Cyprus
University of
Technology

Faculty of Health Sciences

Doctoral Dissertation

Brain Stimulation and Computerized Working Memory Training on Language Recovery in People with Aphasia

Despina Kranou-Economidou, B.S., M.S., CCC-SLP

Limassol, June 2020

CYPRUS UNIVERSITY OF TECHNOLOGY

FACULTY OF HEALTH SCIENCES

DEPARTMENT OF REHABILITATION SCIENCES

Doctoral Dissertation

Brain stimulation and computerized working memory training on language recovery in people with aphasia

Despina Kranou-Economidou, B.S., M.S., CCC-SLP

Limassol, June 2020

Approval Form

Doctoral Dissertation

Brain stimulation and computerized working memory training on language recovery in people with aphasia

Presented by

Despina Kranou-Economidou, B.S., M.S., CCC-SLP

Supervisor: Faculty of Health Sciences, Professor Maria Kambanaros

Signature _____

Member of the committee: Professor Christakis Damianou

Signature _ _____

Member of the committee: A/Professor George Spanoudis

Signature _____

Cyprus University of Technology

Limassol, June 2020

Copyrights

Acknowledgements

ABSTRACT

Conventionally, aphasia, the language disorder following brain damage which is frequently accompanied by deficits of working memory (WM), is treated with traditional language therapy to improve receptive and expressive language skills. Many times, though improvement of language abilities for people with aphasia (PWA) is slow, and PWA end up in rehabilitation programs for long periods of time with a big economic burden and a slow improvement. As technology is improving though, it is essential for research to look into other ways to support aphasia rehabilitation. The modern technology of non-invasive brain stimulation equipment, the Transcranial Magnetic Stimulation (TMS) and a well-established computerized cognitive training program, *RehaCom,* were used as a joint treatment method to facilitate language recovery, and in turn have a positive effect on quality of life (QoL). The treatment reported in this thesis is the first to be used in PWA.

The specific goals were to investigate whether the application of excitatory TMS to the left dorsolateral prefrontal cortex (LDLPFC) followed by computerized WM training lead to near-transfer on WM tasks and non-verbal intelligence, and far-transfer on language tasks, narratives, functional communication and QoL.

Although the results revealed a mixed and indistinct pattern of training and transfer effects across participants this treatment showed a positive effect in neurorehabilitation of PWA. While all participants showed improvements in cognitive and linguistic tasks, the most noteworthy observation was that two of the participants with global aphasia significantly improved in non-verbal intelligence and three participants showed a modest improvement in the WM screening task, specifically in the number of correct responses. Overall findings showed a significant trend for improvement and a significant difference between the treated and untreated periods in non-verbal intelligence, accompanied with significant and non-significant trend for improvement in language abilities. The treatment results are encouraging, and it is clinically and theoretically important to further investigate whether this treatment will be taken on as an innovative method for post-stroke aphasia rehabilitation in the future and convert it from an efficacious to an efficient treatment in the clinical setting to improve language functions.

Keywords: Aphasia, Language, Working Memory, TMS, Non-verbal intelligence

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACC	Anterior Cingulate Cortex
BcoS	Birmingham Cognitive Screen
BDI-II	Beck's Depression Inventory
CACR	Computer Assisted Cognitive Rehabilitation
Cc	Circular Coils
cTBS	Continuous Theta Burst Stimulation
CUT	Cyprus University of Technology
CVA	Cerebrovascular Accident
DLPFC	Dorsolateral Prefrontal Cortex
ECT	Electroconvulsive Therapy
EMG	Electromyography
F8c	Figure-Of-Eight Coil
FDI	First Dorsal Interosseous
fMRI	Functional Magnetic Resonance Imaging
Gf	General Fluid Intelligence
HRQL	Health-Related Quality Of Life
IADL	Instrumental Activities Of Daily Living
IST	Internal States
iTBS	Intermittent Theta Burst Stimulation
LDPFC	Left Dorsolateral Prefrontal Cortex
LH	Left Hemisphere
M1	Motor Cortex
MB	Multiple Baseline
MCA	Main Concept Analysis

MEP	Motor Evoked Potential
MEP	Motor Evoked Potential
MNI	Montreal Neurological Institute
NAA	National Aphasia Association
NCD	Non-Communicable Diseases
NHP	Neurologically Healthy People
NIBS	Non-Invasive Brain Stimulation
P-A	Posterior-To-Anterior
PC	Personal Computer
PFC	Prefrontal Cortex
pSTM	Phonological Short-Term Memory
PWA	People With Aphasia
QoL	Quality Of Life
RCTs	Randomized Controlled Trials
RMT	Resting Motor Threshold
rTMS	Repetitive Transcranial Magnetic Stimulation
SAH	Subarachnoid Haemorrhage
SAQOL-39	Stroke and Aphasia Quality of Life Scale-39 Item
SAQOL-39g	Stroke and Aphasia Quality of Life Scale-39 Item Generic
SBR	Spontaneous Biological Recovery
sSTM	Semantic Short-Term Memory
STM	Short-Term Memory
TBI	Traumatic Brain Injury
TBS	Theta Burst Stimulation
TES	Transcranial Electrical Stimulation

TiDier	Template for Intervention Description and Replication
TMS	Transcranial Magnetic Stimulation
WEST	WEighted Statistics
WEST-ROC	WEighted Statistics Rate of Change
WHO	World Health Organization
WM	Working Memory
WOME	Working Memory

1   GENERAL INTRODUCTION

1.1   Prevalence

According to the World Health Organization (WHO), among the 17.5 million deaths due to Non-communicable Diseases (NCD) an estimated 6.7 million were due to strokes (WHO, 2014). While globally stroke is the second leading cause of death above the age of 60 years, it is also the second leading cause of disability, after dementia leaving five million people permanently disabled with loss of vision and / or speech, paralysis and confusion (Stroke, 2017). In Greece an estimate of 30,000-35,000 new cases of stroke occur annually (Neuroradiology, 2017). In Cyprus, an estimate of 1,200-1,400 new cases of stroke per year are recorded (Demetriou, 2016). A stroke or cerebrovascular accident (CVA) is caused when the blood supply to the brain is interrupted either when a blood vessel bursts (haemorrhagic) or is blocked by a clot (ischemic) causing damage or death to the brain cells. The National Stroke Association (2017) accounts the 87% of strokes to be ischemic and while haemorrhagic strokes are less common, they are accountable for about 40% of all stroke deaths. One of the most common consequences of CVA is aphasia, which is a loss of the ability to produce and/or understand spoken or written language, and it affects up to 38% of ischemic strokes (Pedersen et al., 1995). Evidence indicates that language function recovery is stable within 2 weeks in those with initial mild aphasia, within 6 weeks in those with moderate, and within 10 weeks in those with severe aphasia (Pedersen et al., 1995).

1.2   Theoretical Background

Although working memory (WM) was linked to be at fault for language-processing difficulties seen in people with aphasia (PWA) for over 20 years, initial indications of this relationship were dated almost 100 years ago (Kasselimis, 2015). There is now a better understanding of how a WM impairment at the level of information maintenance and manipulation interacts with language abilities, as it clearly has an impact on communication, which in turn has a negative chain reaction in the person's quality of life (Nicholas, Hunsaker, & Guarino, 2017). A great deal of research is moving away from the traditional notion that aphasia is considered to be an acquired language disturbance and is exploring it as a cognitive disorder with pronounced language deficits (McNeil, Odell, & Tseng, 1991). Related to that, verbal WM training has been found to modulate prefrontal and parietal activity levels and structural connectivity in

healthy adults (e.g. (Olesen, Westerberg, & Klingberg, 2004; Takeuchi et al., 2010) and these neural regions have been found to also support language functioning and aphasia recovery (e.g. (e.g. Cornelissen et al., 2003; Fridriksson, 2010; Meinzer et al., 2008). Based on the evidence, memory training may have a positive effect for many individuals with aphasia in terms of both neural and behavioural outcomes. In this study, the primary objective was to assess the efficacy of a neurorehabilitation program by using Transcranial Magnetic Stimulation (TMS) followed by a computerized WM training program RehaCom, to excite the left dorsolateral prefrontal cortex (LDPFC), the area responsible for WM, to determine if this can improve language deficits in PWA post stroke. Repetitive transcranial magnetic stimulation (rTMS) administered to the left dorsolateral prefrontal cortex (LDLPFC) has shown to improve working memory (WM) abilities (e.g. Pearce et al., 2014), while at the same time, WM is has a relationship with language skills (Wright & Fergadiotis, 2013). Therefore, this research considers it optimal to combine TMS with computerized WM training, in order to improve language abilities in PWA because of neurological damage. Singal, Higgins, and Waljee (2014) advocate that intervention studies can be placed on a continuum, with a progression from efficacy trials to effectiveness trials. They argue that efficacy studies explore an intervention's benefits and harms when performed under highly controlled conditions, while they argue that effectiveness studies investigate interventions under a more real-world practice approach. While more than 1000 randomised controlled trials (RCTs) have been conducted in search for new therapies that can be incorporated into routine clinical practice (McIntyre et al., 2016), their timing seems to be one factor that may limit the RCTs translational impact of stroke rehabilitation (Stinear, 2016). In an earlier review study (Stinear, Ackerley, & Byblow, 2013) found that over half of motor rehabilitation RCTs were conducted with patients who were at least 6 months post-stroke, when rehabilitation services were no longer available. It is therefore important to conduct rehabilitation trials during the initial days and weeks after stroke because this is when spontaneous biological recovery (SBR) is taking place (Krakauer, Carmichael, Corbett, & Wittenberg, 2012) and when rehabilitation is delivered in the 'real world' (Stinear, 2016). Testing an intervention at the time of its intended use is crucial for evaluating its efficacy as well as its feasibility in clinical practice (Stinear, 2016). This study is investigating the efficacy of the iTBS application to the LDLPFC followed by computerized WM training in the subacute and chronic stage post-stroke in PWA.

1.3 Aphasia

Aphasia is one of the most common consequences of stroke and refers to impairments that affect the comprehension and expression of spoken and/or written language, with frequent co-occurring cognitive deficits (Salis, Kelly, & Code, 2015). PWA, who exhibit lesions inside the ''language zone'', demonstrate different characteristics depending on the location and degree of the lesion and their language may be characterized by verbal and/or written production limitations with relatively well-preserved comprehension, as in Broca's aphasia, or by auditory comprehension limitations with relatively preserved verbal production, as in Wernicke's aphasia (Connor & Obler, 2002). To have an adequate definition of aphasia it is critical to mention four primary facts: it is neurogenic, it is acquired, it affects language, and it excludes general sensory and mental deficits (Hallowell & Chapey, 2008). Aphasia ranges from severe, where communication is almost impossible, to very mild. It is possible for aphasia to affect a main single aspect of language use, such as the ability to retrieve the names of objects, or the ability to put words together into sentences, or the ability to read, but usually several aspects of communication are impaired (NAA, 2017).

1.4 Types of Aphasia

Dronkers and Baldo (2009) note that to be deemed with aphasia, the impairment must affect a range of language functions, including speech, comprehension, reading, and writing. A review of the classification subtypes includes Broca's aphasia, Wernicke's aphasia, conduction aphasia, global aphasia, anomic aphasia, and transcortical aphasia. They describe *Broca's aphasia* as a "non-fluent aphasia" due to telegraphic. slow, and deliberate speech, often with omission of grammatical markers but with relatively preserved comprehension. They carry on with *Wernicke's aphasia* which is also described as "fluent aphasia" because the person can speak spontaneously with a normal to fast rate of speech, and their speech rhythm and prosody (melody) are normal, but often unintelligible due to paraphasias which lack meaningful content. Additionally, comprehension is significantly impaired in all language modalities (i.e., spoken or written language. *Conduction aphasia* presents with fluent speech and relatively good comprehension, but with somewhat paraphasic speech and greatly reduced ability to repeat. Reading and writing, and naming, are also affected to a moderate degree (Dronkers & Baldo, 2009). They continue to describe *Global aphasia* as the most severe of all aphasia subtypes, with significant impairments across all aspects of language, namely impaired speech,

comprehension, repetition, naming, reading, and writing. Persons with global aphasia may be able to produce automatic or stereotypic responses (e.g., "yes" and "no") but do so unreliably. While people with any type of aphasia have difficulty naming things, people with *Anomic aphasia* are left with a persistent inability to produce the words for the specific things they want to talk about with vague circumlocutions and expressions of frustration while they have relatively preserved speech fluency, repetition, comprehension, and grammatical speech. Lastly, they describe the *Transcortical aphasias* as a group of aphasia syndromes which all commonly have a relatively preserved ability to repeat, despite other significant language deficits: a) *Transcortical Motor aphasia* is similar to Broca's aphasia characterized with nonfluent speech and relatively good comprehension, but with relatively preserved ability to repeat; b) *Transcortical Sensory* aphasia is similar to Wernicke's aphasia, characterized with fluent speech and poor comprehension but also a relatively preserved ability to repeat; and c) *Mixed Transcortical* aphasia is similar to global aphasia but with relatively preserved repetition.

1.5 Cognition in Aphasia

Cognitive function is impacted after stroke and generalized cognitive problems have been identified across all domains with attention, memory, language, and orientation being the most affected, accompanied by marked deficits in visuospatial skills and abstract reasoning (Tatemichi et al., 1994). Although aphasia is defined as an acquired language disorder, researchers are increasingly recognising the role of cognitive factors, such as attention, memory and executive function, in the rehabilitation of aphasia (Lambon Ralph, Snell, Fillingham, Conroy, & Sage, 2010; Seniów, Litwin, & Leśniak, 2009), Over the last decade, there is a growing interest in the relationship between language deficits and non-linguistic cognitive deficits as a result of left hemispheric stroke (Caplan, Michaud, & Hufford, 2013; El Hachioui et al., 2014; Salis et al., 2015; Vallila-Rohter & Kiran, 2013). Cumming, Marshall, & Lazar, (2013) consider how cognition is not a unitary concept but it integrates several areas, such as attention (focusing, shifting, dividing, or sustaining attention on a particular stimulus or task), executive function (planning, organizing thoughts, inhibition, control), visuospatial ability (visual search, drawing, construction), memory (recall and recognition of visual and verbal information), and language (expressive and receptive). They argue that these domains are not independent, which makes classification very complicated, and what represents a cognitive

domain is unclear - for example remembering a list of grocery items you have been told to buy is not just dependent on memory but also on attention and language. Feldman et al. (2003) showed that memory dysfunction is often not the most pronounced feature after stroke, about half of those with vascular cognitive impairment exhibit amnestic signs. Therefore, they suggest the need for a more useful assessment framework for classifying poststroke cognitive deficits with thorough information, rather than the accepted 'gold standard' of a battery of neuropsychological tests which is appropriate for dementia.

1.6   Working Memory

1.6.1   Working Memory in Aphasia

WM deficits are a significant area of cognitive processing deficits related with aphasia, but with major limitations in research primarily due to lack of established valid WM impairment measures for this population (Ivanova & Hallowell, 2014). Individuals with aphasia frequently show WM and short-term memory (STM) deficits, which in turn may adversely affect language symptoms and recovery, and consequently WM treatment may represent an efficient approach to addressing these individuals' cognitive and linguistic impairments (Martin, Kohen, Kalinyak-Fliszar, Soveri, & Laine, 2012; Murray, 2012). WM treatment for individuals with aphasia, however, has been scarcely studied despite previous studies showing that WM in individuals with aphasia can be improved with training (e.g. Martin et al., 2012; Martin et al., 2009; Mayer & Murray, 2002; Vallat et al., 2005).

1.6.2   Primary Working Memory Theory

Baddeley's theory (1992) defines WM as a multicomponent system that holds information temporarily and mediates its use in ongoing mental activities; it refers to a brain system that provides temporary storage and manipulation of the information required for complex cognitive tasks, including language comprehension, learning, and reasoning. Later, Baddeley (1996) defended that the notion of WM differs from that of STM in two ways: (a) WM is believed to comprise of a number of subsystems, instead of being a unitary module; and (b) substantial importance is given on its functional role in other cognitive tasks such as learning, reasoning, and comprehension.

The current study supports Baddeley's multicomponent system theory which was a theory that was first introduced and promoted by Baddeley and Hitch (1974), which suggested that short-term maintenance of information is controlled by two "slave systems", the phonological loop and the visuo-spatial sketchpad, and the supervision of information integration and the coordination of the slave systems are controlled by the "central executive". The phonological loop keeps phonological information and prevents its decay by constantly rehearsing its contents, resulting to the information being refreshed in an internal rehearsal loop (Baddeley & Hitch, 1974). The other slave system discussed by Baddeley and Hitch (1974), was the visuo-spatial sketchpad, which keeps visual and spatial information, as in constructing and manipulating visual images, or representing mental maps. This sketchpad was further divided into a visual subsystem, dealing with what is seen (i.e. shape and colour), and a spatial subsystem, dealing with location (Baddeley & Hitch, 1974). Furthermore, Baddeley & Hitch, (1974) discussed that the central executive is responsible to assign incoming information to one of the two storage subsystems and to coordinate, monitor, and make use of the information in the two subsystems. The central executive is the achiever and instigator of human cognition which assigns attention to a task and executes information storage and computational tasks within a given task (Caplan & Waters, 1999). An additional fourth component, the episodic buffer, was added by Baddeley (2000), which is responsible to keep representations that combine phonological, visual, and spatial information, and potential information not covered by the slave systems (**Figure 1.6.1**).
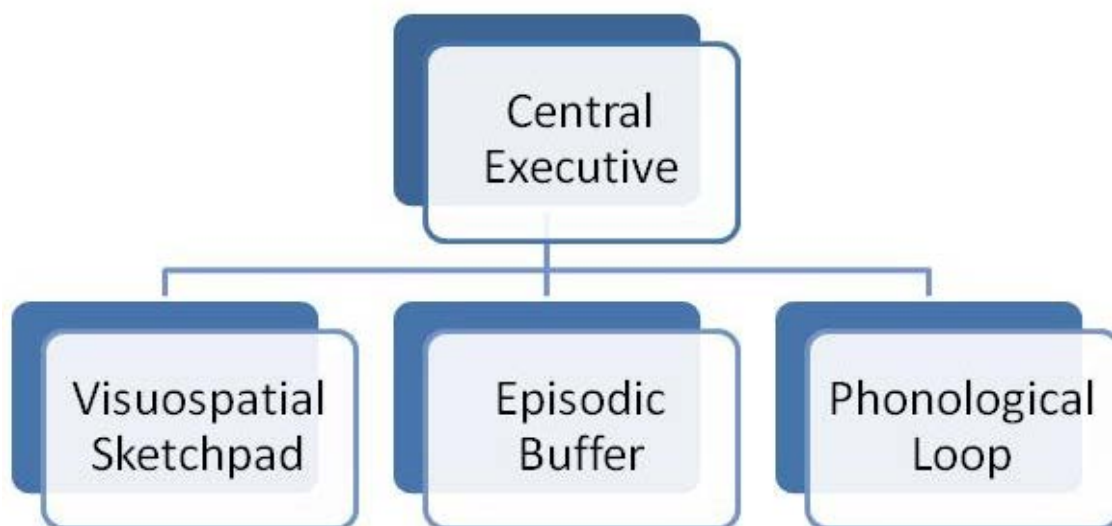
Figure 1.6.1. Baddeley's Multicomponent theory of WM (Baddeley, 2000).

In an attempt to link WM theories with language deficits in aphasia, evidence showed that WM interacts with language abilities and deficits in WM influence language performance (Baddeley, 2003; Murray, 2012). Murray (2012) explored the aphasia literature relating to direct or indirect STM and WM remediation, and found that PWA respond to STM and WM treatment with a possible positive affect on language abilities.

1.6.3   The Role of Dorsolateral Prefrontal Cortex in Working Memory

Kane & Eagle (2002) reviewed the pronounced agreement in the literature that the prefrontal cortex (PFC) paths, and possibly the dorsolateral prefrontal cortex (DLPFC) cells in specific, are critical for WM functions, and they discuss how the role of DLPFC in WM is to maintain information in a highly active, easily accessible state. They argue that this information maintenance is mainly important in the manifestation of interference, and it may be essential in blocking the effects of distraction. In the past, Smith, Jonides, & Koeppe (1996) proposed that the phonological loop primarily engaged regions in the left hemisphere, including the temporoparietal region and Broca's area, while the visuospatial sketch pad primarily engaged regions in the right hemisphere, including the frontoparietal cortex and the occipital cortex. More recently though it was discussed that working memory is the result of various combinations of processes and there are no unique processes or brain structures specific to WM (Eriksson, Vogel, Lansner, Bergström, & Nyberg, 2015), while others can even functionally describe it in different terms than working memory (i.e. D'Esposito & Postle, 2015; Jonides et al., 2008). Neuroimaging research has made advances in identifying the neurological substrates of WM, and functional neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) have been used by researchers to identify neural activation patterns occurring during working memory tasks (e.g. Carpenter, Just, & Reichle, 2000). Carpenter et al. (2000) investigated the neural activation patterns by using n-back task, where letters, spatial positions, or patterns were sequentially presented and were evaluated for their identity to an element that was presented n- items previously. They discussed how this task involves the phonological loop encompassing frontal (i.e. DLPFC) and parietal regions as it requires encoding, temporary maintenance and rehearsal, tracking of serial order, updating, and comparison and response processes. Soon after, Hartley, Speer, Jonides, Reuter-Lorenz, & Smith (2001) reported clear evidence of dissociations among working memory systems through neuroimaging studies, where they discussed presenting exactly the same stimuli with two different memory instructions; in one situation, the individual was to remember one aspect

of the stimulus (i.e. verbal identity) and in the other situation the individual was to remember a different aspect (i.e. location), which resulted in different patterns of cortical stimulation, showing strong evidence for distinct memory systems. Many research studies support that the fronto-parietal network involves the DLPFC, the anterior cingulate cortex (ACC), and the parietal cortex (PAR) as the working memory neural network (Chein, Moore, & Conway, 2011; Kim, Kroger, Calhoun, & Clark, 2015; Osaka et al., 2003; Owen, McMillan, Laird, & Bullmore, 2005). More precisely, the DLPFC has been largely implicated in tasks demanding executive control such as those requiring integration of information for decision-making, maintenance and manipulation/retrieval of information, and information updating (C. Kim et al., 2015). The ACC has been shown to act as an "attention controller" that evaluates the needs for adjustment and adaptation of received information based on task demands (Osaka et al., 2003), and the PAR has been regarded as an area involved in sensory or perceptual processing and in the storage of WM contents (Owen et al., 2005). Chai, Abd Hamid, & Abdullah (2018) attempted to translate the theoretical formulation of the multicomponent WM model (Baddeley, 2010) to specific regions in the human brain as depicted in **Figure 1.6.2** below. The DLPFC is known not only for its involvement in WM but also for its significant contribution to perform tasks correctly (Courtney, 2004; Pessoa, Gutierrez, Bandettini, & Ungerleider, 2002). Due to this involvement in multiple WM components, the DLPFC is a desirable target for neuromodulation in the context of WM training. Given that WM simultaneously participates in information processing and storage in order to achieve a cognitive target such as WM (Kane & Engle, 2002), the ability to carry out many activities of daily living is reduced when WM fails (D'Esposito & Postle, 2015). A large-scale meta-analysis of fMRI studies on WM (Wager & Smith, 2003) identified 86 peak activations reported by working memory studies within the DLPFC, with a geometric center of activation in the MNI coordinates $x = \pm 40$, $y = 34$, $z = 29$. The LH MNI coordinates were used in this study to stimulate the LDPFC ($x = -40$, $y = 34$, $z = 29$).
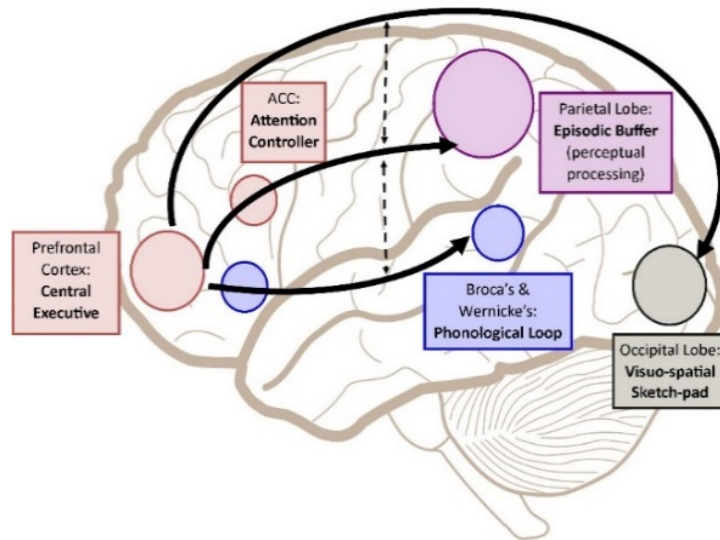
Figure 1.6.2. The multicomponent working memory model (Baddeley, 2010) represented simplified as implicated in the brain, in which the central executive assumes the role to exert control and oversee the manipulation of incoming information for intended execution. ACC, Anterior cingulate cortex. From Working Memory From the Psychological and Neurosciences Perspectives: A Review by Chai et al., 2018, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5881171/figure/F1/ Copyright © 2018 Chai, Abd Hamid and Abdullah.

1.6.4 Working Memory as related to Fluid Intelligence

General fluid intelligence (*Gf*) is the ability to solve novel reasoning problems and it is associated with comprehension, problem solving, and learning (Cattell, 1971). *Gf* is a complex human ability that allows for thinking adaptation to a new cognitive problem or situation (Carpenter, Just, & Shell, 1990), it is essential for a broad range of cognitive tasks (Gray & Thompson, 2004), and it is considered one of the most important factors in learning (Jaeggi, Buschkuehl, Jonides, & Perrig, 2008). Several studies have explored the positive link between WM training and *Gf* (e.g. Engle, Laughlin, Tuholski, & Conway, 1999; Friedman et al., 2006; Unsworth, Fukuda, Awh, & Vogel, 2014), while other studies debate this relationship (i.e. Harrison et al., 2013) Some research supports the notion that WM training is a promising way of increasing *Gf* (Jaeggi et al., 2008; Sternberg, 2008). Specifically, Jaeggi and colleagues (2008) reported gain in *Gf* when a WM training task, the ''dual *n*-back'' task, was used which involved multiple executive processes, including ones required to inhibit irrelevant items, ones required to monitor ongoing performance, ones required to manage two tasks simultaneously, and ones required to update representations in memory. The underlying neural circuitries provide evidence that there is a common ground between WM and *Gf* in that both seem to rely

on similar neural networks, most consistently located in lateral prefrontal and parietal cortices (Gray, Chabris, & Braver, 2003). Furthermore, research in healthy adults (Woolgar et al., 2010) has shown that domain-general regions, associated with attention, WM, cognitive control and *Gf*, are engaged for effortful language processing, including understanding or producing complex syntactic structures or ambiguous words (Fedorenko, 2014).

1.7 Non-Invasive Brain Stimulation (NIBS)

1.7.1 Transcranial Magnetic Stimulation

Merton & Morton (1980) revealed the possibility to electrically stimulate the motor areas of the human brain through the intact scalp [transcranial electrical stimulation (TES)], where a brief, high voltage electric shock was initiated to trigger the motor cortex and produce a rather synchronous muscle response known as the motor evoked potential (MEP). However, TES was painful because of activation of pain fibers in the scalp. Barker, Jalinous, & Freeston (1985) discovered that it was possible to stimulate both nerve and brain using external magnetic stimulation with little or no pain. TMS is a brief and powerful magnetic field formed by a strong electric current which circulates within a coil resting on the scalp, that penetrates human tissue painlessly and, if the current amplitude, duration, and direction are appropriate, it induces electric currents that can depolarize neurons or their axons in the brain (Hallett, 2007). This electric field produces a change in the transmembrane current of the neuron, which results to the depolarization or hyperpolarization of the neuron and the triggering of an action potential (Walsh & Pascual-Leone, 2003). During TMS, the stimulating coil is held over the subject's head and relatively large currents in targeted cortical areas of a person's brain via electro-magnetic stimulation are administered, with almost no resistance and, depending on the targeted brain area, neurons are depolarized and can generate various physiological and behavioural effects (Horvath, Perez, Forrow, Fregni, & Pascual-Leone, 2011). Depending on the stimulation parameters, TMS can excite or inhibit the brain, and can be used to map brain function and explore the excitability of different cortical regions (Hallett, 2000). The equipment comprises of a high current pulse producer, which is able to yield a discharge current of several thousand amperes that flows through a stimulating coil, creating a brief magnetic pulse with field strengths up to several Teslas (Lefaucheur et al., 2014). Large circular coils (Cc) have a wide action radius, but their use is limited if focal stimulation is desired

(Lefaucheur et al., 2014), whereas there is better focusing with a figure-of-eight coil (F8c), which reduces the stimulation zone to a few square centimeters (Thielscher & Kammer, 2004).

TMS can be applied one stimulus at a time (single-pulse TMS), in pairs of stimuli separated by a variable interval (paired-pulse TMS), or in trains, [repetitive TMS (rTMS); Rossi, Hallett, Rossini, & Pascual-Leone, 2009]. Single-pulse TMS can be used, for example, for mapping motor cortical outputs, studying central motor conduction time, and studying causal chronometry in brain-behavior relations; paired pulse TMS can be delivered to a single cortical target using the same coil or to two different brain regions using two different coils, or a peripheral stimulus can be paired with a single TMS stimulus known as paired associative stimulation (PAS), and can provide measures of intracortical facilitation and inhibition, as well as study cortico–cortical interactions; rTMS refers to regularly repeated TMS presented to a single scalp location (Rossi et al., 2009). The aforementioned authors describe 'fast' or 'high-frequency' rTMS states stimulus rates of more than 1 Hz, and the term 'slow' or 'low-frequency' rTMS represents stimulus rates of 1 Hz or less.

Single or paired pulse TMS causes neurons in the cortex under the location of stimulation to depolarize and release an action potential, and it produces muscle activity (motor evoked potential - MEP) if used in the primary motor cortex, which can be recorded on electromyography; but If used on the occipital cortex, 'phosphenes' (flashes of light) might be perceived by the patient, while the participant does not consciously experience any effect in most other areas of the cortex - except some slight alterations of the behavior (e.g., slower reaction time on a cognitive task), or possible brain activity changes if sensing equipment is used (Pascual-Leone et al, 2002). High-frequency rTMS (>1 Hz) has been shown to temporarily facilitate the neural activity, whereas low-frequency rTMS (≤1 Hz) revealed an inhibitory advantage in which rTMS modified the level of excitability of a particular cortical area beyond the duration of the rTMS train itself (Kobayashi & Pascual-Leone, 2003). Low frequency (i.e. 0.2-1 Hz) rTMS results to reduction of excitability in the targeted cortical region, while higher frequency (5-20 Hz) commonly improves brain excitability (Hallett, 2007).

Rothkegel, Sommer, & Paulus (2010) argued the importance of intervals during excitatory high frequency stimulation of conventional rTMS in determining excitatory after effect. rTMS protocols using short bursts of high frequency stimulation such as theta burst stimulation (TBS) (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005) indicate that the manifestation of short

breaks of a specific duration determines whether corticospinal excitability is facilitated or inhibited; while 40s of continuous TBS leads to inhibition, breaking up this sequence every 2s for 8s switches inhibition to facilitation (Rothkegel et al., 2010). It is possible that continued trains of 5 Hz rTMS first increase cortical excitability, resulting to inhibition instead of facilitation and breaks during the standard high frequency protocol after trains of limited duration might prevent the threshold surpass of the level of excitability and could change excitation into inhibition (Rothkegel et al., 2010). They concluded that there is a functional significance of utilizing breaks during high-frequency rTMS, while a prolonged continuous train of rTMS tends towards inhibition vs. the classical block design which leads to facilitation.

Recent developments in non-invasive brain stimulation (NIBS) techniques, such as TMS, have demonstrated interaction with spontaneous brain activity and related sensory-motor and higher order cognitive abilities through the use of a coil to deliver a brief and powerful magnetic pulse to the scalp (Pascual-Leone et al., 2011). TMS is a NIBS method of stimulating neurons by inducing weak electric currents by electromagnetic induction, and synaptic plasticity can be modified to briefly increase or decrease localized cortical activities when it is applied in rTMS patterns. RTMS is used to generate synaptic plasticity (Hoogendam, Ramakers, & Di Lazzaro, 2010) and has shown exploratory potential for post-stroke aphasia neurorehabilitation (Keser & Francisco, 2016). RTMS also signifies a new approach with the potential to regenerate the central nervous system (CNS) by enhancing neurogenesis in adults (Arias-Carrión, 2008). Their study was based on rTMS induced neurogenesis, neuronal viability and secretion of neuroprotective molecules in animal models of Parkinson's Disease.

The use of TMS in the field of cognitive neuroscience largely depends on its ability to transiently interact with the stimulated neural network, and it can be used with two distinct approaches: on-line stimulation and off-line stimulation (Miniussi & Rossini, 2011). The on-line stimulation is one of the two approaches used where there is simultaneous on-going cognitive processing interaction when rTMS is applied during the performance of a task, but with marked deterioration of cognitive performance while there is disruption of cortical activity (Sandrini, Umiltà, & Rusconi, 2011). In an off-line approach, the magnetic stimulation and task performance are dissociated in time, and the task is applied before or after the brain stimulation (Sack & Linden, 2003), in which case rTMS affects the modulation of cortical excitability (increase vs. decrease) and intents to change the cognitive performance (Miniussi & Rossini, 2011). Studies performed in normal subjects have considered that TMS may lead

to enhanced cognitive performance (Vallar & Bolognini, 2011). In their review they discussed how in healthy subjects, most of these effects were temporary (in the range of minutes), but repeated TMS in follow-up sessions, in combination with learning and plasticity processes, may prolong the facilitating effects past the end of the stimulation period and provide important opportunities for long-lasting positive effects (Miniussi et al., 2008). Additionally, Vallar & Bolognini (2011) noted how excitatory stimulation (i.e. intermittent Theta Burst; HF rTMS) systematically resulted in behavioural enhancement, whereas inhibitory stimulation (i.e. continuous Theta Burst; LF rTMS) resulted in a reduction of performance in the task of interest.

Recently though a new approach is being explored through the application of the theta burst stimulation (TBS) protocol as discussed in Huang et al. (2005) report. It's largely believed that TBS protocols produce more reliable, longer-lasting effects on cortical dynamics and on behavior than other standard forms of TMS (Demeter, Mirdamadi, Meehan, & Taylor, 2016). The TBS application is the delivery of very short, high-frequency stimulation pulses to the scalp at intervals, usually three stimulation pulses delivered at 50 Hz (gamma frequency) and repeated every 200 ms (theta frequency intervals of 5 Hz). When gamma frequency stimulation applied at a theta rhythm combination, it is believed to mimic theta-gamma coupling which in turn is assumed to play a role in cognitive functions such as working memory. In continuous TBS (cTBS) protocols, TBS is delivered in an uninterrupted train for 40 seconds. In intermittent TBS (iTBS), 2-second trains of TBS are repeated every 10 seconds, for approximately 190 seconds in total (Huang et al., 2005). TBS is the most commonly used method of patterned rTMS that produces a rapid facilitation of synaptic transmission in the stimulated cortex and can persist for over an hour after the initial stimulation session (Huang et al., 2005). These findings suggest that iTBS may lead to changes in ongoing neural dynamics at larger spatial scales that reflect changes in the functional organization of distributed functional networks (Papazachariadis, Dante, Verschure, Giudice, & Ferraina, 2014).

