs, including extrinsic and intrinsic information (Wolpert et al., 2013)

Sonification:

- Mapping physiological and physical data onto psychoacoustic parameters to access, either on- and/or offline, biomechanical information that would otherwise not be available (Schaffert et al., 2019)

Synergy:

- A group of individual degrees of freedom behaving as a single functional unit (Turvey, 2007)

- Pathological synergy – reduction in number of coordinated muscle patterns; remaining coordinated muscle patterns are more fixed or constrained (Santello & Lang, 2015)

Task-specific training:

- Rehabilitation approaches involving repeated practice of specific functional tasks (Langhorne et al., 2011)

Therapeutic Instrumental Music Performance:

- Simulation through structured musical instrument playing of fundamental movement patterns that form the basis for functional task performance. The basic design is comprised of three key elements: 1) the organization and planning of movement in time and space, as well as force dynamics, is facilitated by a clearly pulsed musical structure, with melodic, harmonic, and dynamic components (2) instruments are selected and played in a manner that will enhance therapeutic goals (3) instruments are positioned or spatially arranged to facilitate optimal mapping of the targeted movement (Thaut, 2005).

Appendix B: Protocol for TIMP Study

All participants receive 30 minutes of active TIMP. Exercises will involve playing a variety of instruments (e.g., drums, rototom, tambourine, maracas, cabasa, castanet, electronic digital touch tablet, keyboard) targeting gross and fine motor control. Spatial configurations of instruments and therapeutic sequences of playing will be adjusted according to each participant's needs.

Gross Motor Control Exercises:

1. shoulder abduction/adduction
2. shoulder flexion (0-90 degrees)/extension
3. elbow flexion/extension

Fine Motor Control Exercises:

4. wrist pronation/supination
5. wrist dorsiflexion/volar flexion
6. digit flexion/extension
7. digit abduction/adduction

Improvisatory activity:

8. improvisation on electronic digital touch tablet or percussion instruments

Instruments are arranged in advance so that only minor adjustments are needed.
An accelerometer is placed on the participant's wrist prior to beginning the exercises.

Session 1:

A. Therapist demonstrates the target movement on instrument(s) for the first gross motor task, then asks participant to play. The therapist uses a tap metronome to determine the tempo selected by the participant and records beats per minute (BPM) for the exercise. The therapist also adjusts the positioning of instrument(s) if required.
B. Therapist sets the metronome on subdivisions for the BPM selected so that the participant will hear the subdivisions of the beat while performing the exercise. The therapist asks the

participant to listen to the beat/musical facilitation, then begin the exercise. The therapist observes the participant to note if further positioning adjustments are needed.

C. Therapist provides rhythmic musical facilitation at the tempo established by the participant. The therapist observes the participant closely throughout to monitor and respond if there are any signs of distress.
D. Repeat A-C for remaining gross motor exercises followed by fine motor exercises.
E. The participant is invited to improvise on the electronic digital touch tablet or percussion instrument(s) at a self-selected tempo, with music facilitation provided by the therapist, who maintains a steady beat at the participant's self-chosen pace.

Sessions 2 – 12:

A. Using the tempo previously selected by the participant for the first gross motor movement, the therapist demonstrates the task. The participant is then invited to play at the same tempo with the metronome, while the therapist makes any necessary adjustments to instrument positioning.
B. The therapist provides rhythmic musical facilitation while continuing to monitor the participant closely.
C. Complexity of the task may be increased; e.g. changing positioning of instruments, altering tempo
D. Repeat A-C for remaining gross motor exercises followed by fine motor exercises.
E. The participant is invited to improvise on the electronic digital touch tablet or percussion instrument(s) at a self-selected tempo, accompanied by the therapist, who maintains a steady beat at the participant's self-chosen pace.

Final fifteen minutes:

Group 1 participants review gross and fine motor tasks practiced in the first thirty minutes through active playing. The therapist first demonstrates the task to be reviewed using a metronome set at the tempo previously selected by the participant. The participant is then asked to play at the established tempo. The therapist provides rhythmic musical facilitation.

Group 2 participants review motor tasks practiced in the first thirty minutes using sensory enhanced motor imagery (SEMI). The therapist first demonstrates the task to be mentally rehearsed using a metronome set at the tempo previously selected by the participant. The participant is then asked to engage in motor imagery of the exercise while listening to the metronome. Gross and fine motor exercises are each rehearsed using SEMI.

Group 3 participants review motor tasks practiced in the first thirty minutes using motor imagery (MI). The therapist first demonstrates the task to be mentally rehearsed. The participant is then asked to engage in motor imagery of the exercise. Gross and fine motor exercises are each rehearsed using MI.

Appendix C – Detailed Protocol

Detailed Protocol for TIMP Study: **ID#: ___________________________** **Date: _____________________________________**

Metronome beat to be played at participant's preferred pace for each exercise, using subdivision function.