1.7.2   rTMS in Aphasia Therapy

Recent studies have been conducted in order to determine whether rTMS might be used as a therapeutic option in stroke rehabilitation (Georgiou, Phinikettos, Giasafaki, & Kambanaros, 2020). Szaflarski et al. (2011) used an excitatory stimulation protocol called intermittent theta burst stimulation (iTBS) to apply rTMS in moderate to severe chronic aphasia patients for 10 daily treatments of 200 seconds, targeting the left Broca's area. Their study resulted significant

improvements in language function after 2 weeks of stimulation that were associated with significant shifts of fMRI signal to the affected hemisphere. Allendorfer, Storrs, & Szaflarski (2012) performed a pilot study in order to investigate whether excitatory rTMS is able to stimulate changes in white matter structural integrity in language regions of aphasic stroke patients that were targeted with excitatory rTMS intervention using Diffusion Tensor Imaging (DTI). Their study resulted in left hemispheric increases in fractional anisotropy (FA) near the target stimulation sites for excitatory rTMS and near the regions that showed increased language fMRI activation in the previously reported fMRI and behavioral study (Szaflarski et al., 2011). These outcomes support their hypothesis that rTMS may stimulate improvements in the integrity of the white matter tracts underlying residual left hemispheric language areas. Allendorfer et al. (2012) concluded that the alterations in cortical excitability induced by excitatory rTMS may have improved neuronal function at the stimulation site, which resulted in improved cognitive performance. They reported that the increased integrity of the underlying white matter may reflect this improved cortical function. Cotelli et al. (2011) reported results from a pilot study of three chronic stroke patients who had non-fluent aphasia, where placebo or real rTMS was applied immediately followed by 25 minutes of individualized speech therapy. In their study, real rTMS consisted of high-frequency 20 Hz rTMS over the left dorsolateral prefrontal cortex for 25 minutes for a total of four weeks of intervention. Assessments took place at 2, 4, 12, 24, and 48 weeks post-entry/baseline testing, where they found a positive effect still present at 48 weeks after the beginning of the combined rTMS-speech therapy intervention. While their study provided supporting evidence of a long-lasting effect of combined rTMS and behavioral therapy to achieve successful outcomes in aphasia therapy, the small patient number was a major limitation (Cotelli et al., 2011). In another study, Thiel et al. (2013) explored the possibility to support recovery from post-stroke aphasia when rTMS is combined with SLT. They recruited post-stroke aphasia patients in the subacute phase who were randomized to a 10-day protocol of either 20-minute inhibitory 1 Hz rTMS over the right triangular part of the posterior inferior frontal gyrus or sham stimulation. In their study both groups received 45 minutes of speech and language therapy subsequent to rTMS. The participants in their study demonstrated a highly significant treatment effect with the intervention group experiencing a significantly larger improvement in language test scores than the sham group. Thiel et al. (2013) concluded that inhibitory rTMS in the unaffected hemisphere, combined with SLT improves recovery from post-stroke aphasia and promotes recruitment of left-hemispheric language networks. Similarly, Rubi-Fessen et al. (2015) also

explored how rTMS combined with speech language therapy (SLT) might improve both basic linguistic skills and functional communication in individuals with subacute aphasia. Their study provided a 2-week treatment to patients with subacute aphasia after stroke. Half of the participants received 10 sessions of 20-minute inhibitory 1-Hz rTMS over the right inferior frontal gyrus (Brodmann area 45), and the other half received sham stimulation. All the participants of that study received 45 minutes of speech and language therapy immediately after the 20-minute stimulation application. Results showed significant improvement in participants who received real rTMS with respect to all 10 measures of basic linguistic skills and functional communication, whereas sham-treated participants significantly improved in only 6 of 10 measures (Rubi-Fessen et al., 2015).

1.7.3 Dorsolateral Prefrontal Cortex (DLPFC) Stimulation as a treatment method to improve Working Memory

Contemporary neuroscientific techniques such as TMS are just beginning to be explored for the purpose of cognitive enhancement. TMS is one of the most utilized methods for the purpose of altering cognitive function including WM, for a number of neurological disorders including, stroke (Kim, Hong, Kim, & Yoon, 2019). Recently, Georgiou, Lada, & Kambanaros (2019) conducted a systematic review to assess the efficacy of rTMS in the field of post-stroke aphasia rehabilitation. In total, 10 RCTs underwent review for their methodological quality and comprehensive summaries of the best available evidence on this topic. Even though there is evidence that low frequency (1 Hz) rTMS has the potential to improve aphasia post-stroke irrespective of severity, the evidence was inconclusive.

Recently, Georgiou, Konstantinou, Phinikettos, & Kambanaros (2019) reported the findings of neuronavigated cTBS over the right pars triangularis (Tr) for two individuals with chronic aphasia post-stroke. Baseline linguistic and quality of life measures were collected prior to the treatment study. Continuous TBS was carried over 10 consecutive days for 40 secs per sessions. Immediately post-treatment and later at 3-months follow up, participants were reassessed on baseline linguistic and quality of life measures. Results from one individual revealed improvement in language skills in the post-treatment phase, but language abilities reverted to baseline scores at follow-up. Results from the second participant revealed neither improvement nor decline in language abilities at baseline to post-treatment and follow-up stages. Furthermore, improvement in quality of life was reported by one. An investigation performed

in healthy subjects compared sham and active iTBS to the LDLPFC (Hoy et al., 2016). Their study results were acquired from the classic n-back task with the use of letter stimuli (2-back and 3-back memory loads) and showed that iTBS significantly improved WM, producing a robust improvement in 2-back accuracy at 20- and 40-minutes post-stimulation. In a different study to explore the ability of cTBS and iTBS to modulate working memory and executive functions, Marron et al. (2017) applied a single session of either active cTBS, active iTBS or sham TBS to the left DLPFC of healthy participants. In their results, both, iTBS and cTBS, yielded improvements in the Digit Backward task and the Word score of the Stroop test and they concluded that TBS over the DLPFC modulates working memory performance and executive processes.

Demeter et al. (2016) investigated the relationship between the LDLPFC activity during encoding and successful subsequent memory with TMS. In their study the participants received 2 s of sTBS to either left DLPFC or to the control region (Vertex) followed by the item-encoding task (viewing three sequential nouns on the screen). Participants were asked to think about the meaning of the word and indicate whether the item was best categorized as concrete or abstract. Following the encoding, the participants performed an item recognition test to indicate whether the word was studied or unstudied and to indicate how confident they were of their decision. Demeter et al. (2016) found that subsequent memory was enhanced on the day left DLPFC was stimulated, relative to the day Vertex was stimulated, and that DLPFC stimulation also increased participants' confidence in their decisions during the recognition task.

Relevant studies intended to verify the hypothesis that the DLPFC plays a crucial role in WM by using the TMS technique, commonly agreed that the DLPFC is involved in the performance of WM tasks, mainly in tasks involving maintenance and manipulation of information (Balconi, 2013; D'Esposito, Postle, & Rypma, 2000). As executive function and working memory were attributed to prefrontal cortex, it is expected that rTMS will influence significantly these cognitive domains (Guse, Falkai, & Wobrock, 2010). Miniussi & Rossini (2011) argue that the overall notion of brain stimulation is that by generating changes in cortical excitability, recovery or reorganization of the functional network responsible for the impaired cognitive function will result. Numerous research articles discuss how the application of high frequency rTMS of >5 Hz targeting the LDLPFC of patients with major depression, resulted with a positive output on working memory skills (Boggio et al., 2005; Demirtas-Tatlidede,

Vahabzadeh-Hagh, & Pascual-Leone, 2013; Kuroda et al., 2006; Martis et al., 2003; Schulze-Rauschenbach et al., 2005). Boggio et al. (2005) performed 10 sessions of rTMS over the left DLPFC, aiming to treat depression in patients with Parkinson's disease, and specifically investigated the cognitive effects. The authors compared the effects of real rTMS and placebo drug with sham TMS and fluoxetine, with both groups showing improvements in executive functions and visuospatial ability domains. The rTMS protocol used in their study included placing the coil over the left DLPFC, using 40 trains of 5 seconds each, at an intensity of 110% of motor threshold and 15 Hz frequency. This protocol was applied in each patient for 10 days over a 2-week period. Over the 2-week period, there was no significant deterioration in any neuropsychological score in both groups. On the contrary, both treatments (rTMS and fluoxetine) were associated with improvement of neuropsychological performance. Results showed a significant effect of time point for Wisconsin perseverative errors, Hooper, Stroop (colored words), and Stroop (interference card) scores.

As far as open studies are concerned, all of them investigating the cognitive effects of rTMS in depression stimulated the left DLPFC via high frequency rTMS, with remarkable improvements in one or more cognitive domains in most of these trials (Demirtas-Tatlidede et al., 2013). In Martis et al. (2003) open study the aim was to investigate a potential treatment for depression. Participants were 15 subjects with treatment-resistant major depression received high frequency rTMS on a daily basis (Monday–Friday). Left prefrontal rTMS was delivered for 10–20 sessions over 2–4 weeks. In their study they applied 20 5-s trains of 10 Hz at 110% motor threshold (MT), with 30-s inter-train intervals. Subjects received a particular series of neurocognitive tests either the day before or the morning preceding to the first rTMS treatment (baseline) and nearly 3 days following the last rTMS treatment. Their study resulted in improved working memory, executive function, objective memory, and fine motor speed.

Another study (O'Connor et al., 2003) investigated two procedures with 14 subjects undergoing treatment with electroconvulsive therapy and 14 with rTMS. The participants who received rTMS were administered 1600 stimuli in 20 trains of 8-second during with 24-second inter-train intervals, at 10 Hz at an intensity of 90% of the motor threshold, in daily sessions for 2-4 weeks. The participants were first tested on the first day of treatment, then at the end of the treatment course, and lastly 2 weeks after the final treatment session. Their results indicated that although the rTMS participants did not show significant mood improvement, they showed improvement in the working memory tasks during letter-number sequencing, improvement in

new learning tasks during acquisition, retention, and retrograde memory. The group of subjects who received the electroconvulsive treatment protocol had a better improvement in mood but demonstrated deficits on tests of working memory, acquisition, retention and retrograde memory, with significant cognitive recovery 2 weeks later.

Rektorova, Megova, Bares, & Rektor (2005) applied one session of high frequency rTMS over the left DLPFC to determine if this would induce any measurable cognitive changes in patients with cerebrovascular disease and mild cognitive deficits. The study was performed on seven patients with cerebrovascular disease without dementia, who had mild executive deficits. One session of rTMS involved 3 rTMS blocks, each block separated by a 10-min break. In each block, fifteen 10-pulse trains, each of 1 s duration, were delivered at a stimulation frequency of 10 Hz, with a between-train interval of 10 s, at a motor threshold intensity. Overall, the protocol delivered 450 stimuli over a period of 30 min. Each patient received two rTMS sessions, on day 1 and day 4, either over the left DLPFC (active stimulation site) or over the left motor cortex (control stimulation site). While the only mild but significant stimulation site-specific effect of rTMS was observed in the Stroop interference after the stimulation of DLPFC, improvement was also noted in other neuropsychological tests results, including the Trail Making Test, the Digit Span, and the Rey-Osterrieth Complex Figure Test-Delayed Recall.

Another study intending to compare the neurocognitive effects of unilateral electroconvulsive therapy (ECT) and rTMS in major depression, 30 patients received 10 treatment sessions of either therapy (Schulze-Rauschenbach et al., 2005). The group of patients receiving rTMS received therapy 2 or 3 times per week and the protocol involved stimulation application over the left dorsolateral prefrontal cortex with an intensity of 100% and a frequency of 10Hz, 20–30 trains of 2 seconds duration per treatment session, 5 seconds intertrain interval. After treatment, significant differences between the ECT and rTMS treatment groups emerged for specific memory functions and were in favor of rTMS. In the rTMS group, some objective memory measures and the subjective memory rating improved in parallel with the improvement in mood and reached normal performance levels.

Although TMS is being used to investigate the relationships between brain correlates, memory functions and behavior, very few studies have investigated how TMS may impact memory performance in order to restore language functions in PWA.

1.8 Computerized Assisted Cognitive Training in Adult Rehabilitation

There are many treatment methods to train and improve cognitive functions, including computer assisted cognitive rehabilitation (CACR). In a very early study where CACR was used as a cognitive rehabilitation method, the purpose was to improve the memory of patients with closed-head traumatic brain injury (TBI; Glisky et al., 1986). In this study, four participants with TBI and related memory impairments, were trained to learn new computer commands while performing multiple trials in each of the three sessions. Gliskly et al., (1986) found that the participants were able to acquire and retain the knowledge necessary to perform a variety of computer functions.

Westerberg et al. (2007) examined the effects of WM training in adult patients with stroke (chronic stage) using a computerized WM training method based on the software product RoboMemo (Cogmed Cognitive Medical Systems AB, Stockholm, Sweden). The WM training tasks involved: (a) maintenance of multiple stimuli at the same time, (b) short delays during which the representation of stimuli should be held in WM, and (c) the unique sequencing of stimuli order in each trail. The software adapted the difficulty level based on individual performance. The training plan required the participants to complete 90 trials each day for about 40 minutes, five days a week for five weeks., on a personal computer (PC) at home. Westerberg et al. (2007) found that even one to three years after a stroke, intensive training can improve an individual's WM and attention performance with generalized results to cognitive functioning in daily living. A further study (Lundqvist, Grundstrm, Samuelsson, & Rönnberg, 2010), used computer-assisted training called "QM" (formerly called ReMemo) to train working memory in brain-damaged patients. The participants were diagnosed with trauma, stroke, infection (encephalitis), tumour, and subarachnoid haemorrhage (SAH). QM presented memory stimuli in a computerized system with visuospatial and verbal WM tasks on a PC. WM training included 45–60 minutes of intense training per day, 5 days per week, for 5 weeks. The visuospatial WM tasks required the participant to remember the position of the presented stimuli and reproduce it; the verbal WM tasks required the subject to remember verbally presented sequences of letters and digits forwards and/or backwards and respond by localizing and remembering the stimuli. Their findings revealed that the participants showed improvement on computer exercises, neuropsychological tests and overall health ratings, but not on quality of life ratings.

Łojek and Bolewska (2013) examined the effects of CACR in craniocerebral and cerebrovascular brain-damaged patients with attention and memory dysfunction, using the "RehaCom" program and the Polish computer therapy program for people with aphasia called "AfaSystem". The participants were divided into two groups: (a) Patients with attention and memory dysfunctions and (b) Aphasia patients. Participants in group (a) received the RehaCom training and participants in group (b) received the AfaSystem treatment. RehaCom training included attention (pick one picture from a group which is identical to the model) and memory tasks (memorizing and recognizing objects from a set of pictures moving horizontally across the screen). The AfaSystem involved oral expression, comprehension, and therapy in reading and writing. The participants with memory and attention dysfunctions patients showed significant improvement only in the trained functions of the RehaCom exercises but did not show generalized improvement in these functions; some improvement was found, in the patients with aphasia group with respect to oral expression and speech functions involving writing. Another study (Yoo, Yong, Chung, & Yang, 2015), used the RehaCom software examined the effect of CACR for the rehabilitation of stroke patients. The cognitive training program was applied for a total of 5 weeks, 5 times/week, 30 min each session. It was composed of attention, focus, memory, spatial imagination, visual impairment, and visuomotor coordination. Participants were divided in two groups: (a) a training group which received rehabilitation therapy and an additional CACR and (b) a control group which received rehabilitation therapy only. Their results of the training group presented statistically significant improvement on some cognitive tasks, including in digit span, visual span, visual learning, auditory continuous performance, and visual continuous performance, but not in verbal learning, trail making, and functional independence measure.

1.9 Quality of Life related to Aphasia

Quality of life (QoL) is defined as 'a person's sense of well-being resulting from satisfaction or dissatisfaction with the areas of life that are important to them (Ferrans & Powers, 1992). When focusing on the health-related quality of life (HRQL), the attention is on the impact of a health state on a person's ability to lead a fulfilling life (Bullinger, Anderson, Cella, & Aaronson, 1993), and it incorporates the individual's perception of and satisfaction with his/her physical, mental/emotional, family and social functioning (Berzon, Hays, & Shumaker, 1993). It is well known that stroke and aphasia can seriously affect communication related QoL (Mile,

2018) while PWA encounter substantial changes of their communicative functioning that can lead to reduced activities and participation in everyday life (i.e. Howe, Worrall, & Hickson, 2008). Consequently, aphasia – and especially limitations of functional communication – were shown to cause reduced QoL (Cruice, Worrall, Hickson, & Murison, 2003; Hilari, Needle, & Harrison, 2012). It is well documented that people with aphasia are often among the most severely affected stroke survivors as they portray high levels of depression and social exclusion, and low levels of leisure and other social activities, social contacts and quality of life (Hilari et al., 2009). The study of QoL in aphasia is a growing subject, and it is considered as a highly important topic as there is a common agreement among speech-language pathologist that effective communication is integral to a good quality of life: a) improving quality of life is the ultimate goal of aphasia rehabilitation; b) understanding the patients' perspective of their own quality of life is essential in targeting appropriate and effective interventions; c) the relative impact of aphasia, compared to other impairments, can most clearly be seen through measures of quality of life; and d) measuring quality of life is a very important outcome measure that can be used for accountability purposes (Worrall & Holland, 2003). Studies have shown that HRQOL issues indicate the impact of health on a person's ability to live a generally fulfilling life (Bullinger et al., 1993). While quality of life refers to the level of comfort, enjoyment, and ability to pursue daily activities, stroke rehabilitation programs aim to produce changes in people's sense of well-being and quality of life (Intercollegiate Stroke Working Party, 2012). Lam and Wodchis (2010) studied health-related factors affecting quality of life and results showed that aphasia has the largest negative impact on quality of life, more than cancer and Alzheimer's disease. They indicated the negative effects of aphasia on an individual's quality of life included their inability to communicate and engage with their family, friends, doctors and their wider community. In a different study, Spaccavento et al. (2013) focused particularly on difficulties in interpersonal relationships, on loss of independence, and on abilities in daily life as a result of language disorders. They found that improvement in the severity of language deficits also causes an improvement in quality of life.

1.10 Reporting Working Memory Interventions as the sole therapy strategy in post-stroke aphasia: A critical review of the literature using the TIDieR checklist

For several years, language impairments were considered isolated impairments from other cognitive domains. However, recent studies have exposed the relationship between language and other cognitive domains, such as memory, attention and executive functions (Caplan et al., 2013). Studies explored the relationship between language and memory processing, indicating an extensive variety of memory deficits in the aphasia literature while implicating STM and WM (Potagas, Kasselimis, & Evdokimidis, 2011), with early indications of this relationship dated almost 100 years ago (Kasselimis, 2015). These findings underline the importance of exploring WM treatment in PWA.

Over the last decades, increased attention has been given in understanding how interventions work (Ferguson, 1999), which was linked to the concept of treatment theory i.e., "the actual nature of the process that transforms received therapy into improved health" (Keith & Lipsey cited in Turkstra, Norman, Whyte, Dikers, & Hart, 2016, p. 164). They suggest that interventions should be specified according to three elements of treatment theory: targets (functioning intended to change following intervention), ingredients (clinician's actions that effect change in target); and mechanisms of action (known or hypothesised ways that ingredients exert effect) (Turkstra, Norman, Whyte, Dijkers, & Hart, 2016). Recently, the Template for Intervention Description and Replication (TIDieR) checklist was developed to assist with specifying interventions in a way to enable comparison, replication and implementation (Hoffmann et al., 2014). This checklist includes 12 items, considered to be the minimum needed to describe an intervention: (1) brief name of the intervention; (2) the rationale, theory, or goal of intervention; (3) intervention materials; (4) intervention procedures; (5) who provided the intervention; (6) delivery mode; (7) place of delivery; (8) when and how much intervention provided; (9) tailoring (i.e., personalisation); (10) modifications (i.e., unforeseen modification at a study level); (11) planned intervention adherence/fidelity measures (how and by whom); and (12) actual intervention adherence/fidelity measures (see Hoffmann et al., 2014, for further description of items).

This review is aiming to support the research community for a better understanding of how WM impairments at the level of information maintenance and manipulation interact with

language abilities. It is clear that WM impairments have an impact on communication, which in turn has a negative chain reaction in the person's quality of life. The main purpose of this review paper is to determine: 1) what type of WM treatment procedures have been used specifically with PWA to improve language skills in the last decade and 2) how successful were these WM treatments.

During the current investigation it became apparent that there is limited scientific evidence where the WM training approach was used as a sole treatment method. For the purposes of this study a systematic search was undertaken, and data was retrieved from electronic databases, specifically from PubMed search (**see Figure 1.10.1**) to investigate whether WM training was used in PWA as the only treatment method to improve language abilities. A comprehensive search of existing peer-reviewed studies was conducted using multiple strategies. First, keyword database inquiries were conducted in PubMed database. In the search, the keywords used were "working memory intervention in aphasia" and all possible combinations of keywords were used. Database filters limited the search to articles published between 2009 and May 2019. To be eligible for inclusion in the systematic review, each study was required to meet all of the following inclusion criteria. First, studies must have included a sample of adults who were diagnosed with aphasia due to stroke. Second, studies must have involved an intervention which used only WM as a treatment method aiming to improve language. Third, study designs were limited to trials that included at least two points of measurement, one at baseline and another at a point in time afterward to measure the efficacy of the intervention. Finally, studies must have been published in English. Studies involving other neurological disorders (e.g. traumatic brain injury) or a combination of interventions (e.g. WM training and speech-language therapy) were excluded. The process of study selection and determination of eligibility is summarized in graphical form consistent with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines in **Figure 1.10.1**.
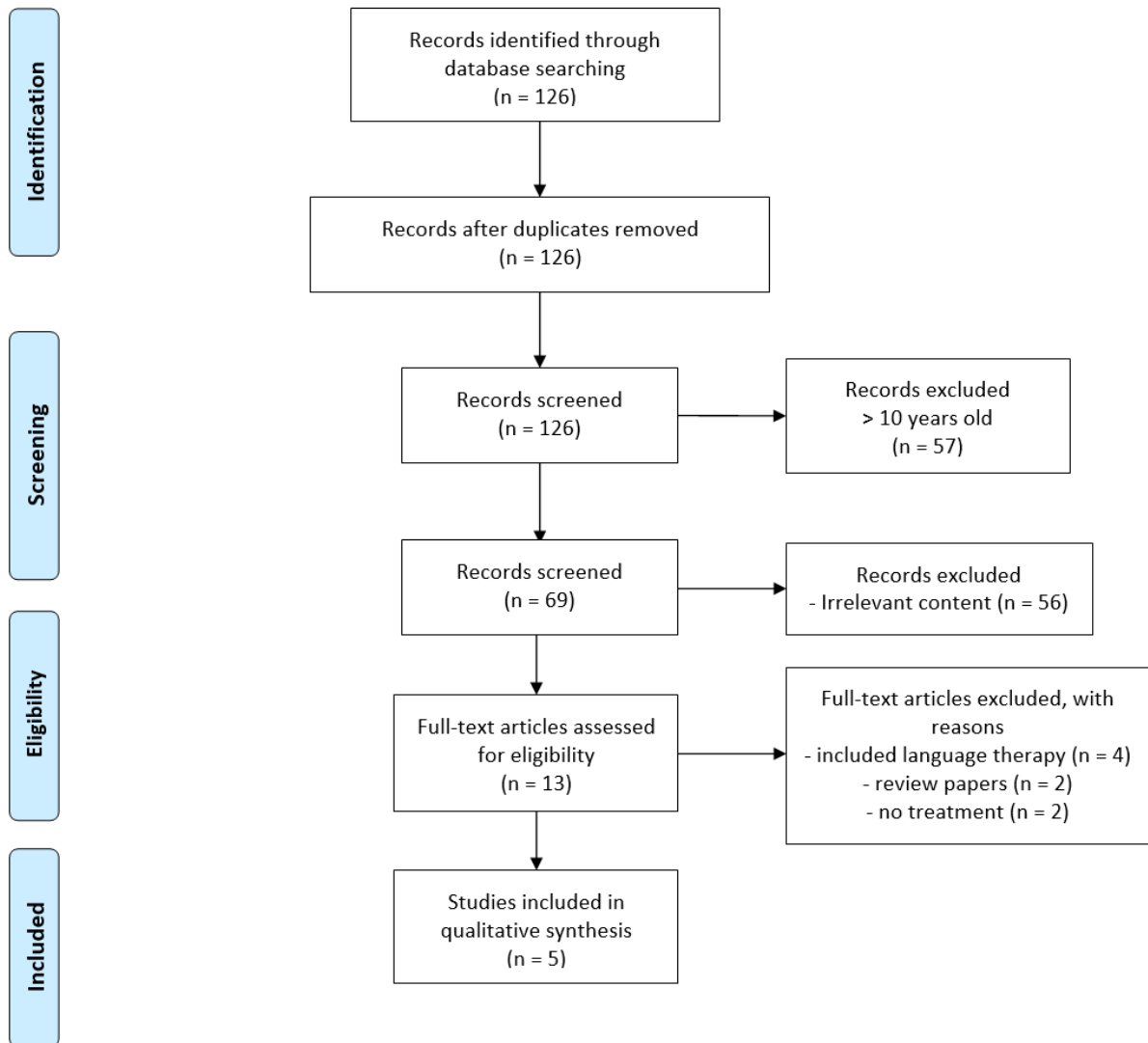
Figure 1.10.1. PRISMA (Liberati et al., 2009) flow chart for the selection of studies investigating WM as a sole treatment for rehabilitation of aphasia

During the last 10 years, only five studies report using a WM intervention in PWA, because of stroke as the sole method of treatment for the language deficits. The findings of this research are summarized in **Table 1.10.1**, with regards to the type of WM treatment, the frequency of the treatment, the dosage of the treatment, and the effects of the treatment on WM (near transfer outcomes) and language abilities (far transfer outcomes).

Table 1.10.1. Studies using WM interventions in PWA as the sole method of intervention to improve language abilities.

Study	N	Aphasia Type	Native Language	Treatment duration	WM training tasks	Near transfer Treatment Outcomes	Far transfer treatment outcomes
Eom & Sung, 2016	6	3 Anomic 2 Broca 1 Wernicke	Korean	4 weeks (12x 1-hour sessions)	Sentence Repetition-Based Working Memory	Improved significantly in: - sentence repetition accuracy of treated and untreated items - digit-forward, digit-backward, and word-forward	Improved significantly in: - sentence comprehension accuracy Improved aphasia quotient - repetition and naming Improved numerically in fluency and comprehension
Zakariás, Keresztes, Marton, & Wartenburger, 2018	3	1 Anomic 2 TMA	Hungarian	4 weeks (13x 20-minute sessions)	Modified n-back task with "lures"	1 PWA improved significantly in the visual 1-back; tendency for an increase in the visual 2-back 1 PWA improved significantly in the visual 1-back	2 PWA improved significantly in TROG-H sentence comprehension 2 PWA improved significantly, 1 PWA showed tendency for improvement in TROG-H number of blocks correct

							1 PWA did not show significant improvement in either n-back task	2 PWA remained stable on the BNT
								1 PWA showed tendency for improvement on the BNT
Salis, 2012	1	TMA	English	13 weeks (26X 30-minute sessions)	- listening span tasks of serial word recognition	Numerical improvement in Digits forward and Digits backward from the WMS	Subtest 1 "Touch the green square" from the TT did not change
					- matching listening span that required judgment of sameness	Numerical improvements in Digit listening span from PALPA	Numerical improvement in Subtest 2 "Touch the large green square" from the TT
							Significant improvement on the TROG
							Significant improvement in the number of repetitions requested in the TROG
Salis, Hwang, Howard, & Lallini, 2017	5	Not specified	Not specified (English)	13 weeks (26X 30-minute sessions)	- listening span tasks of serial word recognition	no statistically significant changes	no statistically significant changes
					- matching listening span that required judgment of similarity	- Improved digit matching listening span of 3 participants by one or two items	- Improved sentence comprehension of 3 participants in the TROG by 4-5%, and in the TT by 4-10%.
							-

| Harris, Olson, & Humphreys, 2014 | 2 | 1 Broca's

1 expressive aphasia | Not specified (English) | 2 treatments, each lasted 10 weeks (10 x 90-minute sessions) | Treatment 1:
- pSTM training

Treatment 2:
- sSTM training | Both participants improved significantly in nonword recall after nonword (pSTM) treatment

significant improvement following the real word (sSTM) therapy | evidence of type-specific generalisation to sentence comprehension
- the pSTM patient showed improvement on sentence repetition after the pSTM treatment
- the sSTM patient improved sentence anomaly judgement after the sSTM but not the pSTM treatment. |

Key: TMA = Transcortical Motor Aphasia; TROG = Test for the Reception of Grammar; H = Hungarian; BNT = Boston Naming Test; WMS = Wechsler Memory Scale; TT = Token Test; STM = Short-Term Memory; pSTM = Phonological short-term memory; sSTM = Semantic short-term memory

This review uses narrative synthesis (Barnett-Page & Thomas, 2009) organised by the systematic application of the TIDieR checklist (Hoffmann et al., 2014) to the 5 studies appraised. The use of a narrative method allows for flexibility and accommodation of a range of study types (Mays, Pope, & Popay, 2005), whereas the synthesis part attempts to move beyond textual summary and description in order to generate comparative understanding, new insights and knowledge (Barnett-Page & Thomas, 2009; Mays et al., 2005). As the purpose of this review is to investigate what has been done so far regarding the use of WM as the preferred intervention method in aphasia, the TIDieR checklist was used as a framework to organise the investigation of intervention reporting, and not with the purpose to replicate any of the studies. A particular focus was given on reporting the commonalities among treatments and their outcomes. The review of the 5 selected publications is organised below in the order it appeared in the search results.

1.10.1 *Primary paper: The Effects of Sentence Repetition–Based Working Memory Treatment on Sentence Comprehension Abilities in Individuals with Aphasia* (Eom & Sung, 2016)

Item #1: BRIEF NAME

Sentence repetition–based working-memory (SR-WM) treatment - maintenance and computation of linguistic units by facilitating a chunking strategy.

Item #2: WHY

To increase sentence-repetition abilities and the treatment effects to elicit generalization to sentence-comprehension abilities, WM-span tasks, and general language-assessment tasks.

Item #3: WHAT

Materials: Sentence stimuli for the current treatment included five different syntactic structures: (a) active sentences with two-argument verbs (five words, 10–11 syllables), (b) passive sentences (five words, 12–13 syllables), (c) active sentences with three-argument verbs (seven words, 13– 15 syllables), (d) conjoined sentences (eight words, 16–17 syllables), and (e) centre-embedded sentences with a subject-relative clause (eight words, 16–17 syllables). A total of 30 sentence stimuli served as treatment sentences with six items for each syntactic structure.

Item #4: PROCEDURES

Six individuals with aphasia participated in the study. All participants with aphasia suffered a single left-hemisphere stroke, were right-handed, and were native speakers of Korean, were in chronic status (post-onset > 6 months), had no serious dysarthria and apraxia of speech, and no history of neurological disease and sensory deficits.

The major principles of this WM treatment protocol included two components: (a) maintain information in a short-term storage buffer while sentence length increases and (b) compute syntactic structures while syntactic complexity increases. The current protocol consisted of four steps: (1) Sentence Repetition; (2) Chunking Strategy; (3) Reading a Whole Sentence; and (4) Sentence Repetition.

During the first step, auditory repetition was involved for the presented verbal sentence and it implicated short-term information maintenance and rehearsal in order to perform step 2, regardless of participants' response accuracy.

During the second step, the WM component of computing the segmented linguistic units was involved. Written stimuli cards were randomly presented by the examiner on a desk, in which sentences were separated word-by-word through chunking linguistic information on the basis of the word. The participants were asked to rearrange the cards in the order the verbal sentence was presented in the first step. If the participants produced correct responses, the examiner read the target sentence aloud and proceeded to the next step. When participants showed incorrect responses, they listened to the target sentence one more time and rearranged the cards, trying for the correct order. When participants responded to the task incorrectly even after the second chance, the examiner provided the correct answer by rearranging the cards in the correct order.

During the third step the WM component is implicated by asking participants to rehearse the integrated information as a whole sentence, while the target sentence is presented verbally as the participants were looking at a card written with the whole sentence. The participants were then asked to read the whole sentence aloud. If the response was correct, the examiner read the target sentence aloud and proceeded to the next step. If the participants responded incorrectly, the examiner read the target sentence aloud and asked participants to read it one more time.

Finally, during the fourth step the examiner asked the participant to repeat the target sentence after the examiner, followed by feedback on the participant's accuracy on the target. When participants elicited correct responses, the examiner read the target sentence aloud and

proceeded to the next sentence. When participants showed incorrect responses, they listened to the target sentence one more time and also proceeded to the next sentence.

Two sets consisting of 15 sentences each were designed to give the total of 30 treatment stimuli. Each 15-sentence set contained all five syntactic structures with three for each structure. Each treatment session contained five different syntactic structures by varying the length and complexity in the following order: (a) active sentences with two-argument verbs, (b) passive sentences, (c) active sentences with three argument verbs, (d) conjoined sentences, and (e) center embedded sentences with a subject-relative clause.

Item #5: WHO PROVIDED

The first author (Bora Eom) conducted assessment and treatment for all participants, although both authors designed the experiments and implemented the theoretical framework. They were speech-language pathologists at the Department of Communication Disorders, Ewha Womans University, Seoul, South Korea, and no additional training for this research was specified.

Item #6: HOW

Intervention was provided on a one-to-one and face-to-face basis. The study used a pre-test/post-test design. The pre-test was performed before treatment and the post-test was conducted immediately after treatment. Only single tests for pre- and post-assessment were administered due to the fact that the treatment was based on a repetition protocol and repeated exposures to the stimuli before treatment could have contaminated the treatment data.

Item #7: WHERE

Location was not specified

Item #8: WHEN and HOW MUCH

Treatment consisted of 12 sessions, administered three times a week with each session lasting approximately 1 hr. For each treatment session, the examiner administered a set of treatment stimuli, repeating each set six times over 12 sessions.

Item #9: TAILORING

The sentence stimuli for the repetition-based WM treatment protocol consisted of sentences that varied in length and syntactic structures. Sentence-repetition stimuli used decontextualized vocabulary to maximally tap into a short-term storage buffer.

Item #10: MODIFICATIONS

In the current study, the colours were used as each noun phrase in a sentence to minimize top-down semantic processing.

Items #11 and 12: HOW WELL

Not reported

Summary

Eom and Sung (2016) applied a sentence repetition–based working-memory (SR-WM) treatment to maintain and compute linguistic units by using a chunking strategy. This treatment resulted in substantial increased repetition ability in both treated and untreated sentences and in generalization effects on the WM measures and general language tasks, including improvements in fluency, sentence-comprehension task, repetition, and naming domains. Improved performance on sentence repetition as well as other linguistic domains was noted using the SR-WM treatment approach, by manipulating syntactic structures and minimizing top-down semantic processing. Based on the results, the clinical and theoretical importance of investigating whether WM treatment operates as a potentially underlying treatment approach that facilitates the distributed network associated with language processing.

1.10.2 *Primary paper: Positive effects of a computerised working memory and executive function training on sentence comprehension in aphasia* (Zakariás et al., 2018)

Item #1: BRIEF NAME

Adaptive WM training task (a modified n-back task)

Item #2: WHY

This research was based on recent studies that suggest that WM, together with certain executive functions (EFs), can play a role in sentence comprehension in IWA, and that WM can be improved with intensive practice. The purpose of this study was to investigate whether a combined WM and EF training improves the comprehension of spoken sentences in IWA. The following questions were to be answered: (1) Can WM and EFs be enhanced through training in IWA? If yes, (2) does the training lead to near transfer effects on WM and EFs? (3) Does the training lead to far transfer effects on sentence comprehension as well?

Item #3: WHAT

Materials: All computerised tasks were run by Presentation® software (Version 14.1) on an IBM T40p ThinkPad®. An n-back task with "lures" was created to target both WM and interference control.

Item #4: PROCEDURES

The study recruited three participants with chronic aphasia for the training phase and a control group which consisted of five IWA who participated only in the pre-test and the post-test, but not in the training sessions. All participants had a single left hemisphere infarct, spoke Hungarian as their native language and were righthanded. Their visual acuity was intact and hearing was within normal limits. A pre/post-test case control design was used. All participants underwent an initial assessment of their language skills (Western Aphasia Battery) and intelligence (Raven Progressive Matrices), completed two n-back tasks, and two language tasks as outcome measures. One day after the completion of the training, participants completed two post-test sessions identical to the two pre-test sessions.

The participants were presented with a stream of letters and were asked to press a button when a letter was the same as the one appearing n-trials prior to the current presentation. Training included sequential letter presentation on a computer screen at a rate of 3 seconds (stimulus length: 1000 ms; interstimulus interval: 2000 ms) per trial. In each trial, the stimulus was sampled from a pool of eight letters: B, F, K, H, L, S, C, and N. The participants' response was performed manually by pressing the SPACE bar of the computer's keyboard and a response was not required for non-target items. Each training session included eight blocks consisting of $16 + 5*(n-1)$ trials including 5 targets. The level of difficulty of an upcoming block was set adaptively, based on performance on the previous block.

Item #5: WHO PROVIDED

Three experimenters (two trained speech and language therapists and one trained nurse) conducted the study. They all received the same instructions regarding the training procedures. Each session was conducted by one experimenter.

Item #6: HOW

Intervention was provided individually, face-to-face

Item #7: WHERE

Location was not specified

IWA in the training group participated in 13 training sessions (approximately 20 minutes each session) over a period of four weeks (3-4 times a week for a month). The choice of 20-minute duration was determined by previous studies showing that sessions of this duration were successful in producing training and transfer effects in healthy adults and children, without exhausting participants.

Item #9: TAILORING

This treatment was based on the classic n-back model that focuses on updating WM (Logan, 1994).

Item #10: MODIFICATIONS

This protocol incorporated lures into the classic n-back task; letters that were the same as the one presented n−1 or n + 1 (but not n) trial before (Kane et al., 2007; Novick et al., 2013).

Items #11 and 12: HOW WELL

Not reported

Summary

Zakariás et al. (2018) used a computerised adaptive WM training task with a modified n-back task where the participants were presented with a stream of letters and were asked to press a button when a letter was the same as the one appearing n-trials prior to the current presentation (classic n-back). Additionally, lures were incorporated into the task where letters that were the same as the one presented n−1 or n + 1 (but not n) trial before. Their study included three Hungarian-speaking PWA aiming to improve sentence comprehension, three to four times a week for a month, for a total of 13 20-min sessions. The authors detected a mixed pattern of training and transfer effects across participants in which: (a) one participant improved in the training task as well as untrained WM tasks and spoken sentence comprehension (b) one participant improved in the training task and spoken sentence comprehension but did not show improvement in other measures of WM; and (c) one participant did not show improvement in the training task but did show increases in performance, for sentence comprehension and untrained WM. The results of this study showed that WM and EFs could be improved through computerised training in a sample of individuals with chronic aphasia and this enhancement may have led to the improvement in spoken sentence comprehension.

1.10.3 *Primary paper: Short-term memory treatment: Patterns of learning and generalisation to sentence comprehension in a person with aphasia* (Salis, 2012)

Item #1: BRIEF NAME

STM training using listening span tasks of serial word recognition.

Item #2: WHY

This study was constructed on previous evidence which argue that STM deficits affect phonological encoding, lexical-semantic processing, phrase production, and sentence comprehension. Thus, it supports the supposition that there is a link between STM and sentence comprehension. The research questions were: (1) Would STM training improve STM?

(2) Would improvements from the STM training generalise to improvements in comprehension of sentences?

Item #3: WHAT

Materials: Treatment probes included listening span tasks of different length, i.e., number of nouns. No additional training was provided to intervention providers.

Item #4: PROCEDURES

The study recruited one IWA in the chronic stage. The participant presented with transcortical motor aphasia according to the Western Aphasia Battery but with a marked comprehension deficit. Sentence repetition ability on the PALPA sentence repetition subtest revealed major difficulties with repetition of function words and bound morphemes (omissions in particular). Word order was preserved in the majority of sentences. Language output was non-fluent, typically telegrammatic, with two to three-word utterances comprising mainly nouns, absence of function words and very few verbs. Comprehension demonstrated moderate to severe problems. Pre-test included digits forward and digits backward; Subtests 1 and 2 of the Token Test; the Test for the Reception of Grammar (TROG); and a listening span. Five pre-treatment baselines were taken over two weeks.

Treatment first began with list spans of five monosyllabic words, then six monosyllabic words. There were 18 trials in each of these list spans, followed with list spans of three polysyllabic words (3–4 syllables) with 14 trials. So, in the probes using monosyllabic words there were 18 trials per probe. In the probes using polysyllabic words there were 14 trials per probe.

The participant listened to two lists of nouns (A then B) and had to judge if the two lists were the same or different. The items in each list were presented at a rate of one word per second in a normal speaking voice without prosody. If the participant's response was correct, the next item list was presented. If incorrect, the presentation was repeated and the words that were dissimilar were pointed out to the participant. As part of the feedback, written lists were also shown in conjunction with spoken presentations to clarify where the differences were. No other language tasks were used during treatment.

Item #5: WHO PROVIDED

A speech-language pathologist delivered the treatment in clinic. The person's daughter also delivered part of the treatment at home. The daughter had been provided with training and was present in all treatment sessions.

Item #6: HOW

Intervention was provided face-to-face on an individual basis.

Item #7: WHERE

Clinic and home

Item #8: WHEN and HOW MUCH

There were two treatment probes per week, each lasting about 30 minutes, for a total of 13 weeks.

Item #9: TAILORING

The content was controlled for frequency, concreteness, and number of syllables. In addition, the words in all lists were semantically unrelated to prevent chunking. Items were also phonologically dissimilar and polysyllabic words did not include compound nouns.

#10: MODIFICATIONS

In the different lists either the first two or last two nouns were transposed, so that the different lists were dissimilar either at the beginning or the end.

Items #11 and 12: HOW WELL

Not reported

Summary

Training resulted in improvement in several list spans but not all and in the STM abilities (listening span, forward digit span). There was also evidence of generalisation to untreated sentence comprehension (only on the TROG). Backward digit span, phonological processing and single word comprehension did not improve. It was noted that improvements in sentence comprehension may have resulted from resilience to rapid decay of linguistic representations within sentences (words and phrases), which in turn facilitated comprehension.

1.10.4 *Primary paper: Short-term and working memory treatments for improving sentence comprehension in aphasia: a review and a replication study* (Salis et al., 2017)

Item #1: BRIEF NAME

Replication study based on previous single case study which used STM training using listening span tasks of serial word recognition - matching listening span that required the judgment of whether word-list pairs comprising spoken nouns were the same or different.

Item #2: WHY

The primary purpose of this study was to replicate the original treatment in case series using a more robust design that involved computerized delivery, treatment fidelity measures, as well as treatment-related control probes.

Item #3: WHAT

Materials: The matching listening span tasks were created and delivered with a bespoke computer program. A tablet touchscreen computer with an external mini speaker was used to deliver five pre-treatment baselines and also the treatment itself at a volume level comfortable for each person.

Item #4: PROCEDURES

Procedures: This study included five participants with stroke-induced chronic aphasia. The treatment sessions began immediately after the baselines. Each treatment session used twenty different word-list pairs with the same temporal parameters as in the baselines. The main difference between baseline and treatment sessions was the inclusion of visual and auditory feedback on persons' response accuracy. A correct response produced a visual feedback of a

smile from a face cartoon, simultaneously with auditory feedback. An incorrect response produced a face with a neutral expression and the auditory feedback stated that the response was incorrect, followed by repetition of the word-list pair. If after the second presentation the person's response was correct, the visual and audio feedback acknowledging the correct trial was presented (as previously described). If the response was incorrect, the program repeated the word-list pair and the speech-language pathologist (who delivered baseline and treatment sessions) would write down the word list and explain which words had (or not) been in the same order as in the first word list before moving on to the next trial. Level of difficulty was determined by the person achieving 80% correct (at first attempt) or above on two consecutive training sessions. Level of difficulty increased by one word in the word-list pairs.

Item #5: WHO PROVIDED

Speech-language pathologist

Item #6: HOW

Intervention was provided face-to-face on an individual basis.

Item #7: WHERE

Either at their homes or in testing rooms at Newcastle University.

Item #8: WHEN and HOW MUCH

There were two treatment probes provided per week, each lasting about 30 minutes for aa total of 13 weeks. Sessions started immediately after the baselines were completed.

Item #9: TAILORING

This intervention was adapted based on the previous study.

Item #10: MODIFICATIONS

Not reported

Items #11 and 12: HOW WELL

Not reported

Summary

This was a replication of a previous study (Salis, 2012) with positive findings based on one individual with aphasia. Salis et al., 2017 provided 27-30 sessions of training involving a

recognition memory task (matching listening span) in five participants with aphasia. The authors reported changes in short-term memory (near transfer) only in one outcome measure (i.e., digit matching listening span), and with regards to the spoken sentence comprehension abilities, the changes observed were not statistically significant.

1.10.5 *Primary paper: The link between STM and sentence comprehension: a neuropsychological rehabilitation study* (Harris et al., 2014).

Item #1: BRIEF NAME

Recall of memory lists training

Item #2: WHY

This study is based on previous evidence linking verbal STM with language processing, which suggest that rehabilitation methods aiming to improve verbal STM may produce generalised benefits in language. It was also proposed that there may be distinct semantic and phonological components of STM, in which phonological and semantic STM patients differ from cases of impaired phonological and semantic processing. Additionally, evidence was found showing differential effects of working memory load on language processing tasks in sSTM and pSTM patients. This proposes a relation between verbal STM deficits and language impairments, specifically by showing verbal STM effects on semantic judgement tasks, although verbal STM did not impact on phonological judgements. The purpose of this study was to explore the effects of improved sSTM and pSTM on sentence processing and STM tasks. Specifically, to test (1) whether phonological and semantic STM treatments can improve phonological and semantic STM and (2) if this improvement leads to generalised gains on sentence comprehension tasks thought to use pSTM and sSTM, across pSTM and sSTM patients.

Item #3: WHAT

Materials: For the assessment a set of 128 sentences were used (Hanten & Martin, 2000). Half of the sentences were anomalous (involving a violation of semantic or pragmatic relationship). Presentation order of the sentences was randomised.

For the treatment, lists of 5-letter words and nonwords were created for the treatment sessions and at home exercises.

Item #4: PROCEDURES

This study included two participants at the chronic stage post CVA. During the assessment the examiner read out loud the sentences in a pseudorandomised order. During the repetition task (pSTM), participants were required to repeat as much of each sentence as possible immediately after the examiner's presentation. Response accuracy was recorded at the word level, which measured whole sentence accuracy (correct or incorrect), and proportion of words accurately read in the sentence (expressed as a percentage). In the comprehension condition (sSTM), participants were asked to judge whether the sentence was acceptable or unacceptable. Any score outside of the range for their healthy controls was considered impaired. The Birmingham Cognitive Screen (BcoS), a battery which includes a range of short assessments of cognition (e.g., memory, language, problem-solving) was also used as a control measure of patients' general cognitive abilities over baseline phases. Their treatment procedure implemented an ABACA design where A denotes baseline and B and C denote treatment (pSTM and sSTM, respectively). Assessments of memory, sentence comprehension, and a control task were administered at each baseline stage. The first treatment stage targeted to train pSTM, during which the examiner read aloud lists of nonwords at a list length of one item above each patient's span for nonwords (e.g., 4 where the patient's span was 3). The patients were requested to recall as many nonwords from each list as possible in the order they were presented. Each patient's responses accuracy was recorded by the examiner after each trial. Feedback was provided as the examiner corrected the patients' errors and the correct list was provided at the end of each trial. The same procedure was implemented for real words, using each patient's word span + 1 in the university sessions with the examiner, and word recognition span + 1 for the exercises completed at home. For the real word tasks, the participants were encouraged to think about the meaning of each word as they heard it, to encourage use of sSTM rather than pSTM when encoding the words. During the treatment period, the nonword home exercises were set for the periods in between the pSTM treatment sessions, and the word home exercises during the sSTM treatment phase. Each week, the patients completed 20 trials of the recognition exercises at home.

Item #5: WHO PROVIDED

The researchers were experts in the area of clinical psychology and neuropsychology

Item #6: HOW

It was not clarified, but throughout the method it was implied that intervention was provided face-to-face on an individual basis.

Item #7: WHERE

The weekly treatment sessions were conducted in a testing room at the university

Item #8: WHEN and HOW MUCH

For both participants, repetition and anomaly detection during assessment were completed in two separate sessions (separated by two weeks).

Each treatment lasted 10 weeks and both participants received one 1.5-hour session per week using two types of treatment – a) trained the retention of nonwords to employ phonological STM and b) treatment with real words to involve both phonological and semantic representations, over 10 weeks, followed by post-treatment evaluation.

Item #9: TAILORING

Not reported

Item #10: MODIFICATIONS

To prevent long-term learning of the stimuli (e.g., reliance on long-term rather than short-term memory), the words used in the lists were changed after each session with other word sets matched for frequency, imageability, age of acquisition and concreteness in the real word case, and for length in the nonword stimuli set.

Items #11 and 12: HOW WELL

Not reported

Summary

Harris et al. (2014) used phonological (pSTM) and semantic (sStm) STM treatments, designed to improve the two separate aspects (phonological and semantic) over a period of 10 weeks, in two participants with chronic aphasia. Results of this research reported that the pSTM patient showed post-treatment improvement on sentence repetition after the pSTM treatment, and the sSTM patient showed improved sentence anomaly judgement after the sSTM but not with the pSTM treatment, suggesting that identifying type of STM deficit, and using one type-specific STM treatment (e.g. only sSTM or only pSTM) can result in targeted benefits in STM and generalised, type-specific improvements on sentence comprehension.

1.10.6 Research questions

Based on the combined findings of these five studies it appears that WM training for PWA could be beneficial with regards to language improvement. Across the studies, the number of participants was low, and this could explain why the positive findings did not reach statistical significance. Other limitations include the administration of diverse WM training protocols (e.g., verbal vs. non-verbal), as well as different duration and intensity of the treatment (e.g., 13 sessions x 20 minutes vs. 30 sessions x 30 minutes) hindering the generalisation of the findings on recovery potential.

The aim of this thesis is to address the following research question:

Does intermittent theta burst stimulation (iTBS) applied over the DLPFC combined with computerised working memory training facilitate language recovery in PWA post-stroke?

In order respond to the major research question the following questions were addressed:

(1) Does WM training generalize to trained cognitive areas as measured by untrained WM and fluid intelligence tasks (near-transfer effect)?
(2) Does WM training generalize to untrained receptive and expressive language and functional communication tasks (far-transfer effect)?
(3) Are generalization effects maintained at follow-up 3 months post-treatment?
(4) Does overall QoL improve after treatment?

2 PILOT STUDY

Combining Intermittent Theta Burst Stimulation (iTBS) With Computerized Working Memory Training to Improve Language Abilities in Chronic Aphasia: A Pilot Case Study.

(Under review in *Aphasiology*)

ABSTRACT

Background: Intermittent theta burst stimulation (iTBS) administered to the left dorsolateral prefrontal cortex (LDLPFC) has been shown to advance working memory (WM) abilities. At the same time, WM training is widely used to enhance learning associated with low language skills. An emerging area of research is that of applying cortical stimulation as an adjunct to behavioural therapy to improve language abilities in people with aphasia (PWA) after stroke.

Aim: To pilot the efficacy of the iTBS protocol, targeting the LDLPFC in combination with computerized WM training to improve receptive and expressive language abilities in an individual with stroke-induced chronic aphasia.

Methods & Procedures: The participant was a 31-year old female who presented with chronic non-fluent aphasia, following a left-hemisphere stroke involving the left frontoparietal lobes. She showed prominent anomia with frequent occurrences of word-finding difficulties.

The assessment battery included a screening measure of WM, a standardized aphasia battery, a non-verbal intelligence test, spontaneous speech samples, a procedural discourse task, and a questionnaire addressing quality of life. All measures were administered once at baseline, immediately after treatment was terminated, and once during follow-up testing, at 3 months

post-treatment. The treatment program included 10 consecutive daily sessions of 30-minutes computer-assisted WM training preceded by 3-minutes of iTBS.

Outcomes & Results: Statistically significant improvement from baseline to post-treatment was found only for the non-verbal intelligence measure, suggesting far-transfer effects. There was no improvement on the computerized WM screening measure. Although no other measures revealed a statistically significant difference, there was a trend towards better performance on untreated items of receptive and expressive language tasks (far-transfer).

Conclusions: The findings revealed a trend for improvement in receptive and expressive language abilities in one individual with chronic aphasia. The iTBS protocol in combination with computerised WM training could be a promising treatment but further studies with larger number of participants are needed to establish its effectiveness for improvement of aphasia after stroke.

Keywords: aphasia; Transcranial Magnetic Stimulation (TMS); receptive

and expressive language; working memory; Cognition

2.1 Introduction

Neuroimaging research confirms that language is part of an extensive network of connected brain regions that promote not only language processing, but also working memory and cognitive control processes (Turken & Dronkers, 2011). Research has focused on the role of the fronto-parietal network including the DLPFC, the anterior cingulate cortex (ACC), and the parietal cortex (PAR) serving the working memory neural network (Chein et al., 2011; Kim et al., 2015; Osaka et al., 2003). Specifically, the DLPFC is largely implicated in cognitive tasks (Kim et al., 2015) demanding executive control (e.g., integration of information for decision-making, maintenance and manipulation/retrieval of information, information updating). The DLPFC, is not only known for its involvement in WM, but also for its significant contribution to correct performance of visuospatial tasks (Courtney, 2004; Pessoa et al., 2002). Due to this involvement in multiple WM components, the DLPFC could be considered an attractive target for cortical stimulation in the context of WM training.

Moreover, other research (Jaeggi et al., 2008; Sternberg, 2008) supports the notion that WM training is a promising way of increasing general fluid intelligence (*Gf*), the ability to solve novel reasoning problems associated with comprehension, problem solving, and learning

(Cattell, 1971). The cortical substrates provide evidence that there is common ground between WM and *Gf* in that both seem to rely on similar neural networks, most consistently located in lateral prefrontal and parietal cortices (Gray et al., 2003). Furthermore, research in healthy adults (Woolgar et al., 2010) has shown that domain-general regions, associated with attention, WM, cognitive control and *Gf*, are engaged for effortful language processing, including understanding or producing complex syntactic structures or ambiguous words (Fedorenko, 2014).

Over the last decade, there is a growing interest in the association between language and non-linguistic cognitive deficits resulting from left hemispheric stroke (El Hachioui et al., 2014; Salis et al., 2015; Vallila-Rohter & Kiran, 2013). Several studies have explored this relationship between language and memory processing breakdown in people with aphasia (PWA), including deficits in working memory (Potagas et al., 2011; Salis, 2012; Salis et al., 2015). In fact, there is growing evidence to support the theory that aphasia is a disruption of cognitive processes underlying language tasks (Tippett, Niparko, & Hillis, 2014). Recommendations made to speech and language therapists advocate assessment and treatment of working memory (WM) deficits in PWA in light of word retrieval and sentence level language breakdown to optimize treatment gains (Bonini & Radanovic, 2015; Vallila-Rohter & Kiran, 2013).

The therapeutic potential of working memory training for aphasia however is restricted to very few treatment studies (Eom & Sung, 2016; Harris et al., 2014; Salis, 2012; Salis et al., 2017; Zakariás et al., 2018). This might be because the incidence of working memory deficits in PWA remain underestimated and not systematically explored. It is also possible that the difficulty of assessing nonverbal cognitive functions in the presence of the aphasia itself (El Hachioui et al., 2014; Vallat et al., 2005) is perceived a barrier to carrying out clinically orientated treatment research on WM. Given that WM is active in information processing and storage necessary to achieve a cognitive target (Kane & Engle, 2002), the ability, to carry out many activities of daily living is also reduced when WM fails (D'Esposito & Postle, 2015). This can have a negative impact on quality of life for people with post-stroke language and cognitive deficits (Manning, MacFarlane, Hickey, & Franklin, 2019).

For the purposes of this study, a systematic literature review on the topic of aphasia rehabilitation using WM training as the sole treatment (i.e., no speech and language therapy) was undertaken. A comprehensive search was performed of existing peer-reviewed studies

using multiple strategies. For the search, the keyword phrase "working memory intervention in aphasia" was used for searching in the freely available PubMed interface. Database filters limited the search to articles published between 2009 and May 2019. To be eligible for inclusion the studies had to meet the following criteria: (i) involve adult participants diagnosed with aphasia due to stroke; (ii) report on WM treatment as the sole treatment method; (iii) describe the aim of WM treatment is to improve language abilities; (iv) include at least two points of measurement, one at baseline and a second at a later time point to measure the efficacy of the intervention; and (v) be published in the English language. Studies involving other neurological disorders (e.g. traumatic brain injury) or a combination of interventions (e.g. WM training + speech and language therapy) were excluded. The process of study selection and determination of eligibility is depicted in a flow diagram consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines in **Figure 2.1.1.**
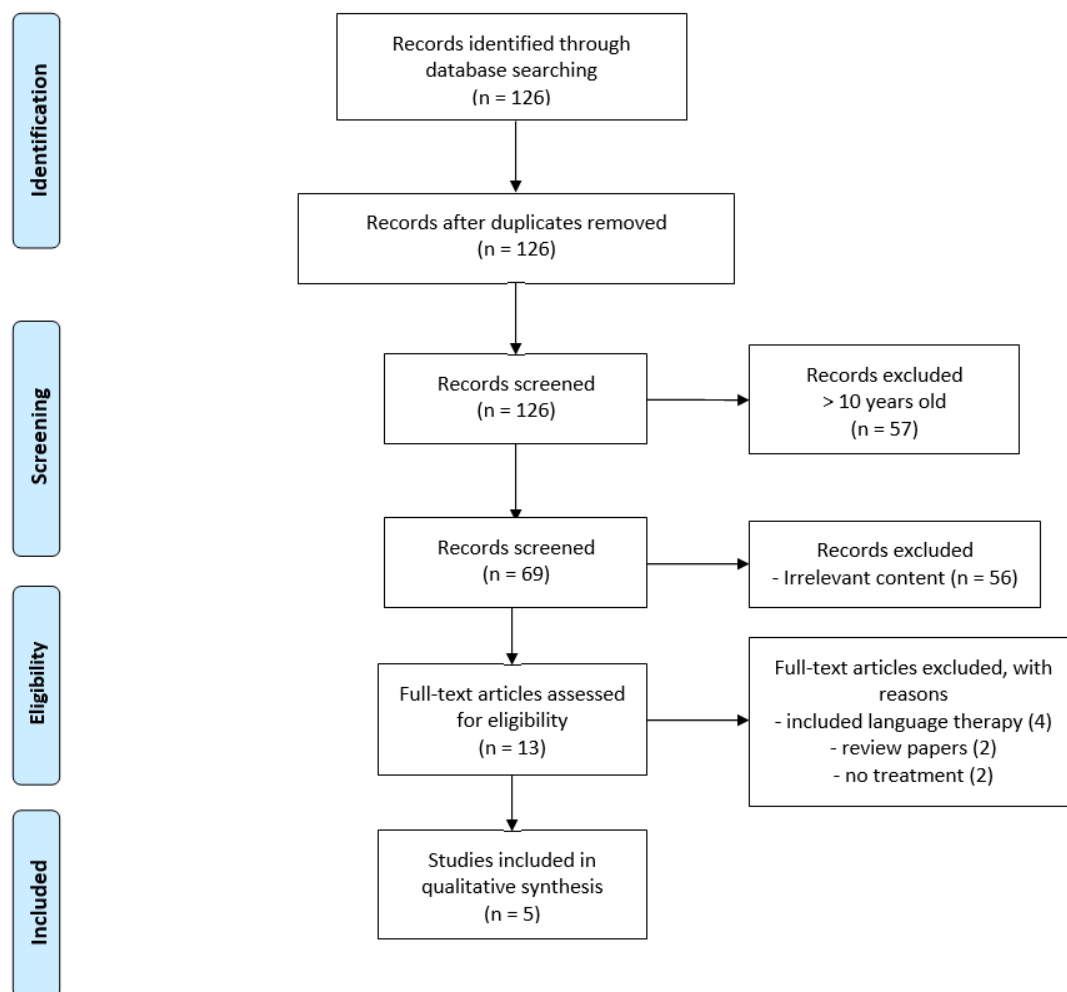
Figure 2.1.1. **PRISMA (Liberati et al., 2009) flow chart for the selection of studies investigating WM as a sole treatment for rehabilitation of aphasia**

During the last 10 years, only five studies report using a WM intervention as the sole method of treatment for the language deficits resulting from stroke-induced aphasia. The findings of this research are summarized in **Table 2.1.1**, with regards to the type of WM treatment, the frequency of the treatment, the dosage of the treatment, and the effects of the treatment on WM (near transfer outcomes) and language abilities (far transfer outcomes). Based on the combined findings it appears that WM training for PWA could be beneficial with regards to language improvement. Across the studies, the number of participants was low, and this could explain why the positive findings did not reach statistical significance. Other limitations include the administration of diverse WM training protocols (e.g., verbal vs. non-verbal), as well as different duration and intensity of the treatment (e.g., 13 sessions x 20 minutes vs. 30 sessions x 30 minutes) hindering the generalisation of the findings on recovery potential.

Table 2.1.1. Studies using WM interventions in PWA as the sole method of intervention to improve language abilities.

Study	*N*	Aphasia Type	Native Language	Treatment duration	WM training tasks	Near transfer Treatment Outcomes	Far transfer treatment outcomes
(Eom & Sung, 2016)	6	3 Anomic 2 Broca 1 Wernicke	Korean	4 weeks (12x 1-hour sessions)	Sentence Repetition-Based Working Memory	Improved significantly in: - sentence repetition accuracy of treated and untreated items - digit-forward, digit-backward, and word-forward	Improved significantly in: - sentence comprehension accuracy Improved aphasia quotient - repetition and naming Improved numerically in fluency and comprehension
(Zakariás et al., 2018)	3	1 Anomic 2 TMA	Hungarian	4 weeks (13x 20-minute sessions)	Modified n-back task with "lures"	1 PWA improved significantly in the visual 1-back; tendency for an increase in the visual 2-back 1 PWA improved significantly in the visual 1-back 1 PWA did not show significant improvement in either n-back task	2 PWA improved significantly in TROG-H sentence comprehension 2 PWA improved significantly, 1 PWA showed tendency for improvement in TROG-H number of blocks correct 2 PWA remained stable on the BNT 1 PWA showed tendency for improvement on the BNT

(Salis, 2012)	1	TMA	English	13 weeks (26X 30-minute sessions)	- listening span tasks of serial word recognition - matching listening span that required judgment of sameness	Numerical improvement in Digits forward and Digits backward from the WMS Numerical improvements in Digit listening span from PALPA	Subtest 1 "Touch the green square" from the TT did not change Numerical improvement in Subtest 2 "Touch the large green square" from the TT Significant improvement on the TROG Significant improvement in the number of repetitions requested in the TROG
(Salis et al., 2017)	5	Not specified	Not specified (English)	13 weeks (26X 30-minute sessions)	- listening span tasks of serial word recognition - matching listening span that required judgment of similarity	no statistically significant changes - Improved digit matching listening span of 3 participants by one or two items	no statistically significant changes - Improved sentence comprehension of 3 participants in the TROG by 4-5%, and in the TT by 4-10%. -

| (Harris et al., 2014) | 2 | 1 Broca's
1 expressive aphasia | Not specified
(English) | 2 treatments, each lasted 10 weeks (10 x 90-minute sessions) | Treatment 1:
- pSTM training
Treatment 2:
- sSTM training | Both participants improved significantly in nonword recall after nonword (pSTM) treatment

significant improvement following the real word (sSTM) therapy | evidence of type-specific generalisation to sentence comprehension
- the pSTM patient showed improvement on sentence repetition after the pSTM treatment
- the sSTM patient improved sentence anomaly judgement after the sSTM but not the pSTM treatment. |

Key: TMA = Transcortical Motor Aphasia; TROG = Test for the Reception of Grammar; H = Hungarian; BNT = Boston Naming Test; WMS = Wechsler Memory Scale; TT = Token Test; STM = Short-Term Memory; pSTM = Phonological short-term memory; sSTM = Semantic short-term memory

2.2 Computerized Assisted Cognitive Training

Other treatment methods to train and improve WM, involve computer assisted cognitive rehabilitation (CACR) programs. For example, Łojek and Bolewska (2013) examined the effects of CACR in patients with WM and attention deficits after stroke, using the RehaCom program and the Polish computer therapy program for aphasia the Afa-System (Seniów et al., 2009). The participants were divided into two groups: patients with WM and attention deficits without aphasia and those with aphasia. Participants in the first group received the RehaCom training and participants in the second group received the Afa-System treatment. RehaCom training included attention (pick one picture from a group that is identical to the target picture) and memory tasks (memorizing and recognizing objects from a set of pictures moving horizontally across the screen). The Afa-System treatment program involved oral expression, comprehension, and reading and writing tasks. The participants with WM and attention deficits showed significant improvement for the trained functions of the RehaCom tasks only, and no generalization to untrained functions. On the other hand, some improvement was reported for PWA on the oral expression and writing subtests after training on the Afa-system protocol but no generalization effects.

Yoo et al. (2015), applied the RehaCom program for a total of 5 weeks, 5 times/week for 30 minutes each session in addition to rehabilitation therapy (physiotherapy and occupational therapy) in a group of stroke patients with cognitive deficits. The RehaCom tasks focused on attention, memory, spatial imagination, visual impairment, and visuomotor coordination. The authors compared their results to a control group of stroke patients who received only the rehabilitation therapy. The group that received the combined treatments (RehaCom & rehabilitation) showed statistically significant improvement on the Computerized Neuropsychological Test (CNT) administered at baseline and post-treatment on digit span, visual span, visual learning, auditory continuous performance, and visual continuous performance, but not in verbal learning, trail making, and the functional independence measure.

2.3 NIBS as a treatment method to improve WM

Contemporary neuroscientific techniques such as transcranial magnetic stimulation (TMS) are beginning to be explored for the purpose of cognitive enhancement. TMS is one of the most

utilized methods for the purpose of altering cognitive function including WM in healthy subjects (Hoy et al., 2016), and for a number of neurological disorders including, stroke (T. D. Kim et al., 2019). Georgiou, Lada & Kambanaros (2019) conducted a systematic review to assess the efficacy of rTMS for treatment of post-stroke aphasia. In total, 10 RCTs underwent review for their methodological quality and comprehensive summaries of the best available evidence for this treatment. Even though there was evidence that low frequency (1 Hz) rTMS has the potential to improve aphasia post-stroke irrespective of severity, the evidence was inconclusive.

A modified form of rTMS known as theta-burst stimulation (TBS), is the most commonly used method of patterned rTMS where short bursts of 50-Hz rTMS are repeated as a continuous or intermittent trains at a rate of 0.1 Hz in the theta range (5 Hz) in short intervals to produce a rapid facilitation of synaptic transmission in the stimulated cortex that can persist for over an hour after the initial stimulation session (Huang et al., 2005). Recently, Georgiou et al. (2019) reported the findings of neuronavigated continuous theta burst stimulation (cTBS) over the right pars triangularis (Tr) as a standalone treatment for two individuals with chronic post-stroke aphasia. Baseline linguistic and quality of life measures were collected prior to the treatment study. Continuous TBS was carried over 10 consecutive days for 40 secs per sessions. Immediately post-treatment and later at 3-months follow up, participants were reassessed on baseline linguistic and quality of life measures. Results from one individual revealed improvement in language skills in the post-treatment phase, but language abilities reverted to baseline scores at follow-up. Results from the second participant revealed neither improvement nor decline in language abilities at baseline to post-treatment and follow-up stages. Furthermore, improvement in quality of life was reported only by one participant. Regarding the use of the iTBS protocol as a standalone treatment for poststroke aphasia only one study was found (Griffis, Nenert, Allendorfer, & Szaflarski, 2016). In this study, 10 sessions of iTBS was applied to the residual language-responsive cortex (left inferior frontal gyrus) in 8 PWA in the chronic stage. The results showed evidence for changes in both the stimulated and unstimulated hemispheres as measured by functional and anatomical MRI data acquired before and after iTBS during covert verb generation tasks. The findings revealed improvements in verbal fluency as a result of iTBS to residual language areas after stroke.

Finally, in healthy subjects, sham and active iTBS to the LDLPFC (Hoy et al., 2016) was compared in combination with the classic n-back task using letter stimuli (2-back and 3-back

memory loads). The results revealed that iTBS significantly improved WM performance, revealing a robust improvement in the 2-back accuracy at 20- and 40-minutes post-stimulation. The findings suggest that iTBS may lead to changes in ongoing neural dynamics at larger spatial scales reflecting changes in the functional organization of distributed cortical networks (Papazachariadis et al., 2014).

2.4 Aims of the study

The primary aim of this study was to investigate the combined effects of iTBS and computerized WM treatment in a young individual with chronic aphasia post-stroke to identify potential recovery mechanisms in WM and language domains. The research is driven by the results from previous studies reported in the introduction section demonstrating the positive effects of NIBS and computerized WM training separately in the context of aphasia, but the combination of the two methods has not been explored before. The following questions were addressed:

(1) Does WM training generalize to trained cognitive areas as measured by untrained WM and fluid intelligence tasks (near-transfer effect)?

(2) Does WM training generalize to untrained receptive and expressive language and functional communication tasks (far-transfer effect)?

(3) Are generalization effects maintained at follow-up 3 months post-treatment?

(4) Does overall QoL improve after treatment?