Legend: **A** – Autoharp; **K** – Keyboard; **V** - Vocals; **D** – Drums; **T** - Tambourine; **R** - Recorded music from drum set

	Beats/ Min	**Goal**	**Activity**		**# of Reps**	**Instruments/Set-up**
1		**Shoulder abduction/ adduction**	a) Chair placed sideways to the table. Place hand tambourine on affected hand. With elbow at 90° and forearm pronated in a comfortable seated position, raise affected arm, placing forearm on table, parallel to table edge; return to initial position. Repeat. b) With pronated forearm and hand on table, parallel to edge of table, raise and place forearm flat on drum, hand and wrist hanging over edge. Return to table top. Repeat. (Height of drum depends on level of difficulty required.)	WMFT 1 WMFT 2		a) hand tambourine b) bongo drum (higher) or bodhran (lower) **K**
2		**Elbow extension/ flexion (side)** (a or b)	a) wrist and forearm may be placed on towel on table for ease of sliding. Place hand tambourine on affected hand. Extend elbow to side so that hand reaches drum. <u>Elbow can be lifted off table</u>. Shoulders are level to prevent leaning with trunk. Return to starting position. b) extend elbow with block touching forearm throughout extension till it comes in contact with drum. Therapist places block in cup of hand for return flexion	WMFT 3 WMFT 4,8		-hand tambourine, bongo drum placed on its side on nonslip surface, towel —wooden block **V**

3		**Elbow extension/ flexion (front)**	-participant is seated facing the table, chair in front-close position, so that participant's back remains in contact with back of chair. Place affected hand on bodhran with heel of hand just inside closest rim of drum. Slide hand towards far rim. Return to starting position and repeat. May assist movement by placing unaffected hand over affected hand.	(warm-up for Ex. #4 and #5)		-bodhran on non-slip surface **K**

4		**Pronation/ supination**	a) participant is seated facing the table, forearm on the table, elbow at 90°, shoulder at 0°. Alternate pronation, supination. Trainer may hold tambourine(s) in fixed position for participants with limited range of motion (ROM). b) Repeat with elbow at 0°, shoulder at 30°-90° flexion.	FM III FM IV		-2 tambourines placed side by side on table, first close (a), then further away (b) **V and/or K**
5		**Elbow flexion/ extension (front), shoulder flexion** (forearm pronated)	a) begin with hand in lap, lift hand to drum, placing heel of hand and fingers on drum, return to starting position b) move hand from closer drum to higher drum(s) and back to closer one	WMFT 5, 6		-drum set **K**
6		**Shoulder abduction/ adduction 0°- 90°- 0°**	-holding drumstick, or with hand tambourine strapped to top of hand, raise arm to side to touch tambourine on stand. Measure height of tambourine. Forearm is pronated, elbow is at 0°.	FM IV		-hand tambourine or drumstick; tambourine on stand with chair positioned beside **V, A**

7		**Shoulder flexion 0°-90°, shoulder extension**	- holding cylindrical shaker, move arm forward to touch tambourine positioned in front of affected arm, then extend back to tap wall (or tambourine held by trainer) behind. Elbow is at 0°, pronation/supination at 0°. Repeat. - measure height of tambourine for front end point; distance of chair from wall for back end point. For the left affected arm, use wall immediately adjacent to small table. For the right affected arm, use wall to left of door, avoiding door area.	FM III		-cylindrical shaker (may be strapped to hand) or rainstick - tambourine mounted on stand - wall or tambourine as end point at back **V, A**

8a 8b		**Flexor synergy /Extensor synergy** **Mixing synergies**	- hand from tambourine on contralateral knee to tambourine by ipsilateral ear and back **or** - participant sits slightly forward in chair so that bodhran can be placed immediately behind the participant. - 1) Participant taps hand on tambourine on lap, then (2) reaches back to tap bodhran, then (3) slides tips of fingers on drum towards drum edge at centre of back. Reverse motion and repeat. Tambourine may be held by trainer at a comfortable distance for participant in place of bodhran to accommodate those with limited ROM	FM II FM III		-tambourine on contralateral knee held by participant's unaffected hand; tambourine by ipsilateral ear held by trainer -tambourine on lap, bodhran positioned by trainer against chair back so that edge of drum reaches participant's spine. Second tambourine or drum may be held by trainer in place of bodhran **V**
9		**Mass flexion/ extension**	-strike drum with fist, then open and extend fingers, striking drum with palm of hand. Variation: a) May practise with (1) fingertips on drum, then (2) lowering palm and fingers to touch drum, (3) flexing fingers, and (4) extending fingers again. Repeat. b) Participant may extend elbow to 0° at side (shoulder at 0°) so that fingers are relaxed at side. Trainer holds hand drum at comfortable angle for exercise.	FM C		- drum set or hand drum **V, K**