2.5 Methods

2.5.1 Participant details

A detailed case history taken by the first author including background and medical information revealed that the participant (A.K.) was a 31-year old woman who had suffered a left haemorrhagic stroke, three years prior to the treatment study. According to the initial MRI scan, damage involved the left parietal lobe, oedema of the basal ganglia (lentiform and caudate nucleus, and internal capsule). A.K.'s current MRI image is shown in **figure 2.5.1**. She presented with chronic, moderate anomic aphasia with verbal perseveration of the Cypriot-Greek expression "potunto" (translation "of this thing"). She had ceased speech therapy 6 months prior to her participation in the study. Her then treatment was implemented in the

United Kingdom (UK), in the English language, and was focused mainly on improving reading and writing skills for English. At the time of recruitment, she was 39 months post-onset and a university graduate with a master's degree in Social Sciences (Social Work), pursuing a PhD degree in the UK. While living abroad, A.K. lived independently in an apartment and used public transportation to commute. Pre-morbidly she was right-handed but had now learnt to write with her left hand. A.K was multilingual as she spoke both varieties of Greek spoken in Cyprus (Cypriot-Greek dialect and Standard Greek) and English.

The study was conducted at the University Rehabilitation Clinic of the Cyprus University of Technology (CUT) in Limassol, Cyprus. Based on case history information, A.K. fulfilled the inclusion criteria as follows: i) native speaker of Cypriot-Greek; ii) chronological age between 21-79 years of age; iii) first-time single left hemisphere stroke, confirmed with MRI; iv) right-hand dominance; v) presence of aphasia; vi) adequate single word comprehension. Exclusion criteria were: i) severe or global aphasia; ii) damaged dorsolateral prefrontal cortex area as identified by MRI; iii) traumatic brain injury; iv) history of psychiatric or other neurological illness; v) depression; vi) epilepsy/seizures; vii) pregnancy; viii) colour-blindness or other visual disorders/visual neglect; ix) hearing loss; x) significant general medical problems including liver, cardiac, or renal dysfunctions; xi) present or past alcohol or drug abuse.
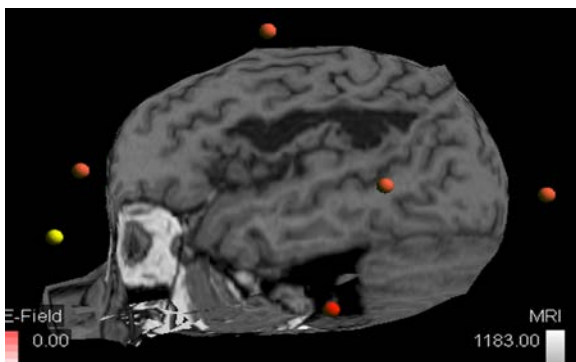
Figure 2.5.1. Lateral view of A.K.'s current MRI scan revealing involvement of the left posterior frontal lobe.

2.5.2 Ethical approval, recruitment and consent

Ethical approval was obtained from the Cyprus National Bioethics Committee. Informed consent was obtained prior to participating in the study.

2.5.3 Procedure and design

All testing was conducted by the first author who is a certified speech-language pathologist trained in the U.S, with 15 years of clinical experience in Cyprus. The assessments were presented in 2 sessions in a predetermined order, and testing was of approximately 2.5 hours in total duration.

2.5.4 Background Tools

A TMS safety questionnaire (Keel et al., 2001) was completed, followed by a screening procedure which included: (a) the *Albert's Visual Neglect Test* (Albert, 1973; Stroke Engine, 2010) to determine unilateral spatial neglect; (b) the *Edinburgh Handedness Inventory* (Oldfield, 1971), aiming to evaluate handedness of the preferred hand for carrying out common activities; and (c) the Greek adaptation of *Beck's Depression Inventory-II* (Beck, 1961; Giannakou et al. 2013), to rule out moderate-severe depression.

2.5.5 Assessment Tools

A battery of tools was administered at baseline, immediately after treatment (same day), and 3 months post-therapy at the follow-up stage as follows:

(1) the Raven's Coloured Progressive Matrices (RCPM; Raven, 2000; Sideridis et al., 2015)
(2) the Greek version of the Boston Diagnostic Aphasia Evaluation–Short Form (BDAE-SF; Messinis et al., 2013)
(3) the RehaCom Working Memory Screening Task (Hasomed GmbH, 2017)
(4) a personal stroke narrative (following Kambanaros, 2019)
(5) the Multilingual Assessment Instrument for Narratives (MAIN; Gagarina et al., 2012)
(6) a Procedural Discourse task (based on Richardson & Dalton, 2016)
(7) the Greek-version of the Stroke and Aphasia Quality of Life Scale-39 (SAQOL-39; Efstratiadou et al., 2012)

The *Raven Coloured Progressive Matrices* (Raven CPM; Raven, 2000) is a test frequently used in measuring abstract reasoning and is regarded as a non-verbal estimate of Gf (Bilker et al., 2012). The RCPM is made up of a series of diagrams or designs with a part missing, and the participant is asked to choose from six alternatives the shape to complete the pattern or shape. The Greek version of RCPM was administered as adapted by Sideridis et al. (2015). Every

correctly solved pattern was given 1 point, with a total score range between 0-36 (Papantoniou et al., 2016).

The *BDAE-SF* (Messinis et al., 2013) is normed for Greek and is culturally appropriate. It includes five subtests: (1) conversational and expository speech such as simple social responses, free conversation, and picture description; (2) auditory comprehension including word comprehension, commands, and complex ideational material; (3) oral expression, such as automatized sequences, single word repetitions, repetitions of sentences, responsive naming, the Boston Naming Test – Short Form (BNT-SF), screening of special categories; (4) reading, including letter and number recognition, picture-word matching, basic oral word reading, oral reading of sentences with comprehension, reading comprehension of sentences and paragraphs; and (5) writing, including mechanics, dictation writing of primer words, regular phonics and common irregular forms, written naming, narrative writing – mechanics, written vocabulary access, syntax, and adequacy of content. For the purpose of this study, subtests 1-4 were administered and results were analysed in accordance with the test manual.

The *RehaCom Working Memory Screening* module (Hasomed, 2017) was used to assess both simple WM span (simple information holding) and the retention and processing of visual-spatial information. The task is similar to the Corsi-block-tapping where the visual-spatial memory span is measured by the maximum length of the memorized dot patterns that can be reproduced immediately without errors (Hasomed, 2017). When the WM screening task is initiated, ten dots are presented in a circular arrangement. Individual dots sequentially turn red and fade. The first sequence consists of two random dots out of the ten lighting up in a particular order to be repeated correctly. When selected correctly, the number of dots increases in the next sequence. Overall, memory span is based on the highest sequence length measured in number of dots, reproduced without position and order errors (z-score value calculated by the software), and confirmed by completing two consecutive sequences with the same number of dots (Hasomed, 2018). The WM screening subtest ends after two consecutive incorrect sequence responses or after 7 minutes. In this study, A.K. had to memorize and reproduce the position and sequence of the coloured flashing dots.

A *personal stroke narrative* was elicited from A.K. by asking her to describe the events of her stroke (Kambanaros, 2019). The first author transcribed and analysed the narrative using the *Shewan Spontaneous Language Analysis* (SSLA) system (Shewan, 1988) protocol. Variables for analysis included number of utterances, time (total speaking time in minutes), rate (syllables

per minute), length (percentage of utterances ≤5 words), melody, articulation, complex sentences (percentage of utterances that contained one independent clause and one or more dependent clauses), errors (percentage of grammatical, syntactic, or morphological errors), content units (units that conveyed information), paraphasias (percentage of substitutions), repetitions, and communication efficiency (content units/time).

The *MAIN* (Gagarina et al., 2012) is a tool designed to evaluate narrative tell and re-tell skills in children but is also used for adults with acquired language deficits associated with neurological disease (see Karpathiou, Papatriantafyllou, & Kambanaros, 2018, on the first MAIN results for an individual with primary progressive aphasia). The MAIN stories consist of coloured picture sequences developed following strict psycholinguistic criteria. While the MAIN examines narrative production at microstructure and macrostructure levels, for this study, only the macrostructure of the generated story was analysed. The primary unit for macrostructure analysis is the episode. The content of each picture sequence was designed to represent three short episodes. Each episode consists of (i) a goal statement for the protagonist, (ii) an attempt by the protagonist to reach the goal, (iii) an outcome of the attempt in terms of the goal, and iv) the internal states (IST) which initiate the goal and also express reactions. Each story is controlled for cognitive and linguistic complexity (Gagarina et al., 2012) and has a moral meaning similar to an Aesop fable. In this study, the "Baby Birds" story was used which depicts a mother bird flying away from the nest to find worms for her hungry baby birds. Six-coloured pictures in the form of a cartoon strip were presented, and one-episode was unfolded each time (2 pictures) for A.K. to narrate based on the pictured stimuli. A setting statement, which gives time and place and introduces the story's protagonist and is scored with zero points for incorrect or no response, 1 point for one correct response, 2 points for reference to both time and place. This component is followed by three episodes. Each episode consists of a) the ISTs which initiate the goal and also express reactions; b) a goal which is a statement of an idea of the protagonist to deal with the initiating event; c) an attempt by the protagonist to reach the goal, which is an indication of action to obtain the goal; d) an outcome of the attempt in terms of the goal, which is the event(s) following the attempt and causally linked to it; and e) the internal states as reaction, which is a statement defining how the protagonist(s) feel or think about the outcome or an action resulting from an emotional response (Gagarina et al., 2012). The first author transcribed the samples verbatim and analysed each sample using a

17-point scoring system following the tool construction guidelines (Gagarina et al., 2012: 126-127).

The *Procedural Discourse* task is considered a semi-spontaneous speech production task that assesses discourse ability following the main concept analysis (MCA) procedure (Richardson & Dalton, 2016). The MCA quantifies the degree to which the speaker is able to communicate the overall gist of an event, and it provides a means to evaluate how accurately and completely the concepts considered to be essential to the shared topic are produced. A.K. was instructed to verbally provide the steps taken in order to prepare a sandwich. The generated language sample was analysed using the MCA procedure referring to the ten main concepts. The total number of main concepts expected to be produced was analysed and measured based on the concept content as listed below:

 (1) Get the bread out.
 (2) Get two slices of bread//halved bread.
 (3) Get the butter.
 (4) Get the (rest of the ingredients i.e. ham, cheese, etc.)
 (5) Get a knife.
 (6) Put/place the bread on the plate.
 (7) Put/spread butter on bread.
 (8) Put the ingredients (i.e. ham, cheese, etc) on bread
 (9) Put the two pieces together.
 (10) Cut the sandwich in pieces

The first five steps comprise of concepts concerning retrieving the ingredients needed, the following four steps include concepts concerning ingredient assembly, and the final concept describes the final appearance of the target (sandwich) prior to serving it. The first author transcribed the samples verbatim and analysed each sample using a binary scoring system of "1" for correct information and "0" for incorrect/missing information.

For all spontaneous and narrative tasks, the second author rated the samples for length, content and structure according to the protocols used as reported above. Point-by-point interrater reliability ranged from 94% to 100% and in the case of disagreement consensus was reached after discussion.

The *SAQOL-39g* has been translated and culturally adapted into Greek for use in Greece with PWA (Kartsona & Hilari, 2007). The Greek SAQOL-39g shows good reliability and validity (Eftsratiadou et al., 2012) as a measure of health-related quality of life in people with stroke, including those with aphasia. An interview with A.K. and the first author took place prior to the therapy study where the SAQOL-39 was used to collect the relevant information.

2.6 Case study design

2.6.1 Baseline phase

During the baseline phase, the six assessment measures were administered one week prior to the treatment phase. At the same time, a T1-weighted MRI image was obtained from the participant in order to accurately locate the stimulation target using the neuronavigation system (ANT NEURO). Neuronavigated positioning of the stimulation coil allowed for repeated accuracy of the stimulation site at all treatment times. Single-pulse TMS was performed to establish the resting motor threshold (RMT) with the Magstim Rapid 2® Stimulator connected to a 70 mm figure-8 air cooled coil (Magstim Co., Wales, UK). Surface electromyography (EMG) leads were placed over the first dorsal interosseous (FDI) muscle of the left hand. A.K. was seated comfortably, with her left arm supported on a pillow. Full muscle relaxation was maintained through visual and online EMG monitoring. The coil was then placed over the primary motor cortex of the right hemisphere at the optimal site for obtaining a motor evoked potential (MEP) in the FDI of at least 50 μV in five or more of 10 consecutive stimulations of the left hand. MEP was projected at intensity 55 by using a computerized adaptive parameter estimation through sequential testing (PEST; Borckardt et al., 2006), with the software TMS Motor Threshold Assessment Tool, MTAT 2.0 (Awiszus & Borckardt, 2010).

2.6.2 Therapy phase

During the therapy phase, the iTBS protocol was applied using the Magstim Rapid2® stimulator (Magstim Co., Wales, UK) with intensity set at 44, which was 80% of the MEP obtained from the right hemisphere. The figure-8 coil was positioned tangentially to the skull, with the handle parallel to the sagittal axis pointing occipitally. Stimulation consisted of bursts of three pulses at 50 Hz given every 200 milliseconds in two second trains, repeated every 10 seconds over 200 seconds for a total of 600 pulses (Huang et al., 2005). Based on A.K.'s MRI images, the Visor 2.0 neuronavigation suite (ANT-Neuro, Enschede, Netherlands) was used

for image pre-processing, tissue segmentation, and registration into standard stereotaxic space. The stimulation target was defined in the left DLPFC by using the Talairach coordinates x=-40, y= 34, z = 29 (Barbey, Koenigs, & Grafman, 2013; Wager & Smith, 2003). This technology enabled reliable three-dimensionally precise reapplication of rTMS throughout the study. A.K. received one session of iTBS each day for 10 consecutive days, followed immediately by 30 minutes WM training with the RehaCom Working Memory (WOME) software (Hasomed GmbH, DE.). The WM training task was a card game making use of a complete card deck (52 cards). During the training AK had to memorise and manipulate an increasing number of cards presented on the computer screen. During the initial levels of training, she was required only to remember the items (e.g., remember a short series of cards and replicate in the same order) whilst at higher levels additional tasks were introduced to influence the memory process (e.g. memorize only the cards of a certain suit from the presentation of various cards). A.K. constantly received feedback driven by the software about her performance, and the degree of difficulty was adapted at each level based on her results.

2.6.3 Post-therapy and Follow-up phases

The post-therapy/follow-up phase consisted of two time points. The outcome (assessment) measures were administered immediately post-therapy and again three months after treatment had ended at the follow-up phase. The purpose of the immediate post-therapy testing was to determine any short-term effects, and of the follow-up phase, to determine any long-term effects. **Figure 2.6.1** represents a schematic overview of the study design.
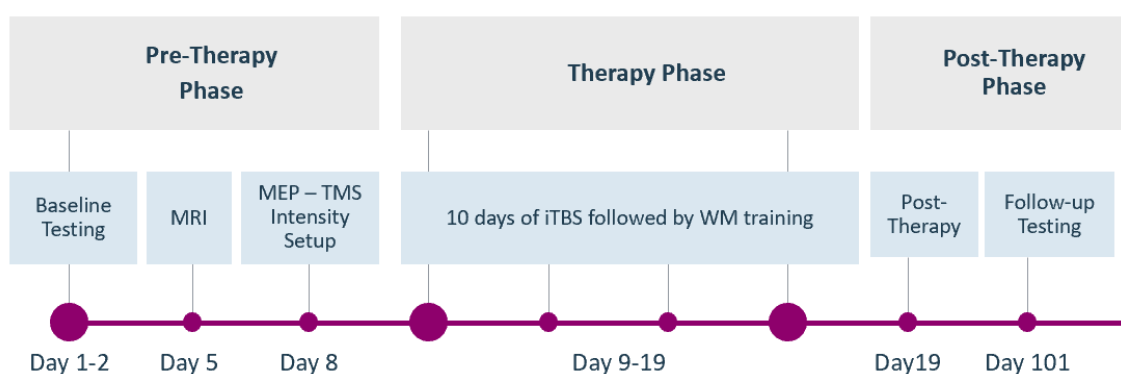
Figure 2.6.1. Schematic overview of the study design

2.7 Results

The McNemar non-parametric test (1947) was used to detect clinical change post-treatment. The McNemar's test was applied to 2×2 contingency tables with a dichotomous trait, with matched pairs of items, to determine whether the row and column marginal frequencies are equal. For this study, each item of the outcome assessment measures (i.e. Word Comprehension, Commands, Complex Ideational Material, etc.) was evaluated and characterized as success or failure taking the values zero and one respectively. For example, in the Word Comprehension subtest, 16 items were identified and characterized as correctly retrieved (success) or incorrectly retrieved (failure) for the three time points (baseline, post-therapy and follow-up) with the McNemar test. The same procedure was carried out for the BDAE subtests, (excluding the cookie theft description), the RCPM, the Procedural Discourse task, and the MAIN narrative. Comparisons were performed between baseline and post-therapy, baseline and follow-up, as well post-therapy and follow-up using the McNemar test.

All assessment measures were completed at three time points – baseline testing was carried out one week prior to the intervention, post-therapy testing was performed immediately following the intervention, and follow-up assessment was completed three-months after treatment was terminated.

With regards to the first research question whether WM training would generalize to untrained WM and fluid intelligence tasks (near-transfer effect), the baseline and post-treatment result from the RehaCom WM screening and the RCPM were analysed. Overall, there was no statistically significant improvement on the RehaCom WM screening measure. A graphic representation of the WM screening results can be seen in **figure 2.7.1.**

RehaCom WM Screening
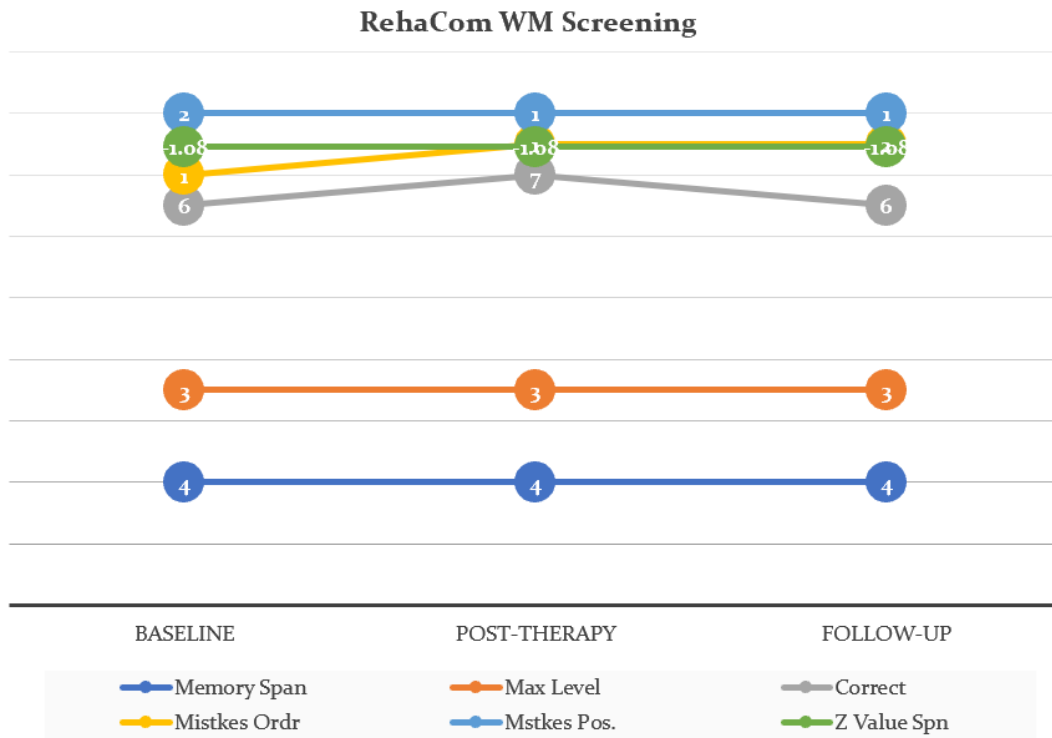
Figure 2.7.1 Schematic representation of the RehaCom WOME screening test results showing (a) an increase in correct responses during the post-therapy phase; (b) a decrease in errors post-therapy; and (c) decrease of positional errors during follow-up.

The results of the RCPM using the McNemar's test, revealed a statistically significant difference in the proportion of correct overall scores between baseline and post-therapy, p = 0.01 (See **Table 2.7.1**). At baseline, A.K. received a raw score of 24/36 (69%) which improved to 34/36 (94%) at the post-therapy phase.

Table 2.7.1. Raw scores (% correct) on the RCPM at baseline, post-therapy and follow-up

	Baseline	Post-therapy	Follow-up	p-value (two-tailed)		
				Baseline & Post-therapy	Baseline & Follow-up	Post-therapy & Follow-up
Raven (Subset A)	67%	92%	83%	p=0.38	p=0.50	p=1.00
Raven (Subset AB)	67%	100%	83%	p=0.13	p=0.50	p=0.50
Raven (Subset B)	75%	92%	83%	p=0.50	p=1.00	p=1.00
Raven	**69%**	**94%**	**83%**	**p=0.01**	**p=0.13**	**p=0.22**

With regards to the second research question whether WM training would generalize to untrained receptive and expressive language and functional communication tasks, statistical analysis was performed on results from (i) the BDAE-SF, (ii) the Procedural Discourse task and (iii) the MAIN telling task but not for the personal stroke narrative. To determine far-transfer treatment effects A.K.'s performance on the above-mentioned language tools was investigated from baseline to post-therapy phases.

2.7.1   A) BDAE-SF

Based on the Summary Profile of the standard subtests of the BDAE-SF (Messinis et al., 2013), improvements were measured in overall percentages and percentiles. Raw scores (% correct) in **Table 2.7.2** show that A.K. improved in four language tasks relative to baseline scores, at post-therapy, and at 3 months follow-up. With regards to overall Auditory Comprehension performance, A.K. improved from 77% (at baseline) to 82% (post-therapy). When looking at the individual subtest percentile ranks, A.K.'s performance on the Commands subtest, improved from the 40th percentile (at baseline) to the 70th percentile (post-therapy). Her performance on the Complex ldeational Material subtest also showed improvement, from the 30th percentile (at baseline) to the 50th percentile (post-therapy). However, the McNemar's test of A.K.'s performance on the overall BDAE-SF Expressive Language scale revealed no statistically significant difference in performance between baseline and post-therapy (p = 0.13). Nevertheless, for the Responsive Naming task A.K. showed a substantial improvement from the 40th percentile at baseline to the 100th percentile post-therapy. Furthermore, the McNemar's test revealed no statistically significant difference in performance related to the Reading subtest between baseline and post-therapy (p = 0.05). Based on the percentile ranks, A.K.'s Oral Sentence Reading improved from the 70th percentile (at baseline) to the 100th percentile (post-therapy).

Table 2.7.2. Raw scores (% correct) on subtests of the *BDAE* at baseline, post-therapy and follow up

	Baseline	Post-therapy	Follow-up	p-value (two-tailed)		
				Baseline & Post-therapy	Baseline & Follow-up	Post-therapy & Follow-up
Word Comprehension	100%	100%	100%	p=1.00	p=1.00	p=1.00
Commands	80%	80%	90%	p=1.00	p=1.00	p=1.00
Complex Ideational Material	50%	67%	83%	p=1.00	p=0.50	p=1.00
Auditory Comprehension	77%	82%	91%	p=1.00	p=0.25	p=0.63
Automated Sequencing	100%	100%	100%	p=1.00	p=1.00	p=1.00
Word Repetition	100%	100%	100%	p=1.00	p=1.00	p=1.00
Sentence Repetition	100%	100%	100%	p=1.00	p=1.00	p=1.00
Response Naming	60%	100%	90%	p=0.13	p=0.25	p=1.00
Boston Naming	100%	100%	100%	p=1.00	p=1.00	p=1.00
Screening of Spatial Categories	100%	100%	100%	p=1.00	p=1.00	p=1.00

Expressive Language	93%	100%	98%	p=0.13	p=0.25	p=1.00

(table 2.3 continued)

Matching Cases & Scripts	100%	100%	100%	p=1.00	p=1.00	p=1.00
Number match	100%	100%	100%	p=1.00	p=1.00	p=1.00
Picture-word match	75%	75%	75%	p=1.00	p=1.00	p=1.00
Oral Word Reading	100%	100%	100%	p=1.00	p=1.00	p=1.00
Oral Reading of Sentences	60%	100%	80%	p=0.50	p=1.00	p=1.00
Oral Reading of Sentences w/ Comprehension	100%	100%	100%	p=1.00	p=1.00	p=1.00
Silent Reading of Sentences w/ Comprehension	100%	100%	100%	p=1.00	p=1.00	p=1.00
Reading	92%	97%	95%	p=0.50	p=1.00	p=1.00

A.K.'s stroke narrative (spontaneous language sample) was analysed using the SSLA protocol (Shewan, 1988) designed to describe and quantify connected speech (see **Table 4**). The language sample collected at each time point, was not sufficient in word length to undergo statistical analysis hence results were compared in raw scores. There was an increase in sentence complexity between baseline and post-therapy (from 10% to 38%), and baseline and follow up. Also, a small improvement in communication efficiency which reflects the rate at which information is conveyed by the speaker (number of content units divided by time), between baseline and post-therapy (from 14.40 to 15.00) was noted but at follow-up, communication efficiency had reverted to baseline performance. No paraphasias were produced in any of the stroke narrative samples. Overall, based on the numerical values collected, there was no increase in the number of utterances, number of words produced, rate of speech, sentence length, melody, articulation, content units, error productions, and repetitions after therapy (see **Table 2.7.3**).

Table 2.7.3. A.K.'s personal stroke narrative analysis based on the *SSLA*.

Phase	Number of Utterances	Number of Words	Rate (No. of syllables/time)	Length (% of utterances < 5 words)	Melody (Scale 1-7; 1=absent, 7=normal)	Artic. (Scale 1-7; 1=always impaired, 7=normal)	Complexity score (% of utterances that contain one independent clause & one more dependent clause)	% of Errors (grammatical/ syntactic/mor phological)	Number of C.U.s	% of repetitions	Communication Efficiency Score (No. of content units/time)
Baseline	20	127	128.40	50%	4	7	10%	25%	35	15%	14.40
Post-Therapy	8	60	110.00	13%	4	7	38%	25%	18	38%	15.00
Follow-up	12	96	111.06	8%	4	7	25%	25%	25	33%	14.42

Key: utt=utterances; artic=articulation; compl=complexity; para's=paraphasias; reps=repetitions

The Cookie Theft picture description was analysed by measuring the total number of words produced (Nicholas & Brookshire, 1993) and number of Content Units produced (Berube et al., 2019) as indicated below (see Figure 5). These results were compared in raw scores. The results revealed an increase in the number of total words produced (at baseline n=57 words, post-therapy n=87 words, follow-up n=56 words) and content units (CUs) produced (baseline n=17 CUs, post-therapy n=27 CUs, follow-up n=18 CUs).

Cookie Theft Analysis
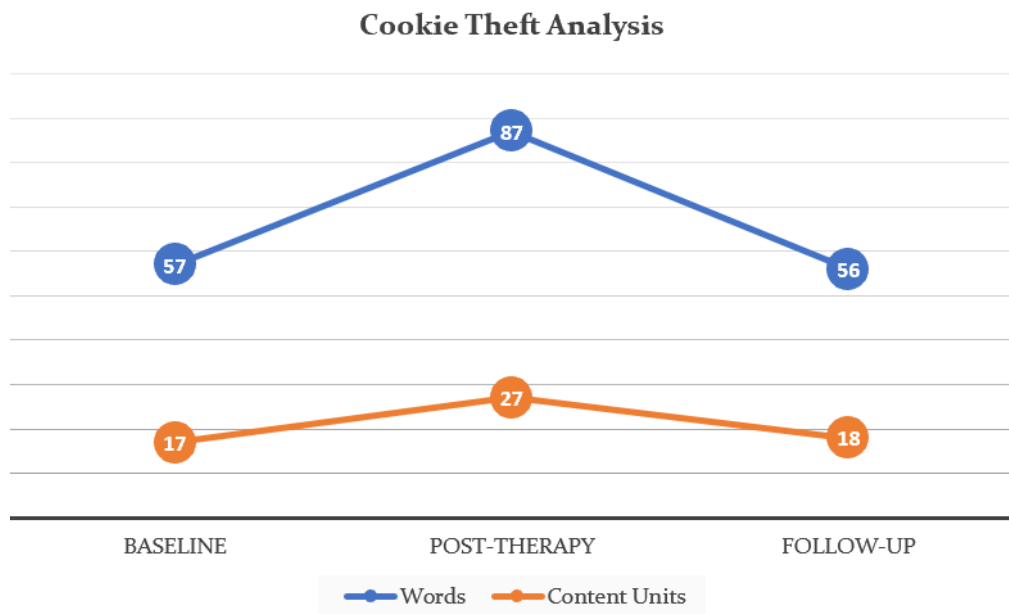
Figure 2.7.2 Results of the Cookie Theft Analysis showing an increase in the number of words and content units produced between baseline and post-therapy phases.

2.7.2 B) Procedural Discourse

Procedural Discourse (see **Table 2.7.4**) was analyzed using the McNemar test. There was no statistically significant difference between baseline and post-therapy performance (p = 1.00), baseline and follow-up (p = 0.50), post-therapy and follow-up (p = 1.00).

Table 2.7.4. Raw scores (% correct) on the procedural discourse task at baseline, post-therapy and follow-up

	Baseline	Post-therapy	Follow-up	p-value (two-tailed)		
				Baseline & Post-therapy	Baseline & Follow-up	Post-therapy & Follow-up
Procedural Discourse	40%	50%	60%	p=1.00	p=0.50	p=1.00

2.7.3 C) MAIN

The McNemar test revealed no statistically significant difference in the proportion of correct outcomes on the MAIN between baseline and post- intervention (p = 0.38). However, improvement was noted for a) the setting statement during post-therapy and follow-up; b) the IST as initiating event and IST as reaction of the second episode during post-therapy and follow-up; c) the outcome of the second episode during post-therapy; d) and IST as initiating event of the third episode during follow-up (see **Table 2.7.5**).

Table 2.7.5. Raw scores (% correct) on the MAIN at baseline, post-therapy and follow-up

	Baseline	Post-therapy	Follow-up	p-value (two-tailed)		
				Baseline & Post-therapy	Baseline & Follow up	Post-therapy & Follow-up
Baby Bird-story	31%	50%	56%	p=0.38	p=0.13	p=1.00

In relation to the third research question regarding whether any generalization effects were maintained at 3 months follow-up, there is evidence of some positive effects and even a trend for further improvement after treatment was terminated as reported below. Although the RCPM follow-up results were lower than at post-therapy, they remained higher than baseline performance (**Table 2.7.1**).

Based on the McNemar's test there was no statistically significant difference in the overall BDAE Auditory Comprehension performance between baseline and follow-up (p = 0.25), and post-therapy and follow-up (p = 0.63). With regards to overall Auditory Comprehension, A.K. continued to improve without receiving any treatment from 82% (post-therapy) to 91% (follow-up). When looking at the individual subtest percentiles the Commands subtest score was maintained at the 70th percentile from post-therapy to follow-up. The Complex Ideational Material subtest score continued to improve from the 50th percentile at post-therapy to the 70th percentile at follow-up.

The McNemar's test regarding the overall BDAE-SF Expressive Language score revealed no statistically significant differences in performance between baseline and follow-up (p = 0.25), and post-therapy and follow-up (p = 1.00).

Similarly, the McNemar's test revealed no statistically significant difference in the proportion of correct words read for the Reading subtest between baseline and follow-up (p = 1.00), and post-therapy and follow-up (p = 1.00).

With regards to the discourse measures, The Procedural Discourse task showed continuation of improvement (**Table 2.7.4**) between post-therapy and follow-up (from 50% to 60%; p = 1.00). The increase in the total number of words and number of Content Units produced during the Cookie Theft picture description was not maintained at follow-up. Analysis of the MAIN revealed a trend for continuous improvement at 3 months follow-up (from 50% to 56%). The McNemar test revealed no statistically significant difference in the proportion of correct outcomes between post-therapy and follow-up (p = 1.00).

With regards to the fourth research question investigating whether overall QoL would improve after treatment, the self-rated SAQOL-39 was analysed by comparing the mean scores (see Figure 6). A.K.'s responses indicated that her QoL improved between baseline (M = 4.69) and post-t therapy (M = 4.90) by 4% and was maintained at follow-up (M = 4.93).
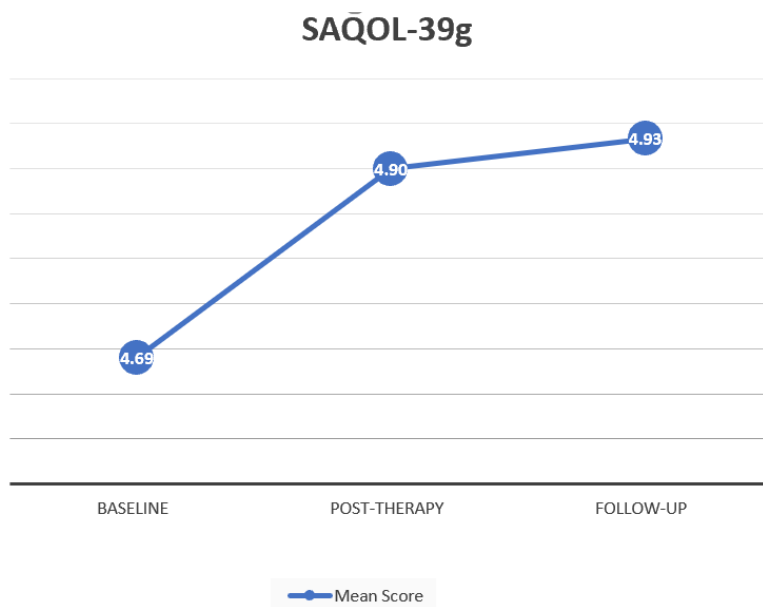
Figure 2.7.3. Mean scores on the SAQOL-39g at baseline, post-therapy and follow-up.

2.8 Discussion

The main aim of the study was to obtain preliminary evidence from a pilot case study on whether using NIBS combined with computerized WM training would boost language recovery in a single participant with post-stroke chronic aphasia. To the best of our knowledge,

the present study is the first to examine the combined effects of applying the iTBS protocol with RehaCom WM training for rehabilitation of aphasia. The effects of the 10-day combined iTBS and WM computerized treatment were measured on the RehaCom Working Memory Screening Task (Hasomed GmbH, 2017), the RCPM (Raven, 2000; Sideridis et al., 2015), the BDAE-SF (Messinis et al., 2013), the MAIN (Gagarina et al., 2012) and the SAQOL-39 (Eftsratiadou et al., 2012) and were analysed to determine the near-transfer effects of WM and the far-transfer effects of fluid intelligence and language functioning, and the effects of the treatment on QoL. The investigation of this proposed treatment is an important issue as it is provided for a short period of time (10 days) and is based on evidence (i.e. Lundqvist et al., 2010; Papazachariadis et al., 2014; Salis et al., 2017) documenting positive treatment effects of NIBS and CACR independently (see introduction), but not combined to address the needs of PWA.

To assess treatment efficacy the outcome measures were compared at the different time points, that is, between baseline and post-treatment, baseline and follow-up, and post-treatment and follow-up. The findings from this pilot study on a single case lend support to the evidence that (i) WM interacts with language abilities and deficits in WM influence language performance (i.e. Murray, 2012); (ii) applying iTBS to the LDLPFC results in improved WM performance (i.e. Demeter et al., 2016; Hoy et al., 2016); (iii) computerized WM training can have positive outcomes on WM tasks (i.e. Lundqvist et al., 2010); (iv) chronic aphasia has a negative effect on QoL (i.e. Manning et al., 2019).

2.8.1   Near-transfer effects of iTBS to the LDLPFC combined with WM training

Results from the RehaCom WM screening (Figure 3) revealed a trend for improvement that did not reach statistical significance. The results are in agreement with previous research showing a non-significant improvement in WM post-training, despite a steady improvement over the duration of the training sessions albeit in healthy ageing adults (Barbu et al., 2017). In general, the RehaCom WM training program has scarcely been used for PWA. Future research is needed to clarify how useful RehaCom as a method of CACR is beneficial for aphasia recovery. In contrast to the expectation that WM would improve after the 10-day treatment, the effect was insignificant with a minor improvement in the number of correct responses (+1) and positional errors (-1) produced between baseline and post-therapy only. These results are in contrast with previous research indicating that computerized WM training improves WM

abilities after acquired brain injury (e.g. Lundqvist et al., 2010; Westerberg et al., 2007), but this contradiction could be due to the short training period (10 days) and/or that only one outcome measure was used to measure WM improvement and multiple baselines were not obtained to provide sufficient information for comparative purposes.

2.8.2 Far-transfer effects of iTBS to the LDLPFC combined with WM training

A.K. had moderate anomia with significant word retrieval difficulties during connected speech. Difficulties were noted also with auditory comprehension, other expressive language abilities and certain cognitive functions. Based on her language and cognitive profile, it was hypothesised that stimulation of the DLPFC combined with WM training would result in improved scores on untreated WM and language tasks. Significant treatment effects were found on the RCPM, a non-trained measure that indicates improvement and far-transfer effects of *Gf* (non-verbal intelligence). This finding is in line with results from a study where significant improvements in *Gf* resulted following cognitive intervention combined with different transcranial electrical brain stimulation protocols (Brem et al., 2018). The findings support the notion that *Gf* can be improved with WM training (Engle et al., 1999; Friedman et al., 2006; Unsworth et al., 2014) and DLPFC stimulation (Brem et al., 2018).

The BDAE-SF results revealed improved language skills on the untrained tasks, even though they failed to reach statistical significance. Specifically, there were improvements in Auditory Comprehension, Commands and Complex Ideational Material subtests. This improvement in auditory comprehension is consistent with results from previous studies that used WM training to improve receptive language abilities in PWA (Eom & Sung, 2016; Harris, et al., 2014; Salis, 2012; Salis et al., 2017; Zakariás et al.,2016). To the best of our knowledge, no other research so far has explored improvements following WM training with regards to responsive naming or sentence reading.

Narrative discourse was elicited with three types of tasks: a spontaneous speech sample and the cookie theft picture description from the BDAE-SF (Messinis et al., 2013), and the baby bird story from the MAIN (Gagarina et al., 2012). A positive trend towards improvement in discourse was noted for all three tasks, with a marked improvement at the post-therapy phase. There is evidence to support higher scores on WM measures are associated with better discourse production abilities in people with brain injury (Youse & Coelho, 2005).

Procedural Discourse analysis was based on the analysis developed by Richardson and Dalton (2016). A.K.'s improved results from baseline, to post-therapy and follow-up are in agreement with research from the aphasia literature on discourse (e.g., Andreetta, Cantagallo, & Marini, 2012; Capilouto, Wright, & Wagovich, 2006; Fergadiotis & Wright, 2011; Ulatowska, North, & Macaluso-Haynes, 1981). From the aforementioned studies, only one study was specifically directed to procedural discourse (Ulatowska et al., 1981), with the more recent studies (Andreetta et al., 2012; G. J. Capilouto et al., 2006; Fergadiotis & Wright, 2011) exploring all aspects of discourse production, including narratives, revealing that as aphasia severity increases, quality and quantity of relevant discourse decreases.

The fact that A.K. did not rate her QoL as severely affected at the time of the study is in line with previous research reporting that PWA in the chronic stage often perceive their QoL as adequate, suggesting that with the passing of time individuals adapt to living with aphasia (Spaccavento et al., 2013). Nevertheless, improvement in her overall QoL was noted from baseline to post-therapy and maintained at follow-up. This is in agreement with the QoL literature that improvement in the severity of language deficits brings about an improvement in QoL (Spaccavento et al., 2014). Moreover, the results are consistent with what has been found in previous research, that non-verbal cognitive impairments may significantly affect QoL in PWA and are potentially important predictors to improvement (Nicholas et al., 2017). In addition to the measured results, A.K. reported noticing improvement in daily word-retrieval tasks, specifically with numbers. Prior to the treatment, she would count her fingers to acquire a number, but post-therapy she and her family noticed that counting was often being done mentally. This translational improvement has real-world meaning for A.K.

Overall, the finding of a significant improvement in non-verbal intelligence and the trends for improvements in language abilities are indicative that computerized WM training and stimulation of the LDLPFC are areas of interest for future exploration towards facilitating language recovery in PWA. This pilot case study may provide insights towards directions for further investigation, and a guide to the design of a more rigorous research program with larger numbers of participants.

2.9 Study limitations

The major limitation of the present study is that the outcome measures were taken only at three time- periods and as such did not meet the criteria for a single subject experimental design. The

single-subject design requires multiple baseline scores with the minimum of two timepoints prior to treatment (see Howard, Best, & Nickels, 2015). In this case, it was not feasible to undertake multiple baseline measures due to A.K.'s time constraints to return to the United Kingdom to resume her studies. This study was a first investigation of the relationship between computerized WM training followed by iTBS application to the LDLPFC in order to investigate potential language improvement in one individual with post-stroke chronic aphasia. It is important to note that results were based on a single WM outcome measure as well as insufficient length of spontaneous speech samples. As such, the results cannot be considered representative of how efficacious computerised WM training and LDLPFC stimulation is towards language improvement in PWA. Nevertheless, the trend for improvement highlights a relationship worthy of continued investigation. Future research should incorporate a wider variety of WM measures, auditory comprehension, and discourse measures.

2.10 Conclusion

This pilot case study suggests that stimulation of the LDLPFC combined with computerized WM training after left hemisphere stroke has the potential to generalize to language improvements. Improvement was not related to spontaneous recovery, since the participant was well in the chronic stage and did not receive additional therapy prior, during or after the treatment phase. A larger number of participants would provide more reliable results. The treatment results are encouraging as this treatment protocol seems to be efficacious towards improvement in non-verbal intelligence that boosts language improvements. The results are promising although the overall level of improvement is small, but this should not be discouraging as these results are based only on one case.

It is clinically and theoretically important to investigate whether brain stimulation and WM training operate synergistically as an underlying treatment approach that enhance cognitive and language processing networks. It is critical to further investigate whether such combined treatment protocols will be taken on as new methods for post-stroke aphasia rehabilitation in the future.

This chapter was a pilot study that preceded the main study, and it was performed in order to appraise the assessment tools and treatment outcomes. This case study projected positive outcomes with statistically significant improvements in non-verbal intelligence (RCPM) and clinical improvements in WM, receptive and expressive language, and QoL, without adverse

side effects. This treatment was deemed worthy to investigate further in the main study while adapting it to a multiple baseline singe-case design to achieve more statistically robust results. The pilot study was submitted for publication in the Aphasiology journal and it is under review. The next chapter elaborates how the main study's data were obtained and analysed, followed by the results, and discussion.

2.11 Treatment delivery fidelity

The treatment protocol is reported in accordance with The Template for Intervention Description and Replication (TiDier) checklist (Hoffmann et al., 2014), which was used to ensure this procedure can be replicated in the future. Treatment was delivered as planned and described in the procedure section without modifications during the implementation.

2.12 Competing interests

2.13 Funding sources

2.14 Acknowledgements

3 METHODOLOGY AND PROCEDURES

Findings from the pilot case study in chapter 2, revealed that stimulation of the LDLPFC combined with computerized WM training after left hemisphere stroke has the potential to generalize to language improvements. A larger number of participants would provide more reliable results. In this chapter the principal study is described as follows: (1) the participant recruitment procedure along with the inclusionary/exclusionary criteria, (2) the study design, (3) the data collection and procedures, along with the equipment used, (4) a description of the iTBS and WM training treatment protocols, and (5) any ethical considerations.

3.1 Participants

The study was carried out at the Cyprus University of Technology (CUT) Rehabilitation Clinic. The participants were obtained through public announcement and advertisement in the media and social networks, by posting in private and public hospital announcement boards, through direct contact with medical doctors, and through rehabilitation centres' and the Cyprus Stroke Association. Ethical approval was obtained from the Cyprus National Bioethics Committee. Informed consent was obtained prior to participating in the study. Participants in the study were residents of Cyprus, diagnosed with mild or moderate aphasia following a first-time left hemisphere (LH) stroke. The inclusion/exclusion criteria were made known as indicated in **table 3.1.1** below.

Table 3.1.1. Inclusion/exclusion Criteria

Inclusion Criteria	Exclusion Criteria
a) Native Cypriot-Greek speakers	a) severe aphasia
b) first-time single left hemisphere stroke, confirmed with an MRI	b) damaged dorsolateral prefrontal cortex area as identified in the MRI
c) fluent or non-fluent aphasia as indicated in their medical file	c) Traumatic Brain Injury
d) presence of aphasia	d) history of psychiatric or other neurological illness
e) right-hand dominance	e) history of depression

g) intact comprehension at the single-word level	f) history of epilepsy/seizures
h) chronological age between 21-79 years	g) pregnancy
	h) color-blindness or other visual disorders/visual neglect
	i) unaided moderate-severe hearing loss
	k) significant general medical problems including liver, cardiac, or renal dysfunctions
	l) current alcohol or drug abuse

The recruitment phase was carried for a period of 20 months and although 30 persons applied to participate in the study (N=30), 7 completed the study (N=7), of which 5 were included in the main study (N=5). The participant selection which relied on the inclusion and exclusion criteria is described in **Figure 3.1.1** below.
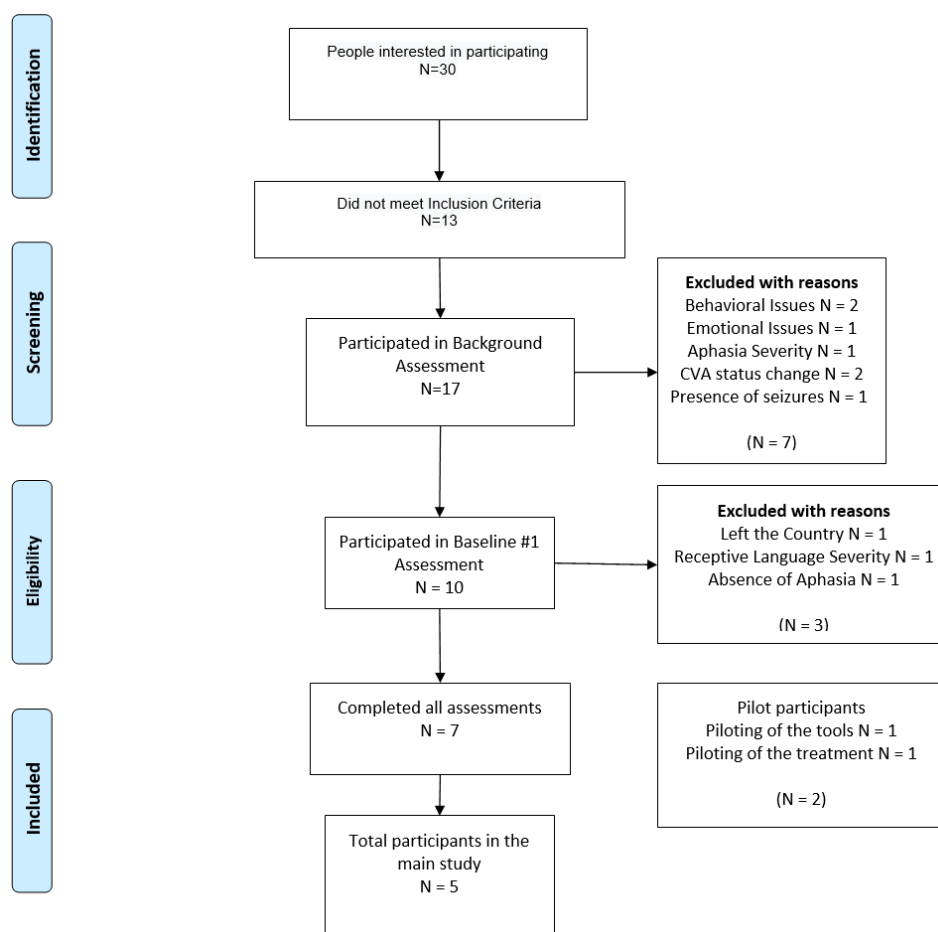
Figure 3.1.1. PRISMA (Liberati et al., 2009) flow chart for the participants selection

The first two participants were recruited for the pilot study to verify that all pre-therapy and therapy procedures were appropriate for prospective participants of the main study. In particular, the first participant suffered a LH stroke but did not exhibit aphasia, and therefore participated in the pilot study to appraise the instrumental and assessment procedure. The second participant fulfilled the criteria and is described as a case-study in chapter 2. The five participants' background details and demographics are listed in **table 3.1.2** below.

Table 3.1.2. Background details of participants.

Participant Initials	Gender	Age	Time post onset	Aphasia type
1) I.A.	M	68	17 months	Mild Expressive
2) C.S.	M	63	1 month	Mild Receptive
3) S.H.	M	54	9 months	Moderate Global
4) C.G.	M	35	1 month	Moderate Expressive
5) F.C.	M	71	3 months	Moderate Global

Participant #1 (I.A.) was a 68-year old male who suffered an ischemic LH ischemic stroke one-and-a-half-years prior to the study. Although the current MRI (**Figure 3.1.2**) did not show visual evidence of CVA damage, the initial medical examination report indicated left hemisphere ischemic stroke, characterized with severe dysarthria. The participant had received speech-language therapy during the acute phase post-stroke but did not continue thereafter. Ever since, he had been experiencing mild expressive aphasia with severe dysarthria and unintelligible speech. He was experiencing increased salivation, with difficulty controlling and swallowing the saliva. Otherwise, he did not report any additional swallowing difficulties. He did not suffer from any paresis or paralysis. He was a retired construction worker with 7 years of elementary school education. He lived with his wife and was able to care for himself. Based on the Instrumental Activities of Daily Living (IADL) questionnaire, which was filled by his wife, he only required assistance for laundry duties. The participant's Beck's Depression Inventory (BDI-II) questionnaire score was 13, which was considered within normal limits (>17 possibility for depression; Giannakou et al., 2013; Kosmidou & Roussi, 2002).
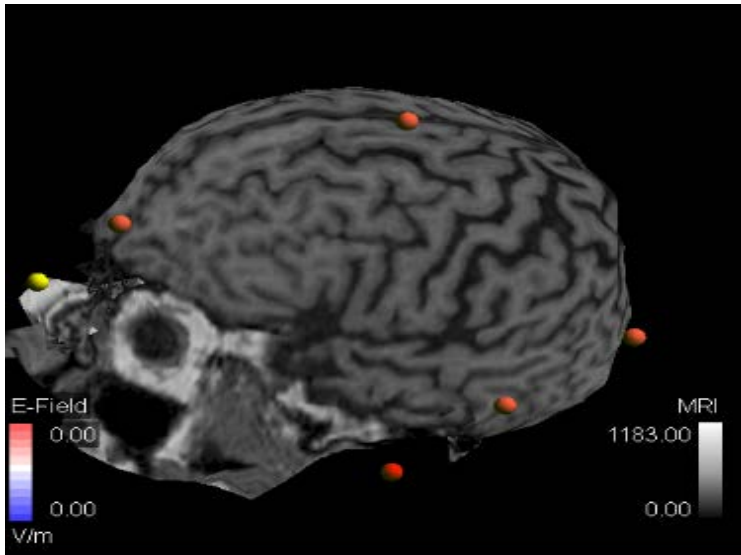
Figure 3.1.2. *Participant #1 (I.A.) MRI. Lateral left view of the participant's brain, which was used with neuronavigation to locate the DLPFC. Post CVA lesion was not visible at MRI. The participant's CVA was confirmed with written medical referral dated February 2017.*

Participant #2 (C.S.) was a 63-year old male who suffered a LH ischemic stroke one month prior to this study. He did not receive any speech-language therapy. He had been experiencing mild receptive aphasia with short-term memory and verbal information comprehension difficulties. He was a retired food and beverage employee and remained as a hobby farmer, with 12 years of school education. Although this participant's brain damage was not visible on the current MRI (**Figure 3.1.3**), the previous MRI report dated 45 days prior to entering the treatment study (dated October 5, 2018), indicated the presence of an acute ischemic stroke in the medial temporal lobe. Mr. C.S. lived with his wife and did not suffer any paresis or paralysis as he was able to drive and to care for himself with minimal assistance. Based on the IADL questionnaire, which was reported by his daughter, 1) he could answer the phone but did not use it spontaneously; 2) he was accompanied by another person during shopping activities; 3) he could prepare a meal if the ingredients were provided; 4) he could carry out some daily housekeeping tasks; 5) he could drive but was always accompanied by someone else; 6) he was able to take his medication if someone prepared it in doses but occasionally forgot; and 7) he was able to independently manage financial tasks. The participant's BDI-II questionnaire score

was 17, which was considered within normal limits (>17 possibility for depression; Giannakou et al., 2013; Kosmidou & Roussi, 2002).
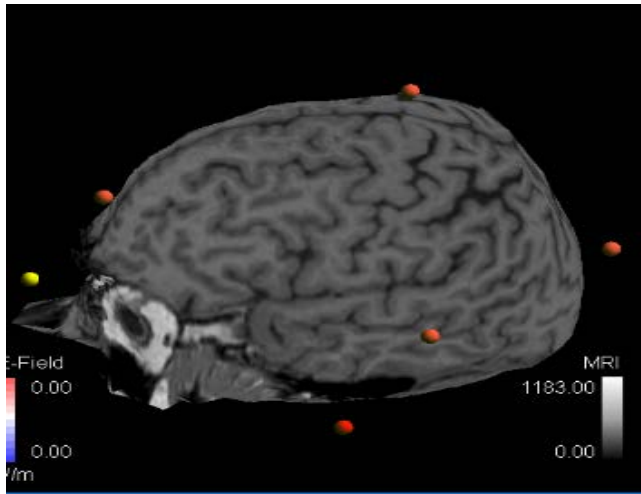
Figure 3.1.3. *Participant #2 (C.S.) Reported findings of the current MRI noted two small areas of low signal intensity involving the subcortical white matter of the left occipital lobe and the left temporal lobe which were compatible with small areas of brain parenchymal loss.*

Participant #3 (S.H.) was a 54-year old male who suffered a LH ischemic stroke nine months prior to entering this study. His MRI report dated March 5, 2018 indicated hypodense area in the left parietal lobe, corresponding to the occipital horn of the left lateral ventricle, indicating the presence of ischemia. His current MRI (**Figure 3.1.4.**) shows the lesion in the left parietal lobe. He was experiencing moderate global aphasia with moderate to severe apraxia of speech. He was an electrician with 12 years of school education. Mr. S.H. lived with his wife and required assistance and supervision to manage his daily activities as he suffered from moderate right-side hemiparesis. Based on the IADL questionnaire, which was reported by his wife, 1) he could answer the phone but did not use it spontaneously; 2) he was unable to perform shopping activities; 3) meals were required to be prepared and served by someone else; 4) he was unable to carry out any daily housekeeping tasks, including laundry; 5) moving and travelling was limited and could be accomplished with assistance; 6) he was able to take his medication if someone prepared the doses; and 7) he could not manage financial tasks. The participant's BDI-II questionnaire score was 2, which was considered within normal limits (>17 possibility for depression; Giannakou et al., 2013; Kosmidou & Roussi, 2002).
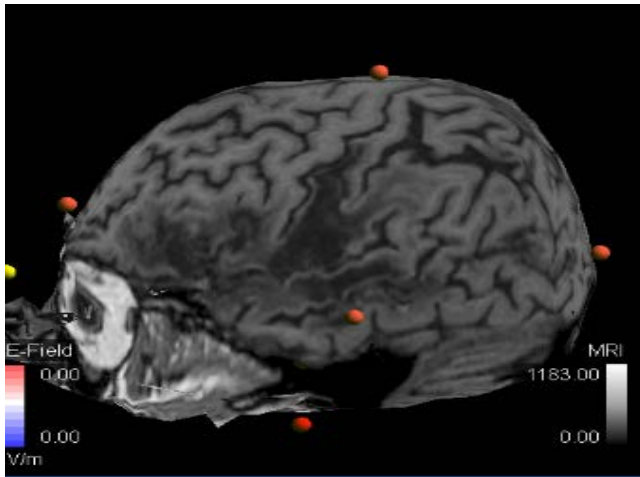
Figure 3.1.4. *Participant #3 (S.H.) MRI. Findings of the current MRI showed an extensive area of brain parenchymal loss associated with perifocal gliosis, involving the left parietal lobe extending inferiorly to the anterior left temporal lobe and also posteriorly to the left occipital lobe. The above caused significant ex vacuo dilatation of the left lateral ventricle. Prominence of the third ventricle was also noted. In addition, subtle hypointensity involving the left corticospinal tract, causing asymmetry of the cerebral peduncles and pons was noted, compatible with a left-sided Wallerian degeneration.*

Participant #4 (C.G.) was a 35-year-old male who suffered a LH ischemic stroke one month prior to entering this study. Therefore, repeated weekly baselines were administered until the participant had demonstrated stable results in the assessments. A total of 5 baselines were administered. The pre-therapy phase was terminated when the tests showed similar results as the last 2 baselines. He did not receive any speech-language therapy. He was experiencing moderate expressive aphasia with major word retrieval difficulties, syntactic impairments, and minor comprehension difficulties. He was a university graduate with a bachelor's degree and was working as a police officer. He did not suffer any paresis or hemiparesis. Based on C.G.'s initial medical report dated December 3, 2018, he suffered an ischemic CVA at the posterior part of left frontal lobe, anterior and middle part of left parietal lobe, part of the temporal and posterior part of the Isle of Reil. His current MRI **(Figure 3.1.5.)** shows the exact area of lesion. He lived with his wife and two toddlers and was able to carry out most daily activities without assistance. Based on the IADL questionnaire, which was reported by his wife, he only required assistance for transportation by car and to manage financial tasks. The participant's BDI-II questionnaire score was 5, which was considered within normal limits (>17 possibility for depression; Giannakou et al., 2013; Kosmidou & Roussi, 2002).
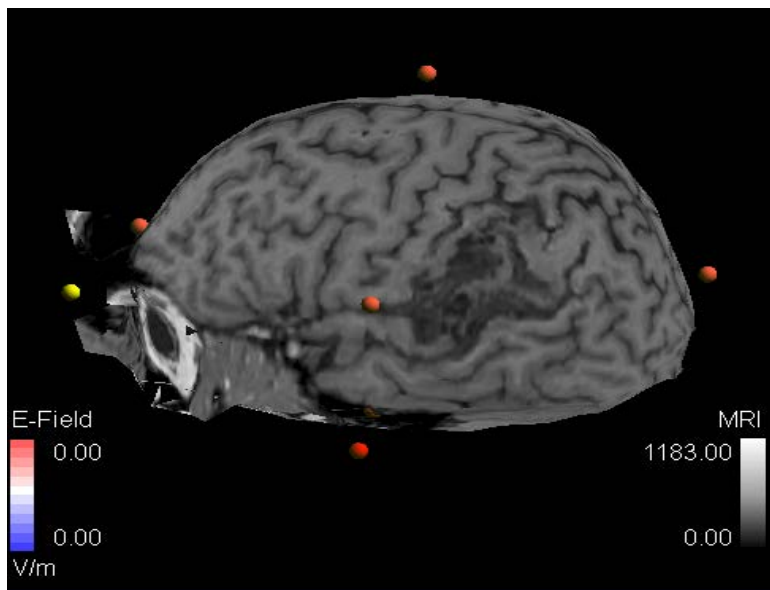
Figure 3.1.5. *Participant #4 (C.G.) MRI. Findings of the current MRI report showed evidence of extensive low signal intensity involving mainly the cortex and subcortical white matter of the left parietal lobe and extending inferiorly to the level of the left insula. Subtle hypointensity of the deep white matter of the left parietal lobe was also noted.*

Participant #5 (F.C.) was a 71-year-old male who suffered a LH ischemic stroke 3 months prior to entering this study. F.C.'s medical report (dated February 2, 2019) indicated damage to the left front-temporal lobe at the head of the caudate nucleus and lenticular nucleus due to ischemic CVA. He was experiencing moderate global aphasia with major word retrieval difficulties and moderate comprehension difficulties. He did not receive any speech-language therapy. His current MRI **(Figure 3.1.6.)** shows the lesion to the LH frontotemporal lobe. Mr. F.C. completed 6 years of elementary education and lived with his wife. Although initially he experienced right side hemiparesis, those difficulties were resolved during the first month of recovery post stroke. He was able to carry most daily activities with minimal assistance. Based on the IADL questionnaire, which was reported by his wife, he only required assistance for transportation by car and to manage financial tasks. The participant's BDI-II questionnaire score was 4, which was considered within normal limits (>17 possibility for depression; Giannakou et al., 2013; Kosmidou & Roussi, 2002).
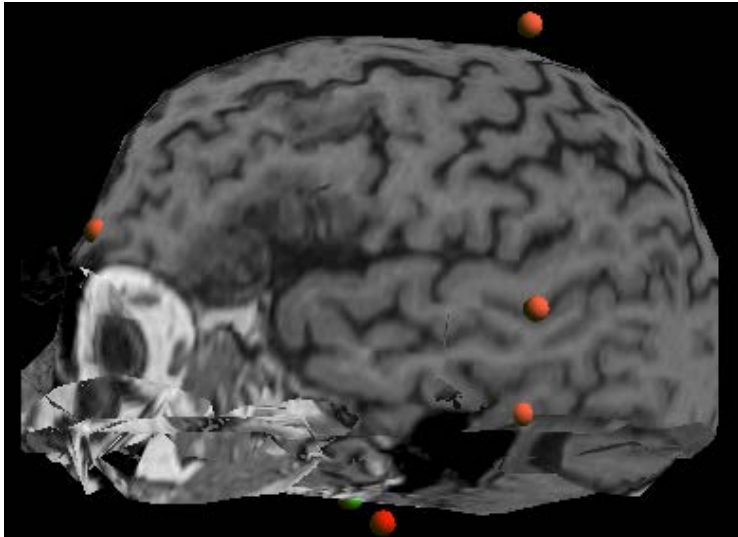
Figure 3.1.6. *Participant #5 (F.C.) Reported findings of the current MRI noted hypointensity of the left basal ganglia. An area of gliosis and scattered areas small areas of parenchymal loss involving the left parietal lobe and the extending slightly to the left frontal lobe were also noted. In addition, there was evidence of mild ex vacuo dilatation of the body and frontal horn of the left lateral ventricle.*

3.2   Study Design

The main study employed a single-case multiple baseline (MB) design comprising of three phases (Howard et al., 2015; Thompson, 2006): 1) Pretherapy or "baseline" testing phase; 2) a therapy phase; and 3) a post-therapy/follow-up phase. Single-case experimental designs are important tools for determining whether improvement is a result of treatment or of some other cause such as passage of time, and usually they are more effective than group studies for evaluating responses to the treatment whilst controlling for the effects of spontaneous recovery or improvements over time (Wilson, 1987). In the MB single case designs the participants serve as their own controls, rather than being compared to a control group (Carr, 2005). That is to say, that the baseline behavior of the participants is measured repeatedly before any type of intervention or treatment occurs and once stability of baseline behavior is established, a phase change occurs where conditions change from baseline to intervention phases. As the baseline is measured repeatedly, it allows for a prediction of the data path while no intervention occurs; this is then compared and contrasted with the intervention data (Carr, 2005). If the person is in a period of spontaneous recovery, the pre-therapy baselines will differ significantly from each other and the repeated testing over time should show improvement without intervention; so,

administering the same test on more than one occasion will project the course of further spontaneous recovery (Franklin, 1997). Likewise, the aforementioned author states that if no spontaneous recovery is occurring (see **Fig.3.2.1.**), then these pre-treatment baseline measures will not differ significantly from each other, and any significant difference in the test score following therapy will have demonstrated a treatment effect.
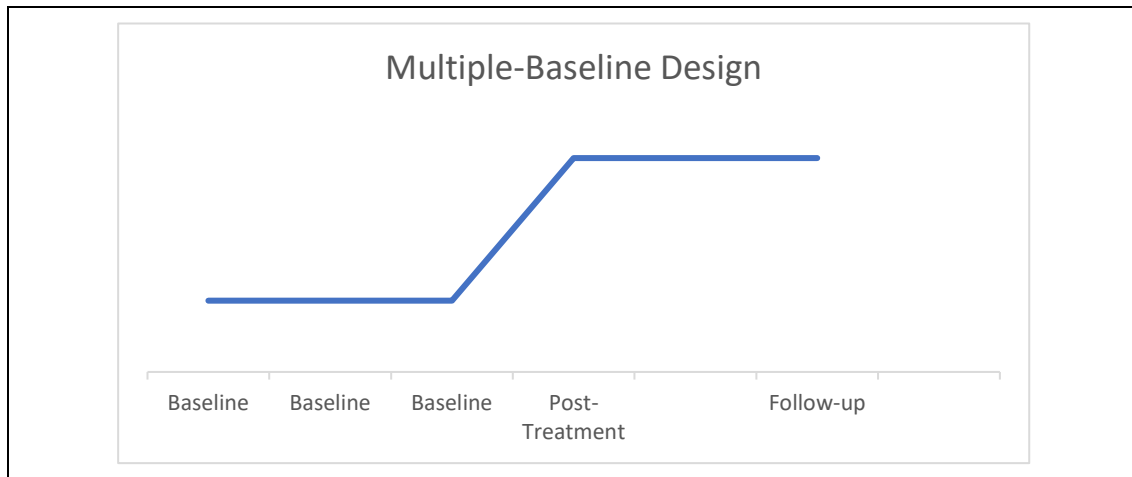
Figure 3.2.1. A schematic figure of a multiple baseline design with a pre-treatment stable baseline.

3.3   Data Collection and Procedures

The main objective was to explore the potential domains of transfer effect after WM stimulation and training, and also to measure how efficacious this treatment protocol was for PWA. Specifically, the purpose was to investigate the combined effects of iTBS and WM training on WM performance as a mediator to language generalization. To address this objective, the following questions were posed:

1)   Does WM training generalize to trained cognitive areas as measured by untrained WM (near-transfer effect) and fluid intelligence tasks (far-transfer effect)?

2)   Does WM training generalize to untrained receptive and expressive language and functional communication tasks (far-transfer effect)?

3)   Are generalization effects maintained at follow-up 3 months post-treatment?

4)   Does overall QoL improve after treatment?

To evaluate treatment efficacy through the precise transfer effects, the outcome measures included specific cognitive (non-verbal) and language (verbal) measures as reported below. The Template for Intervention Description and Replication (TiDier) checklist (Hoffmann et al., 2014) was used to ensure this procedure can be replicated in the future.

3.3.1 Background Tools

The background tools were used to fulfil aspects of the inclusion criteria as it was eminent to detect the presence of unilateral spatial neglect, determine handedness, and determine emotional status in order for the participants to proceed to the pre-testing and treatment stage of this study. A detailed case history was taken including personal and medical information. A TMS safety questionnaire **(figure 3.3.1)** was completed prior to entering the first stage of the inclusion process, followed by a screening procedure which included: (a) the *Albert's Visual Neglect Test* (Albert, 1973) to determine unilateral spatial neglect; (b) the *Edinburgh Handedness Inventory* (Oldfield, 1971), aiming to evaluate handedness of the preferred hand for carrying out daily activities; and (c) the Greek adaptation of the *Beck's Depression Inventory-II* (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961; Giannakou et al., 2013), to measure characteristic attitudes and symptoms of depression.

Figure 3.3.1. The TMS Safety questionnaire completed for all participants prior to the study proper.

3.3.1.1 Albert's Visual Neglect Test

The *Albert's Visual Neglect Test* (**Figure 3.3.2.**) is a screening test for patients with stroke. In this test, patients must cross out the randomly oriented placed lines on a piece of paper (Albert, 1973). Unilateral spatial neglect (USN) is denoted when lines are left uncrossed on the same side of the page as the person's motor deficit or brain lesion is located (Stroke Engine, 2010). The participant was instructed to draw a line through all the lines.
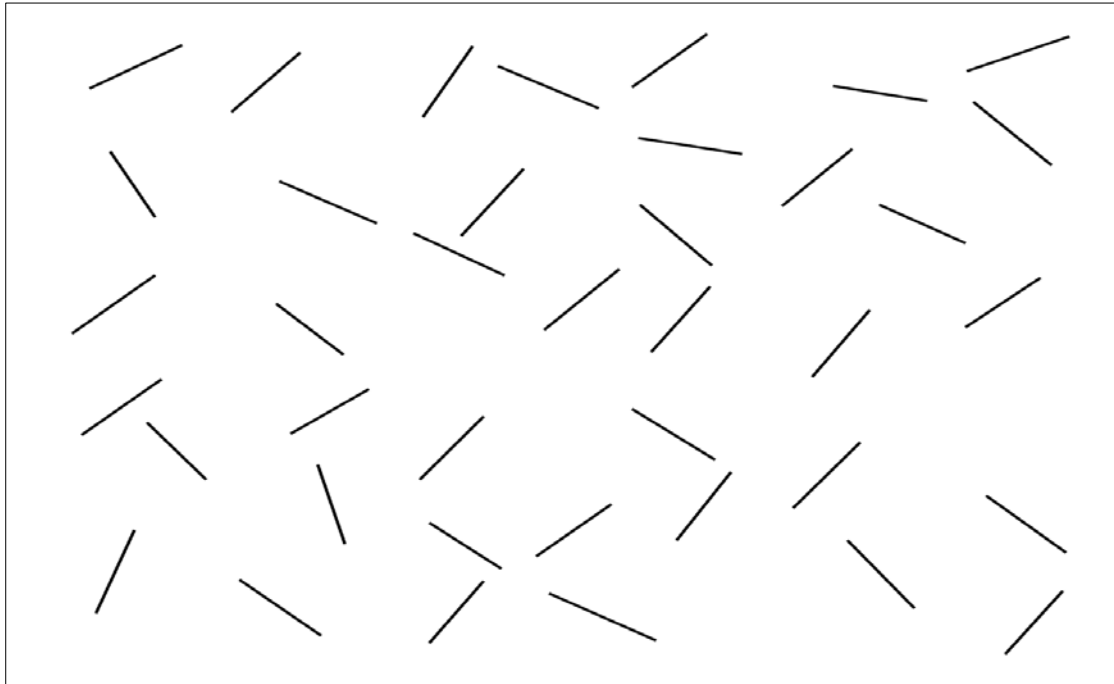
Figure 3.3.2. Albert's Visual Neglect Test

3.3.1.2 *Edinburgh Handedness Inventory*

The *Edinburgh Handedness Inventory* (EHI; Oldfield, 1971) is a ten-item self-report questionnaire aiming to evaluate handedness of the preferred hand for carrying out common activities such as writing and drawing, throwing, and using utensils such as a toothbrush, knife, and spoon (**Figure 3.3.3**). The participant is asked to place 1 or 2 check marks under ''left'' or ''right,'' indicating strength of preference for each activity; 2 checks are to be used if the individual ''would never try to use the other hand unless absolutely forced to'' for the given function. In the clinical context, the EHI offers a quick method for the assessment of expressed hand preference (Caplan & Mendoza, 2011).