10		**Wrist - dorsiflexion/ volar flexion**	-elbow at 90°, forearm resting on arm of chair or angled over corner of table, wrist dangling over edge. Bells strapped to palm of hand or hand tambourine. Alternate dorsiflexion and volar flexion. Hold in dorsiflexion position. Therapist checks to see if person can maintain position against slight resistance. Repeat motion. **or** -Place hand flat on drum. Alternate dorsiflexion and volar flexion, the latter by moving onto fingertips **or** -holding musical spoons or with spoons strapped to affected hand, play spoons by tapping against upper leg (volar flexion) and tapping against unaffected hand (dorsiflexion). Elbow of affected arm may rest on arm of chair.	FM B		-bells strapped around hand or hand tambourine -rototom at appropriate height for seated participant -musical spoons **V, K**
11		**Wrist circumduction**	-rotate wrist holding head of maraca. Tap tambourine on stand at top of movement using handle of maraca. -rotate four x in each direction then switch.	FM B		-maraca, egg shaker, or bells strapped around hand -tambourine on stand
12a		**Cylinder Grip**	- hold end of cabasa in palm with fingers on beads. Rotate cabasa using unaffected hand on handle to encourage active grip in affected hand	FM C - D, WMFT 9,15		cabasa **V, K**
12b		**Cylinder Grip with Elbow flexion**	- Grip large claves, strike together, raise clave in affected hand to just above shoulder height to hit small drum or tambourine held by trainer behind ipsilateral ear. Return to initial position and repeat. **or**			large claves, small drum or tambourine **V**
12c		**Spherical Grip**	-with forearms resting on table or arms of chair, grip head of maraca, fingers in abduction, thumb opposed. Practice wrist dorsiflexion/volar flexion, wrist circumduction, or pronation/supination. Therapist may take handle of maraca in affected hand and give it a slight tug to see if participant can	FM C -E		maraca(s) **V**

			continue to grip. May practice with just affected hand or both hands simultaneously.			

13a 13b		**Grasp - 3 jaw chuck** **Grasp - thumb adduction**	Hold clapper between thumb and 2nd and 3rd fingers - open and close in rhythmic pattern -hold pick between thumb and 2nd MCP joint with thumb and fingers straight, point of pick facing down, Participant plays chord with unaffected hand.	WMFT 10, 12 FM C - B		hand clappers **V, A or K** autoharp, pick **V**
14		**Grasp - flexion in PIP and DIP**	hook grip - hold drum or tambourine in affected hand, and strike drum with increasing intensity with unaffected hand or drumstick	FM C - A, WMFT 17		buffalo drum or tambourine, may use drumstick **K**
15		**Grasp - pincer**	Finger cymbals on thumb and index finger. Forearm resting on arm of chair or diagonally over corner of table. Clap cymbals together in rhythmic pattern. -continue while alternating pronation/supination -with autoharp on lap, hold pick in affected hand between pad of thumb and index finger, and draw across strings, holding chord with unaffected hand.	WMFT 11, 13, 15 FMC C - C		finger cymbals **V, T** (therapist models pronation/supination) autoharp, flexible pick or firmer pick **V**

16		**Finger individuation**	Place castanet on thumb, with strap facing towards participant. Tap the castanet, first with the little finger, then with the fourth, third, and index fingers. Practice playing keys on keyboard successively, beginning with thumb. May practice simple patterns; e.g., alternating thumb and index, third, fourth, or fifth finger. Press and hold key(s) down using one or more fingers. Trainer may gently try to raise key(s) as participant holds key(s) down. Practice playing kalimba with index, third, fourth and fifth fingers. May create simple patterns alternating fingers. Pluck open strings of ukulele using fingers successively Play onscreen keyboard, drums, strings or guitar using successive finger movements	FM C WMFT 10-13		castanet **V, A or K** keyboard **K** kalimba **V, D** ukulele, **V, A or K** Garageband on iPad **V, K**
17		**Shoulder flexion, elbow extension/ flexion** (forearm pronated)	-reach with affected hand to top row, back to closest row, to side, and centre. Repeat pattern. -continue with participant tailored or created pattern	WMFT 16 FM A-III		Sonata **V, A**
18		**Sideways bend**	-participant is seated in chair with arm rests. Buffalo drum is placed to one side and slightly forward. Bend sideways with elbow flexed at 90° until elbow joint is parallel to seat of chair. Extend forearm to hit drum, then flex elbow and tap side of chair by seat. Repeat. Change to other side and repeat.	TIS	4 each side	-2 buffalo drums and rounded drumsticks (may be attached to palm of affected hand) -therapist stands behind to monitor participant's balance **R**

19		**Trunk rotation**	-participant rotates upper trunk to strike drum on opposite side to hand, beginning with hemiplegic side. Shoulder should be moved forward on side of hand that is striking the drum.	TIS	6 (3 each way)	- rototom or drum set **K or R**

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