Edinburgh Handedness Inventory[1]

Your participant ID:_____

Please indicate with a one (1) your preference in using your left or right hand in the following tasks.

Where the preference is so strong you would never use the other hand, unless absolutely forced to, put a two (2).

If you are indifferent, put a one in each column (1 | 1).

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

Task / Object	Left Hand	Right Hand
1. Writing		
2. Drawing		
3. Throwing		
4. Scissors		
5. Toothbrush		
6. Knife (without fork)		
7. Spoon		
8. Broom (upper hand)		
9. Striking a Match (match)		
10. Opening a Box (lid)		
Total checks:	LH =	RH =
Cumulative Total	CT = LH + RH =	
Difference	D = RH − LH =	
Result	R = (D / CT) × 100 =	
Interpretation: (Left-Handed: R < -40) (Ambidextrous: -40 ≤ R ≤ +40) (Right Handed: R > +40)		

Please stop here

[1] Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia, 9,* 97-113.

Figure 3.3.3. The Edinburgh Handedness Inventory

3.3.1.3   Beck's Depression Inventory - II

The *Beck's Depression Inventory - II (BDI-II)* is a 21-item, self-report rating inventory that measures characteristic attitudes and symptoms of depression (Beck, et al., 1961). Examples of these items include questions regarding changes in sleep patterns, difficulty concentrating, sadness, self-dislike, crying, loss of energy, and suicidal thoughts. These items were designed to capture the depression as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth edition (American Psychiatric Association, 2000). The Greek adaptation of

BDI-II (Giannakou et al., 2013; Kosmidou & Roussi, 2002) was given to the participant to self-evaluate their symptoms, by choosing the sentence that was more representative of their emotional status.

3.3.2 Assessment Tools

A battery of tools was administered three to five times prior to treatment initiation (baseline), depending on the participant's stability, on the same day upon completion of the 10-day treatment (post-treatment), and 3 months after completion (follow-up). The single-subject design requires multiple baseline scores with the minimum of two acquirements (Howard et al., 2015; Thompson, 2006). The repeated baselines were 7 days apart. The assessment battery was comprised of:

(1) the Raven's Coloured Progressive Matrices (RCPM; Raven, 2000; Sideridis et al., 2015)

(2) the Greek version of the Boston Diagnostic Aphasia Evaluation–Short Form (BDAE-SF; Messinis et al., 2013)

(3) a personal stroke narrative (following Kambanaros, 2019)

(4) the RehaCom Working Memory Screening Task (Hasomed GmbH, 2017)

(5) the Multilingual Assessment Instrument for Narratives (MAIN; Gagarina et al., 2012)

(6) a Procedural Discourse task (based on Richardson & Dalton, 2016)

(7) the Greek-version of the Stroke and Aphasia Quality of Life Scale-39 (SAQOL-39; Efstratiadou et al., 2012)

3.3.2.1 *Raven's Coloured Progressive Matrices (RCPM)*

The **RCPM** (Raven, 2000) is a non-verbal test and was originally constructed as a test of eductive ability (from the Latin root "educere", meaning "to draw out'), the ability to make meaning out of confusion, the ability to generate high-level, usually nonverbal, representations which make it easy to handle complexity. It is a tool frequently used in measuring abstract reasoning and is regarded as a non-verbal estimate of fluid intelligence (*Gf*; Bilker et al., 2012). Raven's tests have been used in several studies seeking to explain the link between WM and gF (e.g. Engle et al., 1999; Friedman et al., 2006). The RCPM is made up of a series of diagrams or designs with a part missing and is used to assess problem solving skills. The participants were asked to select the correct part to complete the designs from a number of options printed beneath (Raven, 2000). The test consists of 36 items in three sets of 12 (A, AB, and B) of

colored large-print drawings each. Set A required the participant to identify a patch in a continuous pattern and therefore measures the person's ability to complete continuing patterns; set AB required identification of a patch of a discrete pattern, which depends on the person's ability to perceive the separate forms as one gestalt on the basis of spatial relations; and set B required the identification of a patch in a continuous pattern with discrete items which depends on the ability of abstract thinking (Kazem et al., 2007; **Figure 3.3.4.**). The participant's task was to deduce the theme of relations expressed among the designs and choose the missing figure from among the alternative set of six to correctly complete the pattern. The original book form displayed each item on a page in a booklet. As suggested by Raven et al. (2000) no time limit was assigned for either task. Participants were asked to select a piece from six alternatives that completed the pattern for each item by pointing to their chosen response in the stimulus book. The Greek version of RCPM was administered as adapted by Sideridis et al. (2015) to acquire a raw score of the participant's non-verbal intellectual abilities. Performance on the RCPM was calculated according to the number of items correct. Every correct response was given 1 point, with a total score range 0-36.
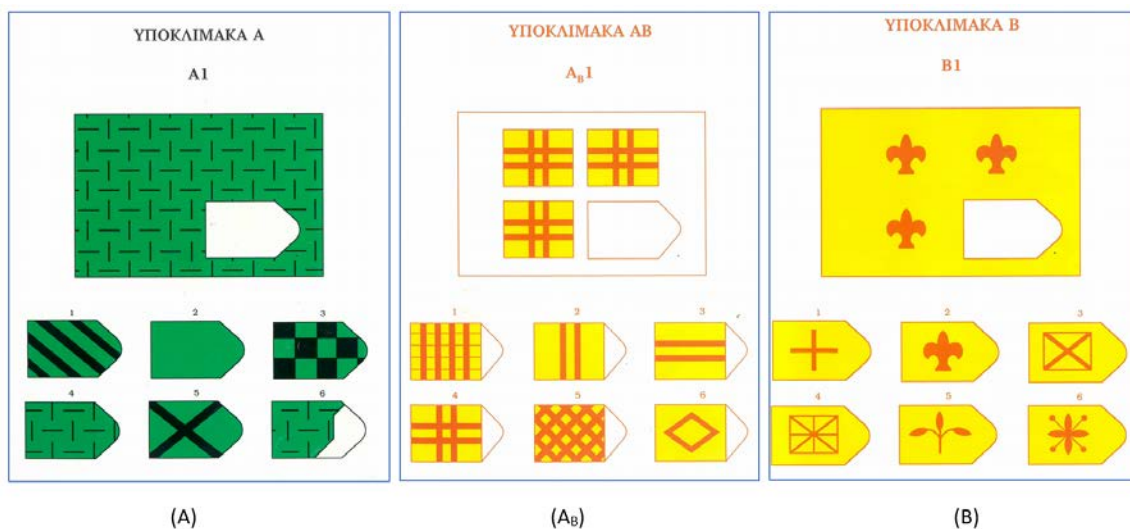
Figure 3.3.4. Examples of RCPM Task Sheets. A: Identification of a patch in a continuous pattern. AB: Identification of a patch of a discrete pattern. B: Identification of a patch in a continuous pattern with discrete items.

3.3.2.2 *Boston Diagnostic Aphasia Examination – Short Form (BDAE-SF)*

The **BDAE-SF** (Messinis et al., 2013) is a brief aphasia assessment tool used in clinical evaluations for the measurement of aphasic language performance for linguistic domains needed to identify the specific language deficits and the exact profile of differential aphasic syndromes. This tool has been adapted into the Greek language and culture, and it includes five subsections: (1) conversational and expository speech such as simple social responses, free conversation, and picture description; (2) auditory comprehension including word comprehension, commands, and complex ideational material; (3) oral expression, such as automatized sequences, single word repetitions, repetitions of sentences, responsive naming, the Boston Naming Test – Short Form (BNT-SF), screening of special categories; (4) reading, including letter and number recognition, picture-word matching, basic oral word reading, oral reading of sentences with comprehension, reading comprehension of sentences and paragraphs; and (5) writing, including mechanics, dictation writing of primer words, regular phonics and common irregular forms, written naming, narrative writing – mechanics, written vocabulary access, syntax, and adequacy of content (Tsapkini, Vlahou, & Potagas, 2009; Messinis et al., 2013). For the purposes of this study, only Auditory Comprehension, Oral Expression, and Reading (See **table 3.3.1**) were administered. Each subtest is described in detail below.

Table 3.3.1. The *Boston Diagnostic Aphasia Examination (BDAE)* scores for Auditory Comprehension, Oral Expression, and Reading.

BDAE-SF	Subtest	Score (maximum)
1. Auditory Comprehension	Word Comprehension	16
	Commands	10
	Complex Ideational Material	6
2. Oral Expression	Automatized sequences	4
	Word Repetition	5
	Sentence Repetition	2
	Responsive Naming	10
	Boston Naming Test	15
	Screening of special categories	12
3. Reading	Matching case/script	4
	Number matching	4
	Word identification	4
	Oral Basic Word	15
	Oral Basic sentence	5
	Oral Sentence Comprehension	3
	Silent Comprehension	4

1) BDAE-SF Auditory Comprehension

1a. Word Comprehension: In this subsection each participant was asked to respond by pointing in a visual multiple-choice task which included samples from four categories of words: body parts, objects, letters, numbers, and colors. The participant was given 1 point for correctly identifying the word within 5 seconds, ½ point for correct identification taking longer than 5 seconds, and no point for incorrect or no response. The maximum score was 16.

1b. Commands*:* The participant was requested to carry out three commands with two to five informational elements. One point was given for of every correct element. The test requires the participant to respond correctly to both the first two commands in order to move the third command. The score in this subscale ranges from 0 to 10.

1c. Complex ideational material*:* The participant was required to understand and express agreement or disagreement in 6 pairs of questions, of which 4 pairs were based on short paragraphs. Each pair consisted of two questions, one having yes and the other no as response options. One point is scored for each item only if both questions were correctly answered. Score ranged from 0 to 6.

2) Oral Expression

2a. Automatized Sequences: The participant was tested on two sequences: days of the week and numbers from one to twenty-one. Two points were given for the production of complete recitation of each series and 1 point was given for unaided runs of 4 consecutive words when reciting days and 8 consecutive words when reciting numbers.

2b. Single Word Repetitions: A sample of different word types was presented, including a color, an object, a noun, an abstract verb of three syllables, and a tongue twister. An item was scored correct if the produced word was intelligible and any misarticulations were noted and coded accordingly. One point was allocated per item for a total of 5 possible points.

2c. Repetitions of Sentences*:* This subtask including two sentences, one high and one low probability sentence. The participant was asked to repeat each sentence and a sentence production was scored as correct if all the words were produced intelligibly. Misarticulations were noted and coded accordingly. One point was given for each correct production for a total of 2 possible points.

2d. Responsive Naming: The participant was instructed to answer a series of questions using single words, including nouns and verbs. Each question contained a key word associated with the expected answer. Two points were given when the response was provided within 5 seconds, 1 point over 5 seconds, and 0 for failed or improper answers. The total maximum score was 15.

2e. Boston Naming Test – Short Form (BNT-SF): The participant was asked to name each of the 15-line drawings, graded in difficulty. The participant was asked to tell the examiner the

name of each picture and was given about 20 seconds to respond for each trial. The participant's response was written in detail and coded accordingly. One point was given for each correct response. If the response was incorrect, no points were given. The total maximum score was 15.

2f. Screening of Special Categories: This subtask included twelve items, representing 3 categories: letters, numbers, and colors. The participant was presented four items per sheet and was asked to name each one. Every correctly named item was awarded one point, for a total maximum of 12 points.

3) Reading

3a. Basic Symbol Recognition: Initially the participant was shown a word or letter centred above four multiple-choice responses and was instructed to select the equivalent, receiving one point for each correct response for a total maximum of four points. Next, the participant was shown a number if fingers and was asked to point to the equivalent arithmetic symbol. Similarly, on the next subtask the participant was shown a pattern made of dots and was asked to point to the equivalent arithmetic symbol. One point was given to each correct item for a total maximum of four points.

3b. Picture-Word Matching: The participant was asked to match by pointing a picture without naming it, from a choice of four options given on the right of the presented picture. One point was given to each correct item, for a total maximum of four points.

3c. Basic Oral Word Reading: The examiner indicated a word that should be read by the participant. Three points were given when the word was read within 3 seconds, 2 points within 3 to 10 seconds, 1 point within 10 to 30 seconds, and 0 if the answer was wrong. The maximum score was 15.

3d. Oral Reading of Sentences with Comprehension: The participant was instructed to read out loud 5 sentences and was informed that questions would be presented about them afterwards. Each question must be read precisely in order to receive a point for each one, for a total of 5 points. Next, the participant was provided with three incomplete sentences regarding the sentences previously read, and was requested to complete the ending of a sentence with a four multiple choice options. One point was given for each correct sentence with the maximum score of 3 points.

3e. Reading Comprehension of Sentences and Paragraphs: In this subtask the participant was instructed to silently read 4 incomplete sentences and was requested to complete the ending of a sentence by pointing to one of the four multiple choice options. One point was given for each correct sentence.

3.3.2.3 *Personal Stroke Narrative - The Shewan Spontaneous Language Analysis (SSLA) system*

For the ***Personal Stroke Narrative*** (Kambanaros, 2019) each participant was encouraged to engage in an open-ended conversation (spontaneous language sample) where they were asked to tell a story about their life before the stroke. The participants were permitted unlimited time and when they appeared to have finished, the examiner gave one prompt by asking if they wished to add anything further. If they continued to talk further, the content was included in transcription; otherwise the sample was considered complete. Each language sample was audio-recorded and transcribed verbatim using orthographic transcription, and phonetic transcription when necessary. The transcription included all the empty and filled pauses (e.g. uumm"). The spontaneous speech sample was quantified using the Shewan Spontaneous Language Analysis (SSLA; Shewan, 1988). The spontaneous language sample was quantified using the 12 variables of the SSLA system: (a) Number of Utterances; (b) Time; (c) Rate; (d) Length; (e) Melody; (f) Articulation; (g) Complex Sentences; (h) Errors; (i) Content Units; (j) Paraphasias; (k) Repetitions; and (l) Communication Efficiency.

a) Number of Utterances: This was a measure of the total number of utterances spoken by a subject. An utterance represented a complete thought, and frequently corresponded to a complete sentence. This could have been expressed in a connected grouping of words, which was separated from other utterances on the basis of content, intonation contour, and/or pausing. On the basis of content, change in content within the sentence was used as one criterion for segmenting utterances (e.g. "*The boy is in the tree... duck on the pond*"). On the basis of intonation contour, a falling intonation signalled the end of an utterance and a rising intonation contour signalled the end of an utterance if it was a question (e.g. "*The boy is in the tree . . ./ Is that a kite?*"). Utterance segmentation based on pauses was used in conjunction with the two previous segmentation criteria and not as a standalone criterion (e.g. "*Boy . . . in the tree/ Boy . . ./ girl waving*"). Additionally, tag questions or tag sentences were not segmented as separate utterances (e.g. "*That's a house, isn't it?*"), parenthetical remarks that were complete thoughts were segmented as separate utterances (e.g. "*I guess this is what I'm supposed to do*"), filled

pauses that occurred at the beginning of an utterance were not segmented as separate utterances, unless no content followed (e.g. "*umm . uuuhhh . . I was a teacher*"), sentence starters ("*Okay*" "*And*") were not segmented as separate utterances when an utterance followed unless accompanied by a falling intonation contour and a distinct pause (e.g. "*Okay, I see a boy*"), and finally, unintelligible utterances were not counted and were indicated by dashes (---).

b) Time: The total speaking time for the language sample was measured with a stopwatch in seconds, beginning with the first syllable and ending with the last syllable. Filled pauses were included in the time measurements. Any spoken material such as interjections or prompts from the examiner were subtracted from the overall time so that only the participant's time was included. The time was converted to minutes (e.g. 86 sec = 1.43 min).

c) Rate: The rate of speech was defined as the total number of syllables spoken per minute by the subject. It was calculated by dividing the total number of syllables counted in the utterances by the time in minutes of the sample. Filled pauses were not counted as syllables in this measure.

$$\text{Rate(syllables/minute)} = \frac{\text{Number of syllables}}{\text{Time(minutes)}}$$

d) Length: The length measure for the sample was computed by dividing the number of utterances that contained five or fewer words by the total number of utterances and multiplying by 100 to express the outcome as a percentage. Consistent with the *Rate* variable, filled pauses were not counted as words.

$$\text{Length} = \frac{\text{Number of utterances} \leq 5 \text{ Words}}{\text{Number of utterances}} \times 100$$

e) Melody: A seven-point melody rating scale, similar to that on the BDAE, was implemented to rate the variable of melody involving the rhythm of speech, the stress patterns employed, and the intonation contours expressed. The rating was independent of pauses, since they could be the result of a word-finding problem, rather than a prosodic disturbance per se.

```
  |--------------|--------------|
  1   2   3   4   5   6   7
Absent      Normal       Normal
melody   melody limited   melody
         to short phrases
      stereotyped utterances
```
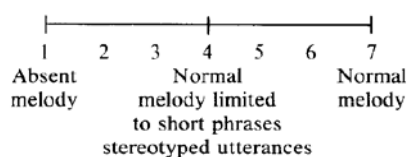
f) Articulation: A seven-point articulation rating scale, similar to that for articulatory agility on the BDAE was used. Articulation was rated using a global judgment of articulatory accuracy which included any speech errors often labelled under the categories of omissions, substitutions, distortions, and/or additions.

```
|—————————————+————————————|
1    2    3    4    5    6    7
Articulation      Normal        Normal
  always       articulation   articulation
 impaired   limited to automatic
                 utterances
```
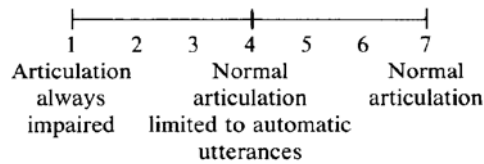
g) Complex Sentences: This syntactic variable measured was computed by dividing the number of complex sentences by the total number of utterances and multiplying by 100 to express the measure as a percentage. A complex sentence was defined as one that contained at least one independent clause and at least one or more dependent clauses. Conjoined sentences and complementing and non-complementing infinitive constructions were not considered complex sentences.

$$\text{Complex sentences} = \frac{\text{Number of complex sentences}}{\text{Number of utterances}} \times 100$$

h) Errors. This variable measured syntactic and morphological errors. It reflected the total number of errors counted for the sample, divided by the total number of utterances, and multiplied by 100 to express the measure as a percentage. Because a subject can make more than one error per utterance, the percentage could exceed 100. An error was defined as an incorrect syntactic and/or morphological form that deviated from a standard adult grammatical system (e.g. *"There's some bushes"*). Incomplete sentences were not counted as containing errors.

i) Content Units: A content unit was described as a grouping of information expressed as a unit. Each content unit was counted only once (e.g. *"There is a girl. The girl is on the stool"*). If two content units had the same action, the action was scored as one content unit for each referent (e.g., *"The boy is looking at the girl. Mom is looking outside")*. If a referent occurred only in the context of a group of information, it was scored as part of that group but not as a separate major content unit. For example, in the utterance *"The water was running on the floor"*, the word "floor" does not score as a separate content unit.

j) Paraphasias: The paraphasia measure was primarily a measure of substitution behaviour to capture what a PWA described when they could not produce the correct content. The percentage of paraphasias reflected a measure of the number of paraphasias relative to the total number of utterances. Similar to the Errors variable, the percentage could exceed 100 if a person made more than one paraphasia per utterance. Paraphasias included several types: literal (phonemic), verbal (semantic), neologism, and jargon.

k) Repetitions: Repetitions were counted only within utterances and not across utterances. Each repeated instance was counted as a repetition. Therefore, a word produced three times counted as two repetitions along with the target (e.g. *"girl . . . girl girl falling off"*). The total number of repetitions was counted, divided by the total number of utterances in the sample, and multiplied by 100 to yield a percentage. Repetitions could occur at several levels: (a) Phonemic (Sound) Repetitions (e.g. *"m. . m. . man"*); (b) Word Repetitions (e.g. *"green green. . . house no no"*); and (c) Phrase or Sentence Repetitions (e.g. *"There's a girl . . . there's a girl"*).

l) Communication Efficiency: This variable was a measure of the efficiency of information transfer. It reflected the rate at which information was conveyed by a speaker. It was calculated by dividing the total number of content units by the time (minutes) for the language sample.

$$CE = \frac{\text{Number of content units}}{\text{Time(minutes)}}$$

3.3.2.4 *The Multilingual Assessment Instrument for Narratives (MAIN)*

The **MAIN** (Gagarina et al., 2012) is a tool designed in order to evaluate narrative skills in children, but may also be used in adults as the pictures used are not considered child-like. It consists of picture sequences, developed based on the use of linguistic and psycholinguistic criteria to measure narrative performance. While the MAIN examines narrative production of microstructure and macrostructure elements, this study only analysed the story's structure of the macrostructure element of the generated story. The primary unit for macrostructure analysis is the episode. The content of each picture sequence was designed to represent three short episodes. The stories begin with a setting statement, which gives time and place and introduces the story's protagonist, and is scored with zero points for wrong or no response, 1 point for one correct response, 2 points for reference to both time and place. This component is followed by three episodes. Each episode is scored with zero points for wrong or no response and 1 point for each correct response regarding: a) the internal states (IST) which initiate the goal and also

express reactions; b) a goal which is a statement of an idea of the protagonist to deal with the initiating event; c) an attempt by the protagonist to reach the goal, which is an indication of action to obtain the goal; d) an outcome of the attempt in terms of the goal, which is the event(s) following the attempt and causally linked to it; and e) the IST as reaction, which is a statement defining how the protagonist(s) feel or think about the outcome or an action resulting from an emotional response (**Figure 3.3.5**). In this study the story "Baby Goats" was utilised. The series of six-coloured pictures presented in a cartoon strip was unfolded one-episode per time (2 pictures). Each participant was instructed to tell a story as each episode was presented. The story portrayed a mother goat wanting to save her baby goat who jumped into the water but a fox jumped forward to catch the other baby goat. Then a bird saw that the baby goat was in great danger and stopped the fox by biting its tail and chasing it way to save the baby goat (**Figure 3.3.6**). The story is controlled for cognitive and linguistic complexity and has a moral meaning similar to an Aesop fable. Each participant produced an original story and the samples were transcribed verbatim and analysed. Each sample used a 17-point scoring system and the tool's construction guidelines were followed (Gagarina et al., 2012: 132-135).

		Examples of correct responses[63]	Score	Comments[64]
A1.	Setting	Time and/ or place reference, e.g. once upon a time/ one day/ long ago... in a forest/ in a meadow/ at the lake/ at the pond...	0 1 2[65]	
Episode 1: Mother/ Goat (episode characters: baby goat and mother/ goat)				
A2.	IST as initiating event	**Baby goat** was scared/ in danger/ drowning/ needed help/ cried/ called the mother **<Mother/ Goat etc.>** saw that baby goat was scared/ in danger/ drowning/ couldn't swim/ was worried about the baby goat in the water	0 1	
A3.	Goal	**Mother goat** wanted to help the baby/ to save/ rescue the baby/ to push the baby out of the water	0 1	
A4.	Attempt	**Mother goat** ran/ went into the water/ is pushing	0 1	
A5.	Outcome	**Mother goat** pushed the baby out of the water/ saved/ rescued the baby **Baby goat** was saved/ out of the water	0 1	
A6.	IST as reaction	**Mother goat** was happy/ relieved **Baby goat** was relieved/ satisfied/ happy/ glad/ not scared any more	0 1	
Episode 2: Fox (episode characters: fox and baby goat)				
A7.	IST as initiating event	**Fox** saw mother looking away/ saw that the baby was alone/ saw that there was food/ fox was hungry	0 1	
A8.	Goal	**Fox** wanted to eat/ catch/ kill the baby goat	0 1	
A9.	Attempt	**Fox** jumped towards/ jumped up/ out/ tried to reach/ grab/ catch the baby goat	0 1	
A10.	Outcome	**Fox** got/ grabbed/ caught the baby goat	0 1	
A11.	IST as reaction	**Fox** was happy **Baby goat** was scared	0 1	
Episode 3: Bird (episode characters: bird, fox and baby goat)				
A12.	IST as initiating event	**Bird** saw that the goat was in danger **Baby goat** was in danger	0 1	
A13.	Goal	**Bird** decided/ wanted to stop the fox, help/ protect/ save the baby goat	0 1	
A14.	Attempt	**Bird** bit/ dragged the fox's tail/ attacked/ chased the fox	0 1	
A15.	Outcome	**Bird** chased the fox away **Fox** let go of the baby goat/ ran away **Baby goat** was saved/ rescued	0 1	
A16.	IST as reaction	**Bird** was relieved/ happy/ proud to have saved/ rescued the baby goat **Fox** was angry/ disappointed **Baby goat/ goats** was/ were relieved/ happy/ safe	0 1	
A17.		**Total score out of 17:**		

Figure 3.3.5. The *MAIN* scoring sheet for the production section of Baby-Goats story structure
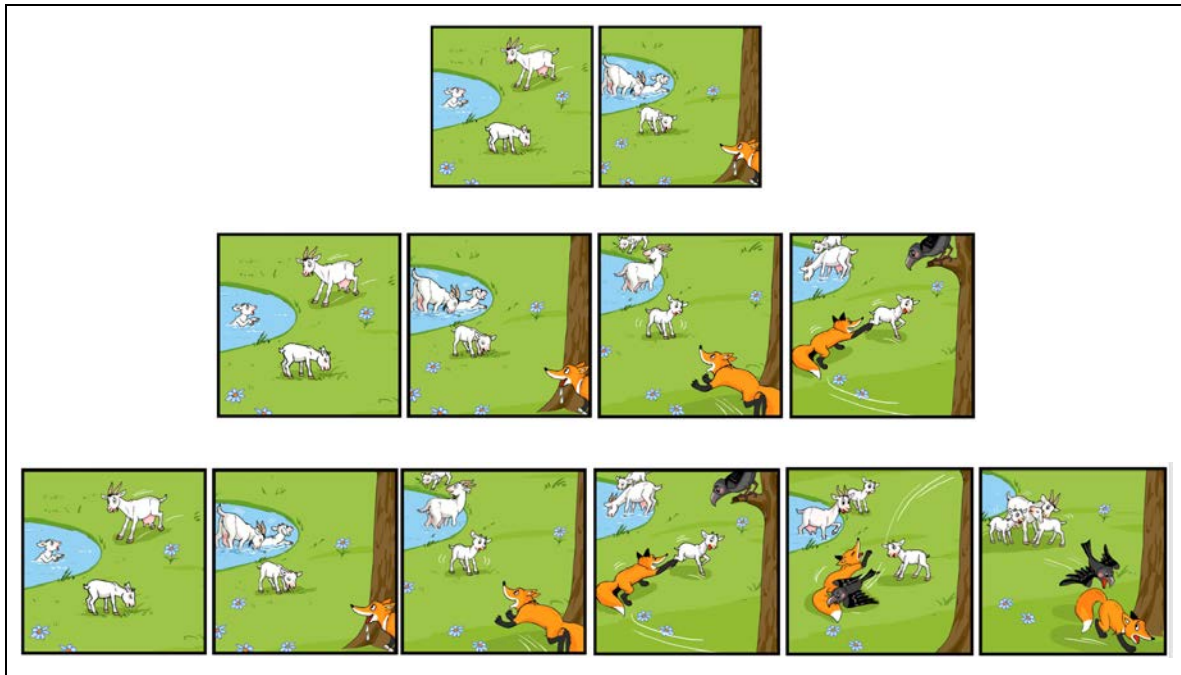
Figure 3.3.6. The Baby-Goat story from the *MAIN* as it unfolds in 3 episodes

3.3.2.5   *RehaCom Working Memory Screening Task*

The *RehaCom Working Memory Screening Task* module (Hasomed, 2017) measures the visual-spatial memory span and visual-spatial memory functions. The task is also used to test the implicit visual-spatial learning and working memory. Before a patient can start training with the software, the screening module can be administered to measure the current performance of the patient. The system recommends a therapy level that the patient can work with. After a certain number of therapy sessions, the screening can be repeated. In the progress analysis is indicated whether the performance of the participant has improved or not. It is recommended to repeat the screening-modules after 10 therapy sessions (Hasomed, 2017). The WM screening test is used for testing simple memory span (simple information holding) and simultaneously checks the retention and processing of visual-spatial information. It is similar to the Corsi-block-tapping where the visual-spatial memory span is measured by the maximum length of the memorized dot patterns that can be reproduced immediately without errors (Hasomed, 2017).

During the WM screening task, ten dots were presented in a circular arrangement (**Figure 3.3.7**). Individual dots sequentially turned red and faded. The first sequence consisted of two random dots out of the 10 lighting up in a particular order. The screening started with a sample exercise, in which a sequence of two dots had to be reproduced correctly in order to proceed to

the actual screening. The participant had to memorize and reproduce the presented position and sequence of the dots lighting up to reproduce them. After the sequence was presented, the participant had to select the same dots in the same order as they were presented. A new sequence was presented every time, meaning sequences did not repeat the previous sequence. The program adapted, adjusting the difficulty according to the participant's performance. Therefore, if the participant selected a sequence of dots correctly, the number of dots increased whenever two consecutive sequences of the same length were reproduced without a mistake. If the response was incorrect the degree of difficulty was reduced. The screening ended after the patient incorrectly reproduced two consecutive sequences or after 7 minutes. Participants used the touchscreen of the laptop to respond to the task.
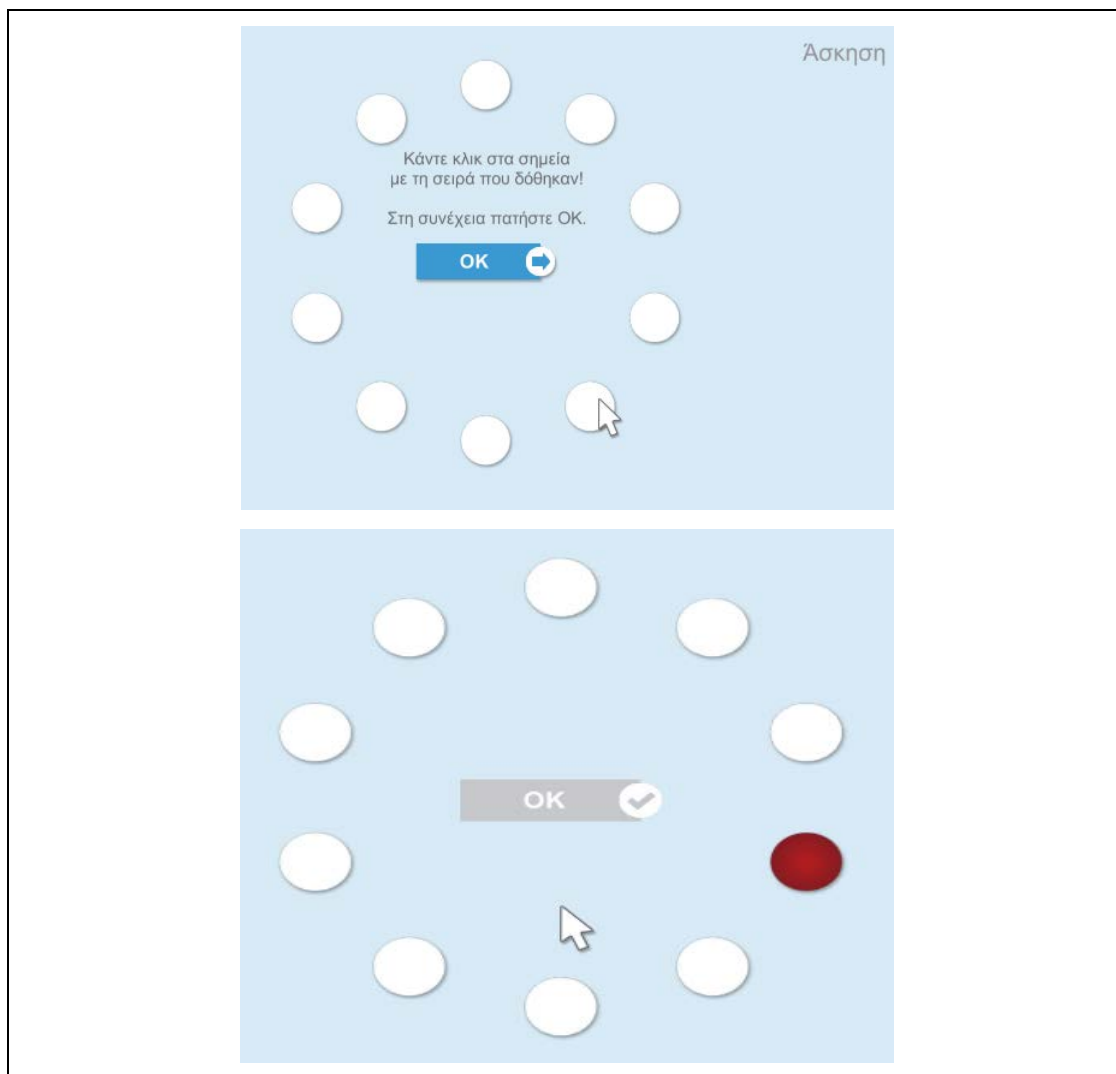
Figure 3.3.7. *RehaCom* Working Memory Screening Task

3.3.2.6   Procedural Discourse

The **Procedural Discourse** task is considered a semi-spontaneous speech production task that assesses discourse ability following the main concept analysis (MCA) procedure (Richardson & Dalton, 2016). How speakers communicate when informing and explaining (i.e. giving instructions) is considered an important skill in contexts where an individual is unable to complete a task autonomously, such as adults who have difficulties completing activities of daily living independently (Pritchard, Dipper, Morgan, & Cocks, 2015). This difficulty can be seen in a speaker with mobility difficulties who wants to instruct a helper how they like their snack to be made (i.e. sandwich), and is an area with very limited research. The MCA quantifies the degree to which the speaker is able to communicate the overall gist of an event, and it provides a means to evaluate how accurately and completely the concepts considered to be essential to the shared topic are produced. Each participant was instructed to verbally provide the steps taken in order to prepare a sandwich. The generated language sample was analysed using the MCA procedure referring to the ten main concepts. The total number of main concepts expected to be produced was analysed and measured based on the concept content as listed below:

(1)   Get the bread out.

(2)   Get two slices of bread//halved bread.

(3)   Get the butter.

(4)   Get the (rest of the ingredients i.e. ham, cheese, etc.)

(5)   Get a knife.

(6)   Put/place the bread on the plate.

(7)   Put/spread butter on bread.

(8)   Put the ingredients (i.e. ham, cheese, etc) on bread

(9)   Put the two pieces together.

(10)   Cut the sandwich in pieces

The first five steps comprise of concepts concerning retrieving the ingredients needed, the following four steps include concepts concerning ingredient assembly, and the final concept describes the final appearance of the target (sandwich) prior to serving it. The first author

transcribed the samples verbatim and analysed each sample using a binary scoring system of "1" for correct information and "0" for incorrect/missing information.

3.3.2.7 *The Stroke and Aphasia Quality of Life Scale-39 (SAQOL-39g)*

The **SAQOL-39g** is a generic stroke scale that determines the patient's health-related quality of life (HRQL) after stroke in three domains: physical, psychosocial, and communication of patients with acute and chronic stroke (Hilari et al., 2009). HRQL questionnaires evaluate the impact of health on a person's ability to lead a fulfilling life, and generally incorporate the individual's perceptions of physical, mental/emotional, family, and social functioning (Spaccavento et al., 2013). The *SAQOL-39* has been adapted and linguistically validated to measure the QoL in Greek speaking people with chronic aphasia after stroke. The psychometric properties of the Greek version of the tool have been tested in its generic form (SAQOL-39g) (i.e. tested with a generic stroke population with and without aphasia) and it was found to be a valid and reliable scale that can be used as an outcome measurement, treatment prioritization and service evaluation (Efstratiadou et al., 2012). The *SAQOL- 39g* has been translated and culturally adapted for use in Greece, where currently there is no other measure for the assessment of HRQL for people with aphasia (Kartsona & Hilari, 2007). The SAQOL-39g consists of 39 items and includes 3 domains: physical (e.g. 'how much trouble did you have walking?'), psychosocial (e.g. 'did you feel that you were a burden to your family?'), and communication (e.g. 'how much trouble did you have finding the word you wanted to say?'). The response format is a 5-point scale ranging from 1 to 5. In the first part, answers range from 'couldn't do it at all' to 'no trouble at all' and in the second part from 'definitely yes' to 'definitely no'. Overall and domain mean scores are calculated with higher scores indicating better quality of life. The information was collected in an interview format. The participants were provided with the questionnaire and all the questions were presented orally by the examiner. Depending on the participant's abilities, the participants responded either verbally, written, or by pointing.

3.4 Treatment

All participants completed ten (10) approximately 45-minute long treatment sessions comprising of iTBS immediately followed by RehaCom WM training over a span of 10 consecutive days, including weekends. Within each treatment session, approximately 15 minutes were devoted for setting up the participant with the TMS equipment and iTBS

application, and 30 minutes were devoted to the RehaCom WM training task. The treatment regimen is depicted in **figure 3.4.1** below.
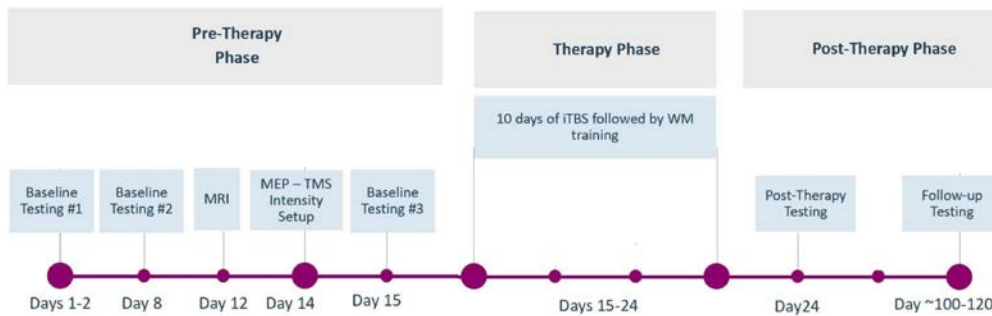
Figure 3.4.1. Timeline representation of the study design

3.4.1.1 *Pretherapy or "baseline" testing phase*

During the pretherapy baseline phase, the purpose was to establish the level of performance prior to treatment so that the effects of treatment on the task could be clearly measured. As referred to in the assessment tools section, six outcome measures were used and the information was collected three times, one week apart, prior to the therapy phase. Preceding the initiation of the therapy phase, a T1-weighted MRI image was obtained from the participant in order to accurately locate the target for the use of Visor 2.0 neuronavigation system (ANT NEURO). Neuronavigated positioning of the stimulation coil allowed for repeated accuracy throughout the study.

3.4.1.1.1 *Transcranial Magnetic Stimulation (TMS) Equipment*

Single-pulse TMS and intermittent theta-burst stimulation (iTBS) were delivered over the motor cortex and the left dorsolateral prefrontal cortex (LDLPFC) respectively, with a Magstim Rapid2® stimulator (Magstim Co., Wales, UK) connected to a 70 mm figure-8 air cooled coil. Biphasic TMS pulses were delivered with a posterior-to-anterior (P-A) current direction in both, single-pulse TMS and iTBS. The treatment intensity of TMS was individually adjusted to each participant's Resting Motor Threshold (RMT). RMT is defined as the minimal intensity at which TMS of motor cortex produces a reliable Motor Evoked Potential (MEP) of minimal amplitude in the target muscle. The MEP was determined with a surface electromyography (EMG) response in the 'target' muscle. EMG leads were placed over the first dorsal interosseous (FDI) muscle of the left hand and the participant was seated comfortably, with left arm supported on a pillow **(Figure 3.4.2)**. Full muscle relaxation was maintained through

visual and online EMG monitoring. The coil was positioned at 45-degree rotation in relation to the parasagittal plane to induce P-A current in the underlying cortex. The motor "hotspot" was determined with a TMS intensity ranging from 45% to 50% of the maximum stimulator output, whereby single pulse stimuli were delivered at varying positions across the scalp near the primary motor cortex (M1) while guided by a neuronavigation system (ANT NEURO) using each participant's recent anatomical MRI image. The motor "hotspot" was defined as the position on the scalp that yielded two consecutive MEPs with greater amplitude than the surrounding positions. The location within the left motor cortex that consistently elicited MEPs in the relaxed right FDI muscle was then defined as the motor hotspot. The coil was then placed over the defined target to obtain a MEP in the FDI of at least 50 μV in five or more of 10 consecutive stimulations of the left hand (Rossini et al., 2015). For this study a computerized adaptive parameter estimation through sequential testing (PEST; Borckardt et al., 2006), with the software TMS Motor Threshold Assessment Tool, MTAT 2.0 (Awiszus & Borckardt, 2010) was used to determine the RMT. The MTAT 2.0 freeware was obtained online (http://www.clinicalresearcher.org/software.html) and the option for assessment without a priori information was selected. No other parameters were changed on the software. The program automatically began at the intensity of 37% and displayed the subsequent TMS intensity to be delivered. The experimenter interacted with the program by indicating the success of a given TMS intensity by pressing the key "Y" on software's laptop: a trial was considered successful if the MEP amplitude was $\geq 50\mu V$. The software then displayed a decreased intensity to be delivered based on the previous response. If the MEP amplitude was $< 50\mu V$, the experimenter pressed the key "N" on the software's laptop and the software displayed an increased intensity. The displayed numbers were color-coded to indicate if the RMT was reached (Red = not reached; Orange = almost reached; Green = Reached) (**Figure 3.4.3.**).
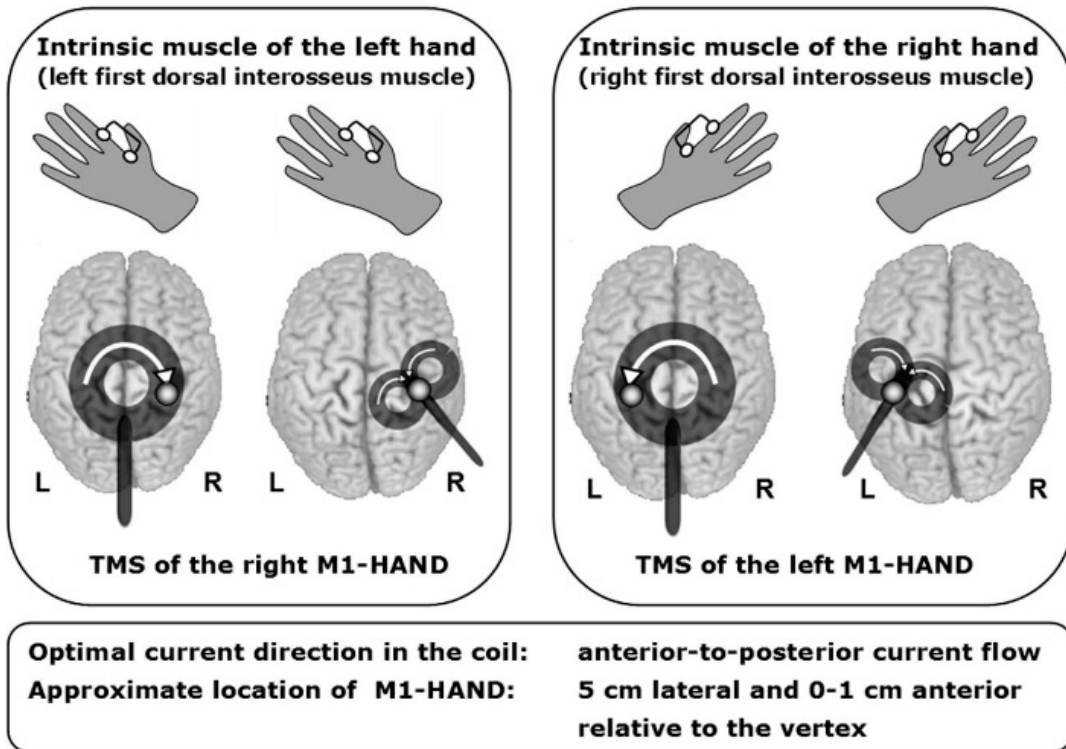
Figure 3.4.2 Coil placement for MT determination of an intrinsic hand muscle (from Groppa et al., 2012 – with online permission).
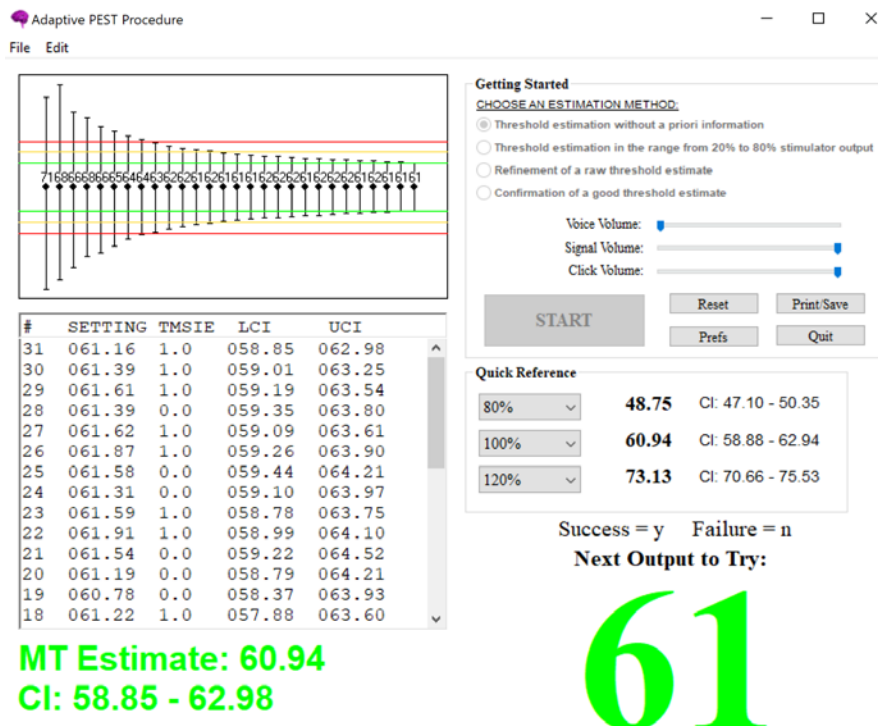
Figure 3.4.3. The Motor Threshold Assessment Tool, MTAT 2.0 illustrating Resting Motor Threshold at intensity 61 (Awiszus & Borckardt, 2010).

3.4.2 Therapy Phase

3.4.2.1 Transcranial Magnetic Stimulation – iTBS application

During the therapy phase the iTBS treatment protocol was administered using Magstim Rapid2® (Magstim Co., Wales, UK) with intensity set at the 80% of the MEP obtained from the right hemisphere. The figure-8 coil was positioned tangentially to the skull, with the handle parallel to the sagittal axis pointing occipitally. The iTBS treatment consisted of bursts of three pulses at 50 Hz given every 200 milliseconds in two second trains, repeated every 10 seconds over 200 seconds for a total of 600 pulses (Huang et al., 2005). Based on each participant's recent MRI images, the Visor 2.0 neuronavigation suite (ANT-Neuro, Enschede, Netherlands) was used for image pre-processing, tissue segmentation, and registration into standard stereotaxic space. The stimulation target was defined in the left DLPFC by using the Talairach coordinates x=-40, y= 34, z = 29 (Barbey et al., 2013; Wager & Smith, 2003). This technology enabled reliable three-dimensionally precise reapplication of rTMS throughout the study. Each participant received one session of iTBS each day for 10 consecutive days, immediately followed by 30 minutes WM training with the RehaCom Working Memory (WOME) software package (Hasomed GmbH, DE.).

3.4.2.2 RehaCom WM Training Equipment

The RehaCom *WOME* (Hasomed GmbH, DE.) software was installed on a personal Lenovo touchscreen laptop to provide the participants a simpler way to respond than using a mouse. RehaCom WOME is a software package developed to train and improve WM performance. The WM training task involved card presentation in the form of a card game, using a complete card deck of 52 cards and consisting of different levels of difficulty. WOME consists of three hierarchically ordered modules that were designed to exercise the main components of WM on the basis of a card game as depicted in **figure 3.4.4**: (a) storage systems, involving the maintenance of information; (b) selective attention, involving memorizing selective parts of information and inhibiting others; and (c) central executive/manipulation processes, involving active operating with the content retained in WM (Weicker et al., 2018). During the training, the participant has to memorise and manipulate an increasing number of visually presented playing cards on a computer screen. During the initial levels of training, the participant is required only to remember the items (e.g. remember a short series of cards and reproduce it in the same order) whilst at higher levels additional tasks are introduced to influence the memory

process (e.g. memorize only the cards of a certain suit from a presentation of various cards). In total, there are 70 levels of difficulty. The participant constantly receives feedback by the software and the degree of difficulty is adapted based on the participant's performance level. The sessions were implemented in a quiet room and the participant was trained on a touchscreen laptop.

	Storage Module: Remember all the cards and choose the matching one from the selection below.
	Selective attention Module: Remember only the clubs and spades shown by the dealer while ignoring the other suits and choose the matching ones from the selection below
	Manipulation Module: Sort the cards in the reversed order they were presented by the dealer

Figure 3.4.4. Graphical interface of the RehaCom WM intervention. (A–C) Show the various modules with their respective instructions that were trained. During the actual training, the dealer shows several cards, which are turned over after 1 second. Here, the cards are illustrated overtly for the purpose of explanation.

3.4.3 Post-therapy/follow-up Phase

The post-therapy/follow-up phase consisted of two points in time. The outcome measures were administered right after the completion of the last day's treatment (10th day), and at 3 months post-treatment at the follow-up stage. The purpose of immediate post-testing was to determine short-term efficacy, and of the follow-up was to determine long-term effects. The exact date of the follow-up depended on the participant's availability when contacted to set-up the appointment. The same battery of tools was used as with baseline as listed below:

(1)   the Greek BDAE-SF (Messinis et al., 2013)

(2)   the RCPM (Raven, 2000; Sideridis et al., 2015)

(3)   the MAIN (Gagarina et al., 2012)

(4)   a Procedural Discourse task (based on Richardson & Dalton, 2016)

(5)   a personal stroke narrative (following Kambanaros, 2019)

(6)   the RehaCom Working Memory Screening Task (Hasomed GmbH, 2017)

(7)   the Greek SAQOL-39 (Efstratiadou et al., 2012)

3.5 Statistical Analysis

Analysis of individual data was conducted using the WEighted Statistics (WEST) method outlined in Howard et al. (2015). Using WEST allows to assess whether there is greater improvement during the therapy period than the baseline and whether improvement is greater for treated items than untreated. The WEST Rate of Change (WEST-ROC) analyses the amount of change in the treated versus the untreated periods or the short versus the long-term periods. Participants' pre-therapy performance for treated and untreated items was compared with post-therapy and at follow-up using a weighted one sample t test. Each item was scored as either correct (1) or incorrect (0) at the pre-therapy phase (baseline) and after the treatment phase (post-therapy and follow-up). The assessment scores were multiplied by the precalculated weightings at each time point, as per Howard et al. (2015). The weighted scores for each item were then summed and used in a one sample t-test. A significant result on the one sample t test indicates that the amount of improvement in the treatment phase is significantly different to that in the baseline phase. The WEST-Trend method was used to confirm the WEST-ROC results and to ensure that treatment effects occurred in the positive direction with an overall

trend for improvement (Howard et al., 2015). Moreover, when there is both a significant WEST-Trend result and a significant WEST-ROC result, the evidence supports a significant effect of intervention (Howard et al., 2015). WEST-ROC and WEST-Trend were used to analyse the data from the RCPM, the Greek BDAE-SF, the MAIN, and the Procedural Discourse task. Results from the SSLA, the RehaCom WM screening, and the SAQOL-39g assessments are reported but no statistical analysis was performed.

4 RESULTS

The Statistical Package for Social Sciences (IBM SPSS 25) was used in the current research for all the data and exploratory analysis. Analyses of individual data were conducted using the WEighted Statistics (WEST) method outlined in Howard et al. (2015), and descriptive results' analysis was used where a statistical analysis was not suitable. The WEST-ROC and WEST-Trend were used to analyse the data from the Greek BDAE-SF, the RCPM, the MAIN, and the Procedural Discourse, where appropriate weights were calculated via the use of an Excel spreadsheet personally provided by Professor Howard (2020). All the data was analysed with SPSS and confirmed via the use of manual formulas in Microsoft Excel for Office 365. Results from the SSLA, the RehaCom WM screening, and the SAQOL-39g assessments are reported but no statistical analysis was performed.

4.1 Participant #1 – I.A.

The participant's oral speech was characterized by severe unintelligible speech due to dysarthria. The BDAE's Oral expression tasks were scored based on word approximations produced that were judged by the examiner as a correct or incorrect response. An attempt was made to transcribe the produced continuous speech with regards to a personal story narration, the MAIN, and the Procedural Discourse but the output could not be analysed nor quantified. Therefore, results were based only on the BDAE-SF, the RCPM, the RehaCom WM screening, and the SAQOL-39.

4.1.1 *BDAE Auditory Comprehension*

Statistical analysis of the *BDAE Auditory Comprehension* subtest showed that the overall trend for improvement in *Word Comprehension* was not significant, $t(15) = -1.00$, $p=.167$, whereas the WEST-ROC was not able to be estimated due to standard deviation being equal to zero. Similarly, there was a non-significant overall trend for improvement in *Commands*, $t(9) = -1.00$, $p= .172$, as well no significant difference between the treated and untreated periods, $t(9) = 1.41$, $p=.097$. Additionally, there was a non-significant overall trend for improvement in *Complex Ideational Material*, $t(5) = 1.17$, $p=.148$, and although there was improvement between the treated and untreated periods, $t(5) = 1.19$, $p=.145$, it did not reach significance. In general, WEST-Trend revealed a non-significant overall trend for improvement in the overall

task of *Auditory Comprehension*, $t(2) = 0.45$, $p = .349$, and a non-significant difference between the treated and untreated periods, $t(2) = 1.55$, $p = .131$ **(Table 4.1.1; Figure 4.1.1).**
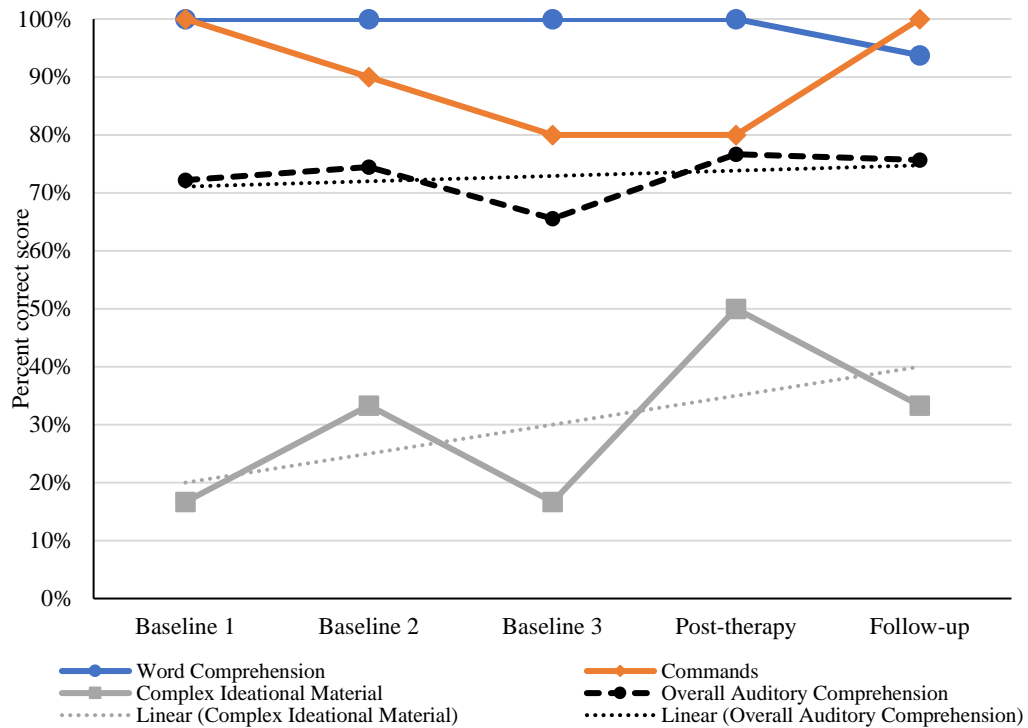
Figure 4.1.1: Percentage (%) correct on the *BDAE Auditory Comprehension* subtests and the overall *BDAE Auditory Comprehension* by study phase (Participant I.A.).

Table 4.1.1: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) on the *BDAE Auditory Comprehension* (Participant I.A.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Word Comprehension	Mean	1.00	1.00	1.00	1.00	0.94	-0.13	0.00
	S.D.	0.00	0.00	0.00	0.00	0.25	0.50	0.00
							t(15)= -1.00, p= 0.167	---
Commands	Mean	1.00	0.90	0.80	0.80	1.00	-0.10	0.30
	S.D.	0.00	0.32	0.42	0.42	0.00	0.32	0.67
							t(9)= -1.00, p= 0.172	t(9)= 1.41, p= 0.097
Complex Ideational Material	Mean	0.17	0.33	0.17	0.50	0.33	0.50	0.83
	S.D.	0.41	0.52	0.41	0.55	0.52	1.05	1.72
							t(5)= 1.17, p= 0.148	t(5)= 1.19, p= 0.145
Overall BDAE Auditory Comprehension	Mean	0.72	0.74	0.66	0.77	0.76	0.09	0.38
	S.D.	0.48	0.36	0.44	0.25	0.37	0.35	0.42
							t(2)= 0.45, p= 0.349	t(2)= 1.55, p= 0.131

4.1.2 *BDAE Oral Expression*

Statistical analysis for the *BDAE Oral Expression* subtest (**Figure 4.1.2; Table 4.1.2**) revealed that there was a significant overall trend for improvement in the *Screening of Special Categories* task, $t(11) = 3.59$, p= .002, with also a significant improvement between the treated and untreated periods, $t(11) = 3.59$, p= .002. The overall trend for improvement in *Word Repetition* was not significant, $t(4) = -0.95$, $p=.198$, and there was also not significant difference between the treated and untreated periods, $t(4) = -0.63$, $p=.281$. The *Sentence Repetition* task did not show significant overall trend for improvement, $t(1) = 1.00$, p= .250, nor significant difference between the treated and untreated periods, $t(1) = 1.00$, p= .250. Similarly, the overall trend for improvement in the *Boston Naming* task was not significant, $t(14) =0.00$, p= .500, and there was no significant difference between the treated and untreated periods, $t(14) = 1.07$, $p=.150$. On the other hand, there were no differences in the responses between the five periods for the participant's *Automated Sequences* and *Responsive Naming*. In general, there was non-significant overall trend for improvement in the overall *BDAE Oral Expression* subtest, $t(5) = 0.80$, $p = .229$, with a non-significant difference between the treated and untreated periods, $t(5) = 0.64$, $p=.276$.
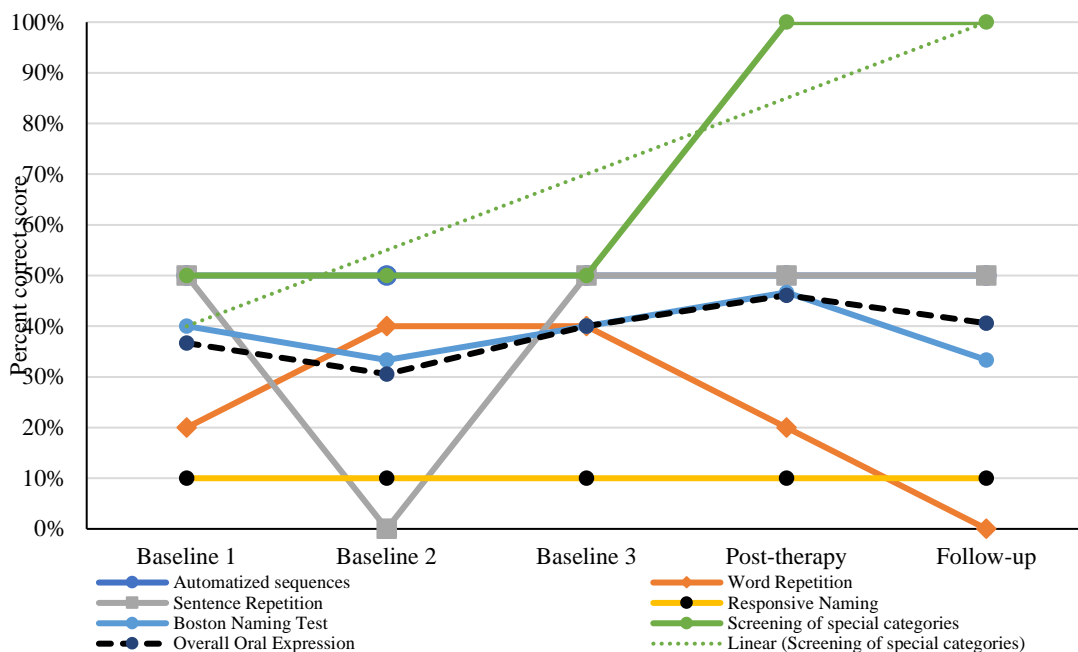
Figure 4.1.2: Percentage (%) correct for the *BDAE Oral Expression* subtests and the overall *BDAE Oral Expression* by study phase (Participant I.A.).

Table 4.1.2: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) on the *BDAE Oral Expression* (Participant I.A.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Automatized Sequences	Mean	0.50	0.50	0.50	0.50	0.50	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Word Repetition	Mean	0.20	0.40	0.40	0.20	0.00	-0.60	-1.00
	S.D.	0.45	0.55	0.55	0.45	0.00	0.89	2.24
							t(4)= -0.95, p= 0.198	t(4)= -0.63, p= 0.281
Sentence Repetition	Mean	0.50	0.00	0.50	0.50	0.50	0.50	0.50
	S.D.	0.71	0.00	0.71	0.71	0.71	0.71	0.71
							t(1)= 1.00, p= 0.250	t(1)= 1.00, p= 0.250
Responsive Naming	Mean	0.10	0.10	0.10	0.10	0.10	0.00	0.00
	S.D.	0.22	0.22	0.22	0.22	0.22	0.00	0.00
Boston Naming Test	Mean	0.40	0.33	0.40	0.47	0.33	0.00	0.27
	S.D.	0.51	0.49	0.51	0.52	0.49	0.65	0.96
							t(14)= 0.00, p= 0.500	t(14)= 1.07, p= 0.150
Screening of special categories	Mean	0.50	0.50	0.50	1.00	1.00	1.50	1.50
	S.D.	0.52	0.52	0.52	0.00	0.00	1.45	1.45
							t(11)= 3.59, p= 0.002	t(11)= 3.59, p= 0.002
Overall BDAE Oral Expression	Mean	0.37	0.31	0.40	0.46	0.41	0.23	0.21
	S.D.	0.18	0.21	0.15	0.31	0.36	0.71	0.81
							t(5)= 0.80, p= 0.229	t(5)= 0.64, p= 0.276

4.1.3 *BDAE Reading*

Statistical analysis of the *BDAE Reading* subtest (**Table 4.1.3**) revealed no differences in the reading tasks of *Matching case/script*, *Number Matching* and *Oral Basic sentence* between the five periods. Analysis showed that the overall trend for improvement in *Word identification* was not significant, $t(3)= 1.00$, p= .196, and there was no significance between the treated and untreated periods, $t(3)= 1.00$, p= .196. Similarly, overall improvement in the *Oral Basic Word* task was not significant, $t(4) = 0.63$, p= .281, and there was also not significant difference between the treated and untreated periods, $t(4) = -0.63$, $p=.281$. Additionally, there was non-significant overall trend for improvement in the *Oral Sentence Comprehension*, $t(2) = 0.00$, p= .500, and with a non-significant difference between the treated and untreated periods, $t(2) = -1.84$, p= .104. Lastly, although there was an overall trend for improvement in the *Silent Comprehension* task, it did not reach significance, $t(3) = 1.57$, p= .108, and the difference between the treated and untreated periods, $t(3) = 1.00$, p= .196 was not significant. In general, there was a non-significant overall trend for improvement in the overall *BDAE Reading* subtest, $t(6) = 1.88$, $p= .054$, and non-significant difference between the treated and untreated periods, $t(6) = -0.94$, $p=.191$ (**Figure 4.1.3).**

Figure 4.1.3: Percentage (%) correct for the *BDAE Reading* subtests and the overall *BDAE Reading* across study phases (Participant I.A.).

Table 4.1.3: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) on the *BDAE Reading* (Participant I.A.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Matching Case/Script	Mean	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Number Matching	Mean	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Word identification	Mean	0.50	0.75	0.75	0.75	0.75	0.50	-0.50
	S.D.	0.58	0.50	0.50	0.50	0.50	1.00	1.00
							t(3)= 1.00, p= 0.196	t(3)= -1.00, p= 0.196
Oral Basic Word	Mean	0.00	0.13	0.13	0.13	0.13	0.80	-0.80
	S.D.	0.00	0.30	0.30	0.30	0.30	1.79	1.79
							t(4)= 0.63, p= 0.281	t(4)= -0.63, p= 0.281
Oral Basic Sentence	Mean	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Oral Sentence Comprehension	Mean	0.33	0.67	0.67	0.00	0.67	0.00	-2.67
	S.D.	0.58	0.58	0.58	0.00	0.58	2.65	2.52
							t(2)= 0.00, p= 0.500	t(2)= -1.84, p= 0.104
Silent Comprehension	Mean	0.50	0.50	0.50	0.75	0.75	0.75	0.75
	S.D.	0.58	0.58	0.58	0.50	0.50	0.96	1.50
							t(3)= 1.57, p= 0.108	t(3)= 1.00, p= 0.196
Overall BDAE Reading	Mean	0.48	0.58	0.58	0.52	0.61	0.22	-0.38
	S.D.	0.41	0.39	0.39	0.46	0.40	0.30	1.08
							t(6)= 1.88, p= 0.054	t(6)= -0.94, p= 0.191

4.1.4 *RCPM*

The results of the RCPM statistical analysis using the WEST-Trend and WEST-ROC (**Table 4.1.4**) revealed non-significant overall trend for improvement in *Subtest A*, $t(11)= 1.60$, $p= .069$, and non-significant difference between the treated and untreated periods, $t(11)= 1.52$, $p= .079$. Also the overall trend for improvement in *Subtest AB* was not statistically significant, $t(11) = 0.90$, $p= .194$, and with non-significant difference between the treated and untreated periods, $t(11) = 1.74$, $p=.055$. Lastly, there was a non-significant overall trend for improvement in *Subtest B*, $t(11)= 1.48$, $p= .083$, and there was non-significant difference between the treated and untreated periods, $t(11) = 0.77$, p= .228. On the other hand, statistical analysis of the overall RCPM showed that there was a significant trend for improvement, $t(35) = 2.14$, $p=.020$, and also significant difference between the treated and untreated periods, $t(35) = 2.31$, $p= .013$ **(Figure 4.1.4)**.
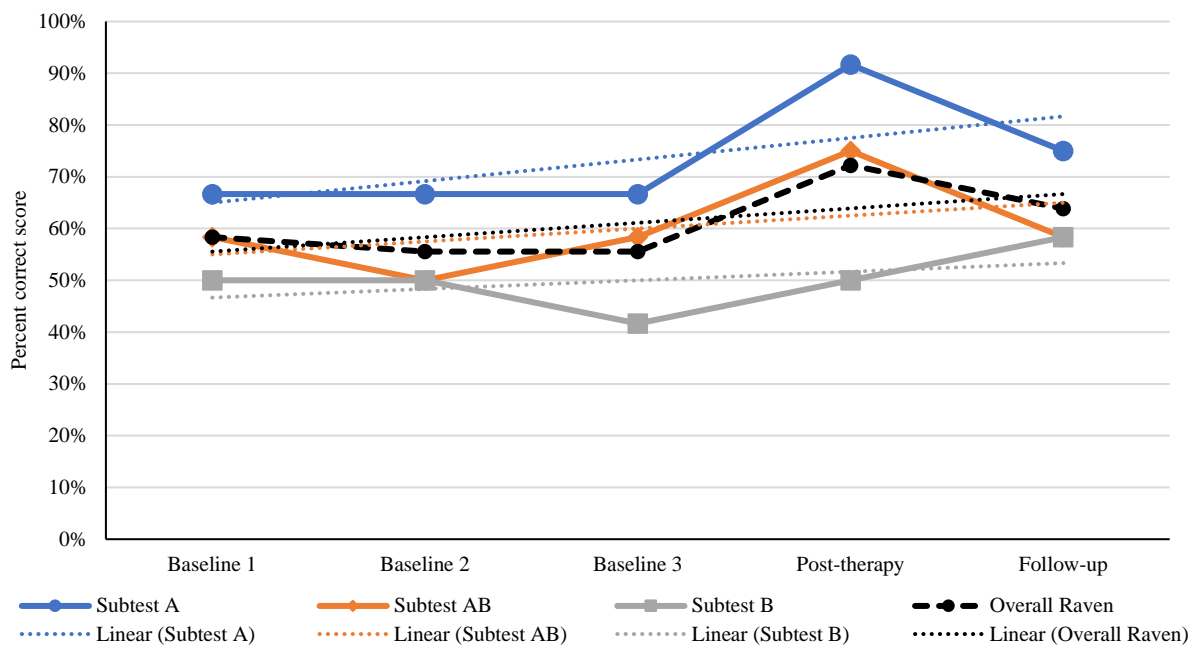
Figure 4.1.4: Percentage (%) correct on the *RCPM* subtests and the overall *RCPM* across the study phases(Participant I.A.).

Table 4.1.4: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) on the *RCPM* (Participant I.A.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
	Mean	0.67	0.67	0.67	0.92	0.75	0.42	0.75
Subtest A	S.D.	0.49	0.49	0.49	0.29	0.45	0.90	1.71
							t(11)= 1.60, p= 0.069	t(11)= 1.52, p= 0.079
	Mean	0.58	0.50	0.58	0.75	0.58	0.25	0.58
Subtest AB	S.D.	0.51	0.52	0.51	0.45	0.51	0.97	1.16
							t(11)= 0.90, p= 0.194	t(11)= 1.74, p= 0.055
	Mean	0.50	0.50	0.42	0.50	0.58	0.17	0.33
Subtest B	S.D.	0.52	0.52	0.51	0.52	0.51	0.39	1.50
							t(11)= 1.48, p= 0.083	t(11)= 0.77, p= 0.228
	Mean	0.58	0.56	0.56	0.72	0.64	0.278	0.556
Overall RCPM	S.D.	0.50	0.50	0.50	0.45	0.49	0.78	1.44
							t(35)= 2.14, p= 0.020	t(35)= 2.31, p= 0.013

4.1.5 *RehaCom WM*

The results of the *RehaCom WM* screening show a negative linear trend line (**Figure 4.1.5**) on all the tasks assessed, and **Table 4.1.5** shows the raw scores attained by participant I.A. Based on the participant's scores, WM did not show improvement.
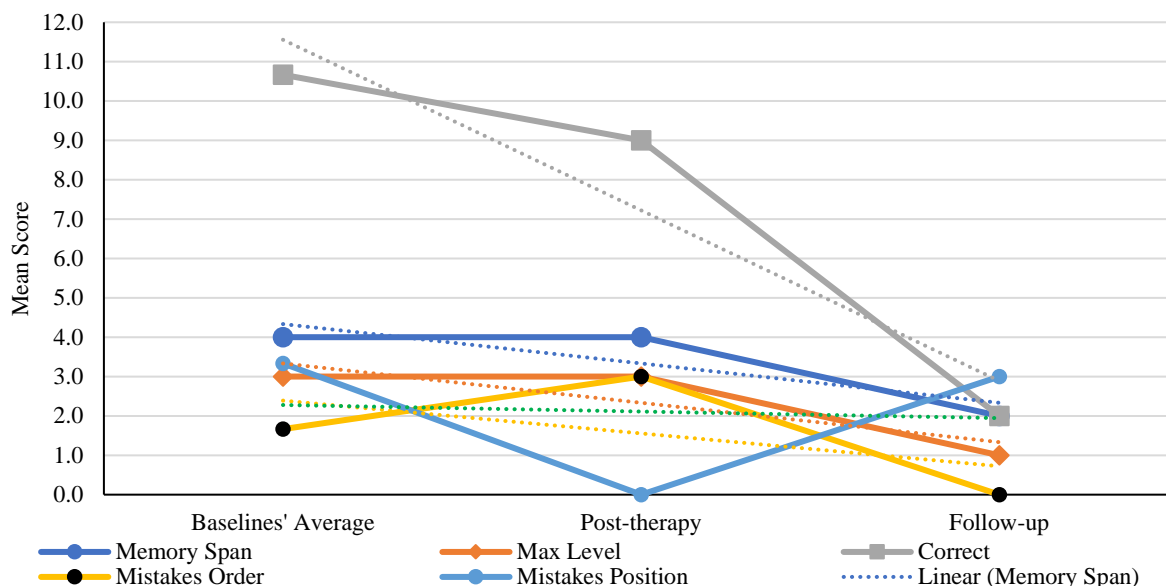
Figure 4.1.5: Schematic representation of I.A.s' raw scores on the RehaCom WM Screening task.

Table 4.1.5: RehaCom WM Screening by subcategory and period

	Baseline 1	Baseline 2	Baseline 3	Baseline Average	Post-therapy	Follow-up
Memory Span	5	3	4	4	4	2
Max Level	4	2	3	3	3	1
Correct	11	10	11	11	9	2
Mistakes Order	3	2	0	2	3	0
Mistakes Position	2	4	4	3	0	3

4.1.6 *SAQOL-39*

With regards to investigating whether the overall QoL would improve after treatment, the self-rated SAQOL-39 was analysed by comparing the mean scores (**Figure 4.1.6.; Table 4.1.6.**).

The participant's responses indicated that QoL improved between the Baseline average (M = 3.64) and post-therapy (M = 4.03) by 8% and increased a further 8% at follow-up (M = 4.41).
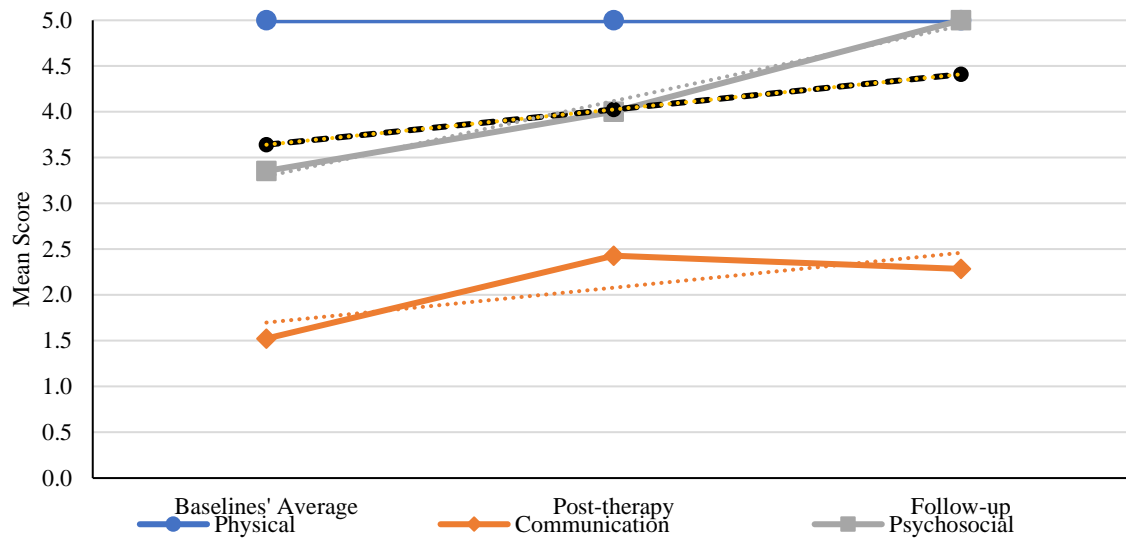
Figure 4.1.6: Schematic representation of the *SAQOL-39g* mean raw score at baseline, post-therapy and follow-up (Participant I.A.).

The mean scores for the overall SAQOL-39 and for each subcategory are shown in **Table 4.1.6.** The Communication self-rated score improved between the baseline average (M = 1.52) and post-therapy (M = 2.43) by 18%, and it was maintained at follow-up (M = 2.29). The Psychosocial self-rated score improved between the baseline average (M = 3.35) and post-therapy (M = 4.00) by 13%, and it was further increased by 20% at follow-up (M = 5.00).

Table 4.1.6: Mean raw scores on the *SAQOL-39g* at baseline, post-therapy and follow-up (Participant I.A.).

	Baseline 1	Baseline 2	Baseline 3	Baseline average	Post-therapy	Follow-up
Physical	5.00	5.00	5.00	5.00	5.00	5.00
Communication	1.14	1.57	1.86	1.52	2.43	2.29
Psychosocial	3.25	3.44	3.38	3.35	4.00	5.00
Overall SAQOL-39	3.56	3.67	3.69	3.64	4.03	4.41

4.2   Participant #2 – C.S.

4.2.1   *BDAE Auditory Comprehension*

During the statistical analysis of the *BDAE Auditory Comprehension* subtest, both WEST-Trend and WEST-ROC (**Table 4.2.1; Figure 4.2.1**) could not be calculated, as there were no differences in the responses between the five periods regarding the *Word Comprehension*. WEST-Trend analysis showed that the overall trend for improvement in *Commands* was not significant, $t(9) = -1.00$, $p= .172$, whereas WEST-ROC was not calculated due to the zero standard deviation. There was non-significant overall trend for improvement in *Complex Ideational Material,* $t(5)=-1.00$, $p=.182$, and non-significant difference between the treated and untreated periods, $t(5) = -1.54$, p=.093. In general, there was non-significant overall trend for improvement in overall *BDAE Auditory Comprehension* subtest, $t(2) = -1,98$, $p= .093$, and non-significant between the treated and untreated periods, $t(2) = -1.00$, $p=.211$.
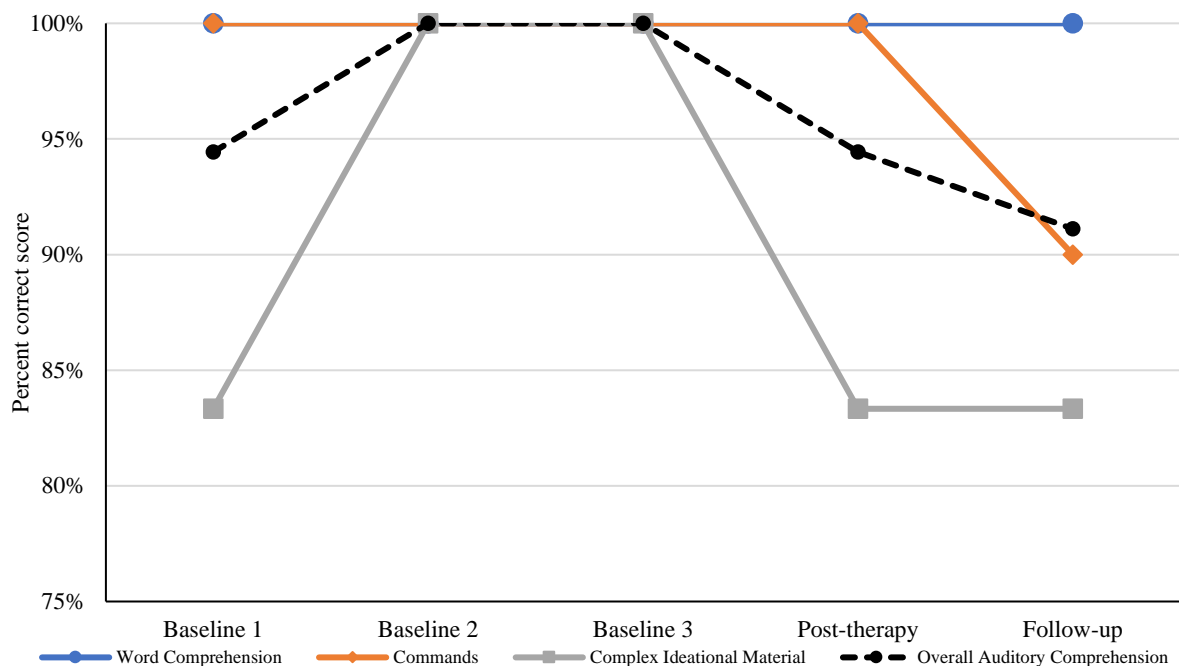
Figure 4.2.1: Percentage (%) correct for the *BDAE Auditory Comprehension* subtests and the overall *BDAE Auditory Comprehension* across study phase (Participant C.S.).

Table 4.2.1: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) for the *BDAE Auditory Comprehension* (Participant C.S.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Word Comprehension	Mean	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Commands	Mean	1.00	1.00	1.00	1.00	0.90	-0.20	0.00
	S.D.	0.00	0.00	0.00	0.00	0.32	0.63	0.00
							t(9)= -1.00, p= 0.172	---
Complex Ideational Material	Mean	0.83	1.00	1.00	0.83	0.83	-0.17	-0.83
	S.D.	0.41	0.00	0.00	0.41	0.41	0.41	1.33
							t(5)= -1.00, p= 0.182	t(5)= -1.54, p= 0.093
Overall BDAE Auditory Comprehension	Mean	0.94	1.00	1.00	0.94	0.91	-0.12	-0.28
	S.D.	0.10	0.00	0.00	0.10	0.08	0.11	0.48
							t(2)= -1.98, p= 0.093	t(2)= -1.00, p= 0.211

4.2.2 *BDAE Oral Expression*

Statistical analysis of the *BDAE Oral Expression* subtest revealed a significant overall trend for improvement was found in the *Boston Naming Test*, $t(14) = 1.82$, p= .045, while the difference between the treated and untreated periods, $t(14) = 0.27$, $p=.396$ was non-significant **(Table 4.2.2; Figure 4.2.2)**. Statistical analysis showed that the overall trend for improvement in *Responsive Naming* was not significant, $t(4) = -0.63$, $p=.281$, and there was non-significant difference between the treated and untreated periods, $t(4)= 0.63$, $p=.281$. The participant's results for the *BDAE Automated Sequence, Word Repetition, Sentence Repetition* and *Screening of Special Categories*, did not show any differences in the responses between the five periods. Overall, there was non-significant trend for improvement in the *BDAE Oral Expression* subtest, $t(5) = 0.10$, $p = .462$, and non-significant difference between the treated and untreated periods, $t(5) =1.19$, $p=.144$.
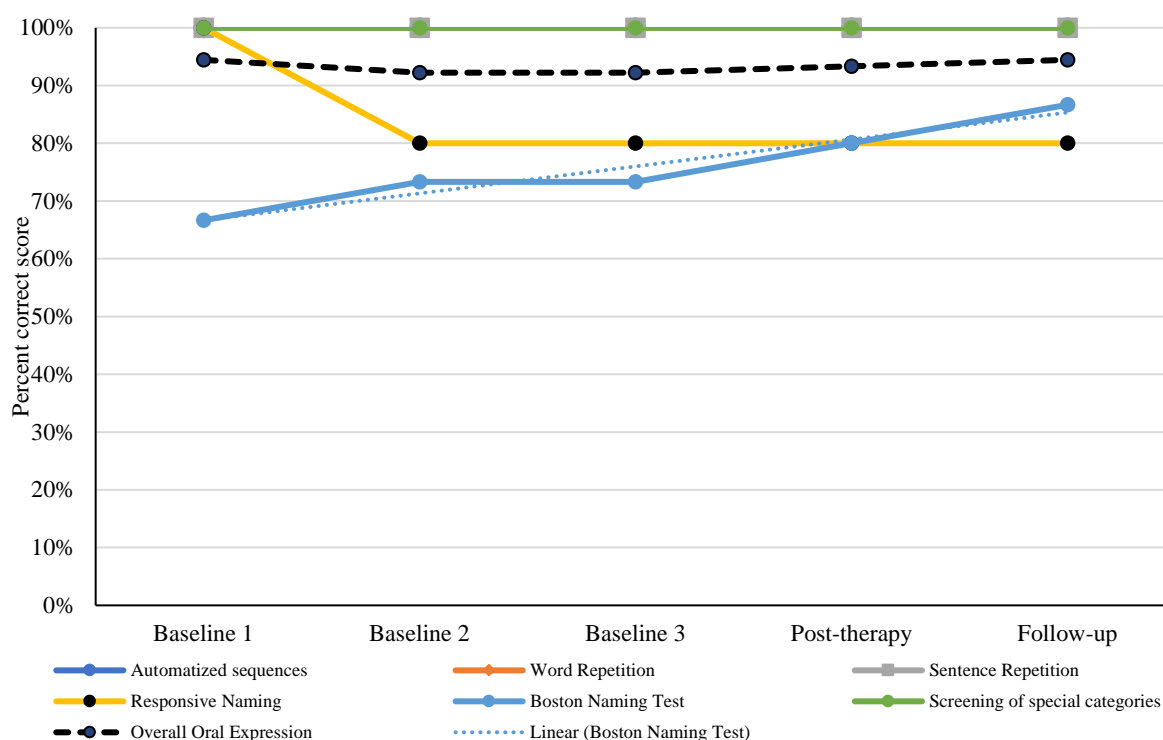
Figure 4.2.2: Percentage (%) correct on the *BDAE Oral Expression* subtests and the overall *BDAE Oral Expression* across study phase (Participant C.S.).

Table 4.2.2: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) for the *BDAE Oral Expression* (Participant C.S.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Automatized Sequences	Mean	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Word Repetition	Mean	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Sentence Repetition	Mean	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Responsive Naming	Mean	1.00	0.80	0.80	0.80	0.80	-0.80	0.80
	S.D.	0.00	0.45	0.45	0.45	0.45	1.79	1.79
							$t(4)= -0.63, p= 0.281$	$t(4)= 0.63, p= 0.281$
Boston Naming Test	Mean	0.67	0.73	0.73	0.80	0.87	0.47	0.07
	S.D.	0.49	0.46	0.46	0.41	0.35	0.99	0.96
							$t(14)= 1.82, p= 0.045$	$t(14)= 0.27, p= 0.396$
Screening of Special Categories	Mean	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Overall BDAE Oral Expression	Mean	0.94	0.92	0.92	0.93	0.94	0.01	0.08
	S.D.	0.14	0.12	0.12	0.10	0.09	0.27	0.16
							$t(5)= 0.10, p= 0.462$	$t(5)= 1.19, p= 0.144$

4.2.3 *BDAE Reading*

Statistical analysis of the *BDAE Reading* subtest (**Table 4.2.3**) showed that overall improvement in *Matching case/script* was not significant, $t(3)= 1.00$, p= .196, and non-significant between the treated and untreated periods, $t(3)= 1.00$, p= .196. Similarly, overall improvement in the *Number matching* was not significant, $t(3)= 1.00$, p= .196, and non-significant between the treated and untreated periods, $t(3)= -1.00$, p= .196. The WEST-Trend could not be calculated for the *Word identification*, whereas the improvement between the treated and untreated periods was non-significant $t(3)= 1.00$, p= .196. Furthermore, overall improvement in the *Oral Basic Sentence* was not significant, $t(4) = 0.63$, p= .281, and the difference between the treated and untreated periods was non-significant, $t(4) = -0.63$, $p=.281$. There were no differences between the five periods for the participant's responses in *Oral Basic Word, Oral Sentence Comprehension* and *Silent Comprehension.* Overall, there was a significant trend for improvement in the *BDAE Reading* subtest, $t(6) = 2.00$, $p= .046$, but difference was non-significant between the treated and untreated periods, $t(6) = 0.30$, $p=.389$ **(Figure 4.2.3)**.

Figure 4.2.3: Percentage (%) correct on the *BDAE Reading* subtests and the overall *BDAE Reading* (Participant C.S.).

Table 4.2.3.: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) for the *BDAE Reading* (Participant C.S.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Matching Case/Script	Mean	0.75	0.75	0.75	1.00	1.00	0.75	0.75
	S.D.	0.50	0.50	0.50	0.00	0.00	1.50	1.50
							t(3)= 1.00, p= 0.196	t(3)= 1.00, p= 0.196
Number Matching	Mean	0.75	1.00	1.00	1.00	1.00	0.50	-0.50
	S.D.	0.50	0.00	0.00	0.00	0.00	1.00	1.00
							t(3)= 1.00, p= 0.196	t(3)= -1.00, p= 0.196
Word Identification	Mean	1.00	0.75	0.75	0.75	1.00	0.00	0.50
	S.D.	0.00	0.50	0.50	0.50	0.00	0.00	1.00
							---	t(3)= 1.00, p= 0.196
Oral Basic Word	Mean	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Oral Basic Sentence	Mean	0.80	1.00	1.00	1.00	1.00	0.40	-0.40
	S.D.	0.45	0.00	0.00	0.00	0.00	0.89	0.89
							t(4)= 0.63, p= 0.281	t(4)= -0.63, p= 0.281
Oral Sentence Comprehension	Mean	0.67	0.67	0.67	0.67	0.67	0.00	0.00
	S.D.	0.58	0.58	0.58	0.58	0.58	0.00	0.00
Silent Comprehension	Mean	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Overall BDAE Reading	Mean	0.85	0.88	0.88	0.92	0.95	0.24	0.05
	S.D.	0.14	0.15	0.15	0.14	0.13	0.31	0.45
							t(6)= 2.00, p= 0.046	t(6)= 0.30, p= 0.389

4.2.4 *RCPM*

The WEST-Trend analysis (**Table 4.2.4**) showed a statistically significant overall trend for improvement in *Subtest AB*, $t(11)= 1.82$, $p= .048$, but the WEST-ROC showed that the difference between the treated and untreated periods was non-significant, $t(11)= 0.64$, $p=.268$ There was non-significant overall trend for improvement in *Subtest A*, $t(11)= -0.32$, $p= .377$, and non-significant difference between the treated and untreated periods, $t(11)= 0.86$, $p= .204$. Lastly, there was a non-significant overall trend for improvement in *Subtest B*, $t(11)= 0.56$, $p= .293$, and non-significant between the treated and untreated periods, $t(11) = 0.22$, $p= .415$. Concluding, there was a non-significant overall trend for improvement in the RCPM, $t(35) = 1.09$, $p=.141$, and also non-significant difference between the treated and untreated periods, $t(35) = 1.06$, $p= .149$ (**Figure 4.2.4**).
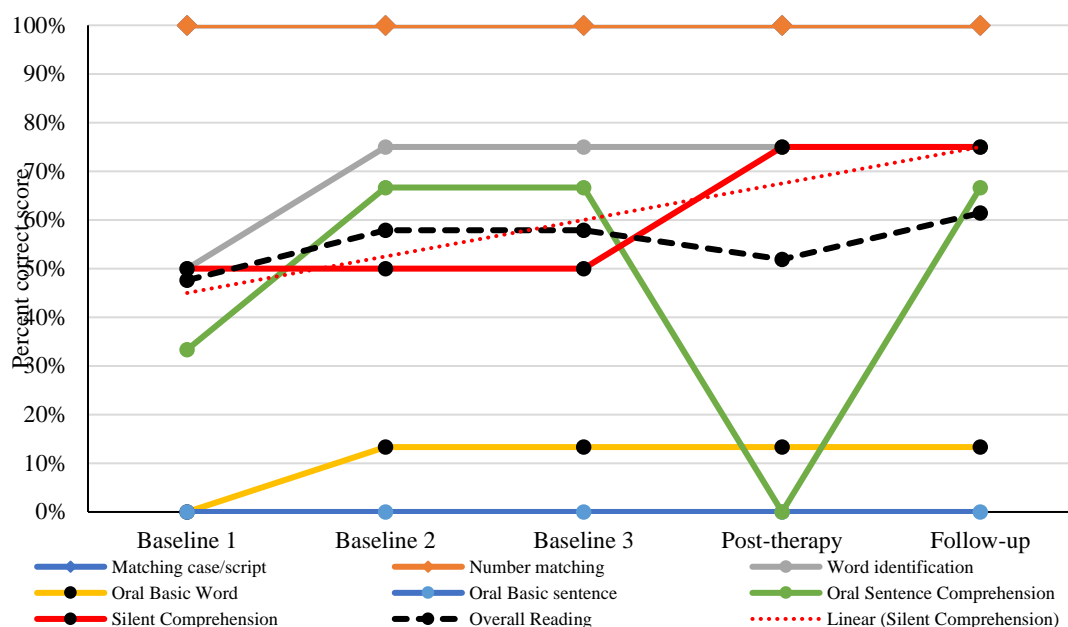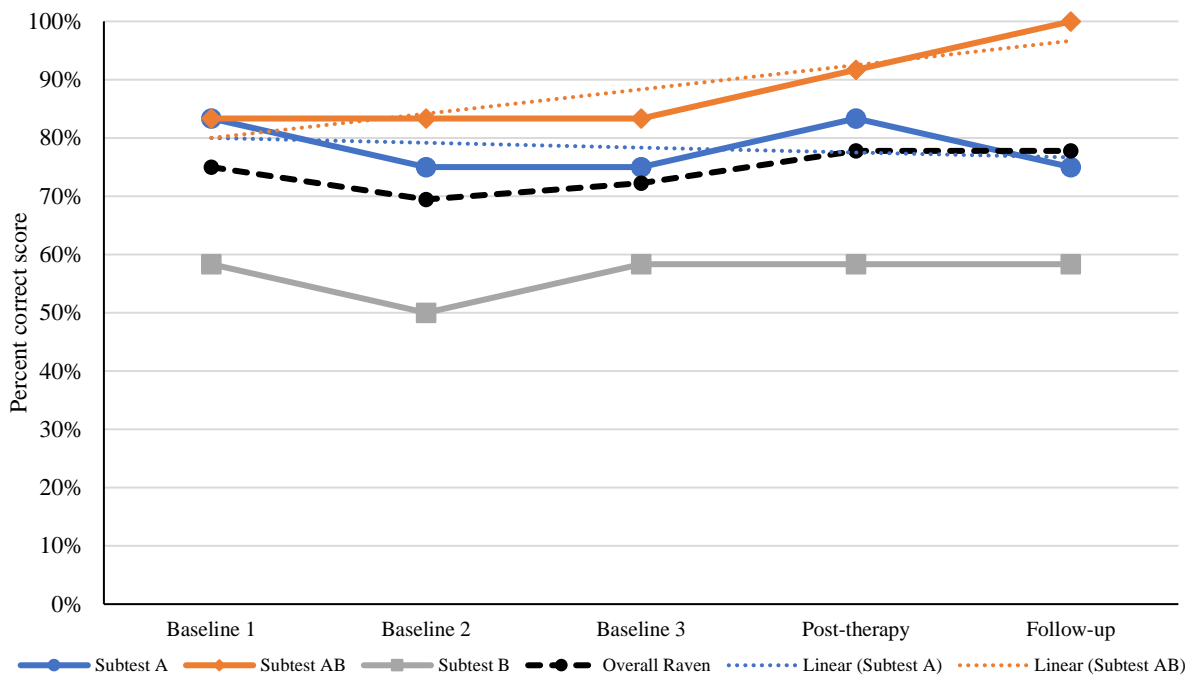

Figure 4.2.4: Percentage (%) correct on the *RCPM* subtests and the overall *RCPM* (Participant C.S.).

Table 4.2.4: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) for the *RCPM* (Participant C.S.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Subtest A	Mean	0.83	0.75	0.75	0.83	0.75	-0.08	0.42
	S.D.	0.39	0.45	0.45	0.39	0.45	0.90	1.68
							t(11)= -0.32, p= 0.377	t(11)= 0.86, p= 0.204
Subtest AB	Mean	0.83	0.83	0.83	0.92	1.00	0.42	0.25
	S.D.	0.39	0.39	0.39	0.29	0.00	0.79	1.36
							t(11)= 1.82, p= 0.048	t(11)= 0.64, p= 0.268
Subtest B	Mean	0.58	0.50	0.58	0.58	0.58	0.08	0.08
	S.D.	0.51	0.52	0.51	0.51	0.51	0.51	1.31
							t(11)= 0.56, p= 0.293	t(11)= 0.22, p= 0.415
Overall RCPM	Mean	0.75	0.69	0.72	0.78	0.78	0.139	0.250
	S.D.	0.44	0.47	0.45	0.42	0.42	0.76	1.42
							t(35)= 1.09, p= 0.141	t(35)= 1.06, p= 0.149

4.2.5 *MAIN*

There was overall trend for improvement in the *MAIN*, but it did not reach significance $t(16)=$ 1.37, $p= .095$, and the difference between the treated and untreated periods was non-significant, $t(16)= 1.24$, $p= .116$.
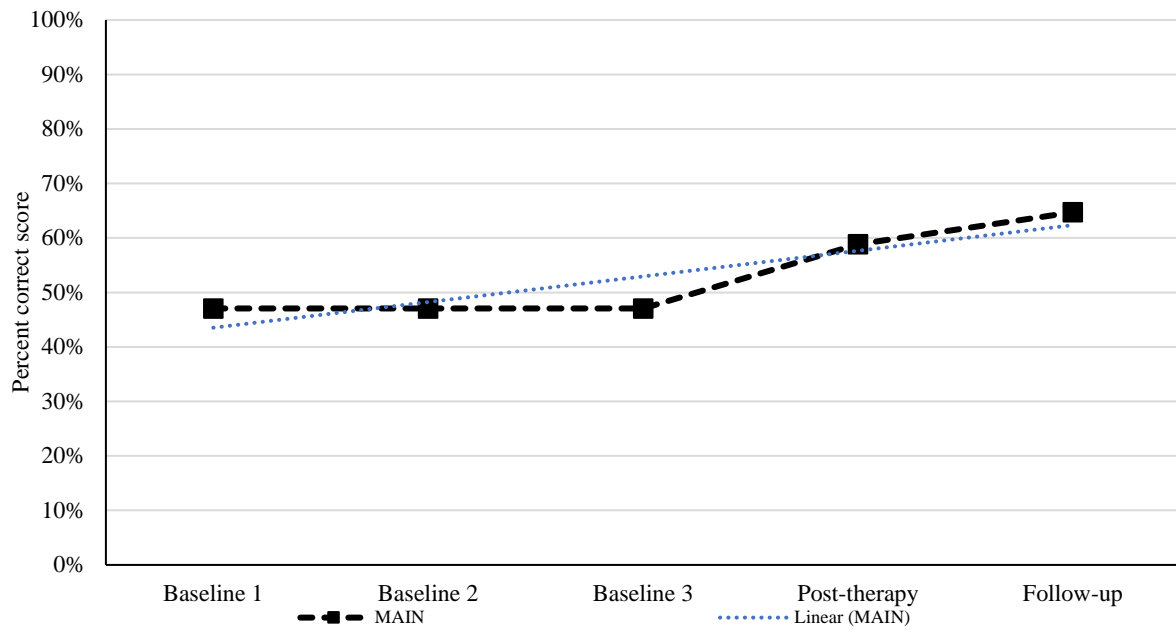
Figure 4.2.5: Percentage (%) correct on the *MAIN* across the study phases (Participant C.S.).

Table 4.2.5: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) for the *MAIN* (Participant C.S.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
	Mean	0.47	0.47	0.47	0.59	0.65	0.47	0.35
MAIN	S.D.	0.51	0.51	0.51	0.51	0.49	1.42	1.17
							t(16)= 1.37, p= 0.095	t(16)= 1.24, p= 0.116

4.2.6 *Procedural Discourse*

Statistical analysis of the participant's *Procedural Discourse* task showed that there were no differences in the number of responses between the five periods.
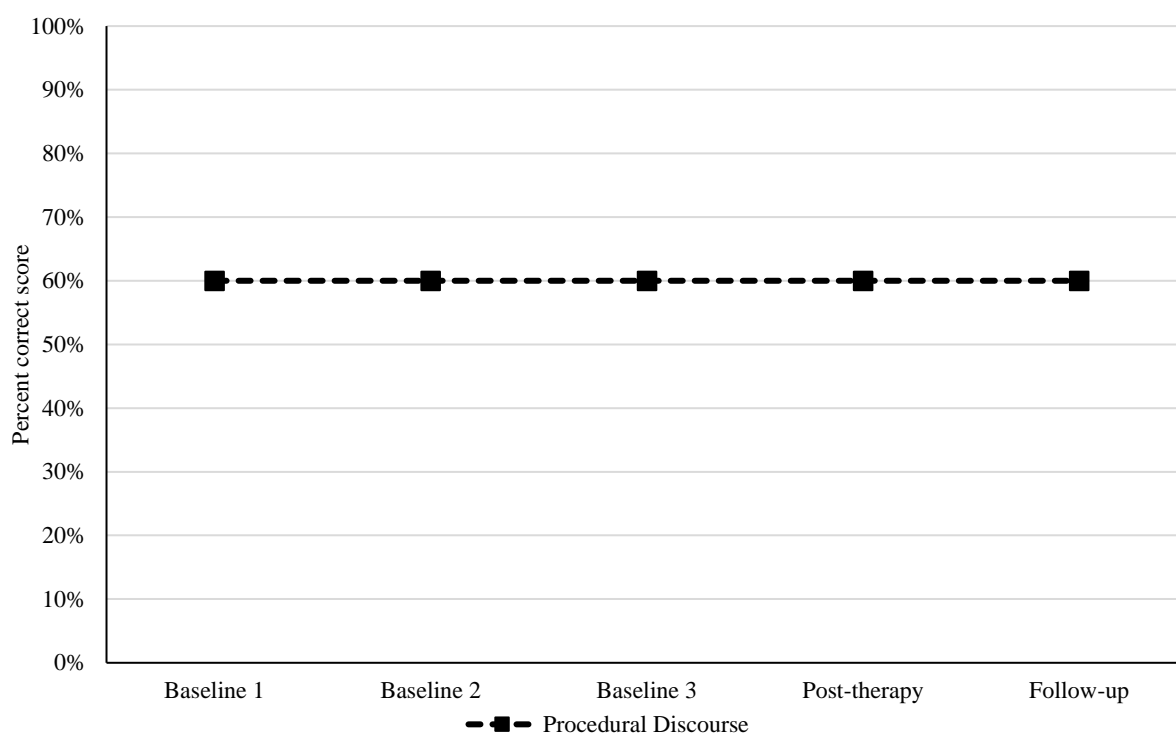
Figure 4.2.6: Percentage (%) correct on the *Procedural Discourse* across study phase (Participant C.S.).

As indicated in the raw scores (**Table 4.2.6**), the participant's raw scores did not change across the five periods.

Table 4.2.6: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) for the *Procedural Discourse* (Case C.S.).

	Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Mean	0.60	0.60	0.60	0.60	0.60	0.00	0.00
S.D.	0.52	0.52	0.52	0.52	0.52	0.94	0.94
						t(9)= 0,00, p= 0.500	t(9)= 0,00, p= 0.500

4.2.7 *SSLA*

C.S..'s stroke narrative (spontaneous language sample) was analysed using the SSLA protocol (Shewan, 1988) designed to describe and quantify connected speech (**Table 4.2.7**). The language sample collected at each time point, was not sufficient in word length to undergo statistical analysis hence results were compared in raw scores. In this case the baseline average (avg) was compared with the post-testing and follow-up results. There was an increase in the number of utterances produced between baseline avg and post-therapy (from 11% to 12%) and baseline avg and follow-up (from 11% to 18%). The rate of speech improved from 116.76 syllables per minute to 141.60 at post-therapy, and to 152.22 at follow-up. The sentence length improved between baseline avg and follow-up (from 39% to 17%), which reflects the use of more than 5 words in the produced utterances. A small improvement was noted in sentence complexity between baseline avg and follow-up (from 54% to 61%). Improvement was also noted between Baseline avg and follow-up in the production of errors (from 44% to 33%). The number of content units improved from 19.33 at baseline avg, to 21.00 at post-therapy, and to 36.00 at follow-up. Improvement in the number of repetitions was noted with a reduction from 7% to 0% between baseline avg and post-therapy. A notable improvement in communication efficiency which reflects the rate at which information is conveyed by the speaker (number of content units divided by time), from 13.33 at baseline avg, to 16.80 post-therapy, and to 17.73 at follow-up. No paraphasias were produced in any of the stroke narrative samples and the overall melody and articulation were judged to be normal.
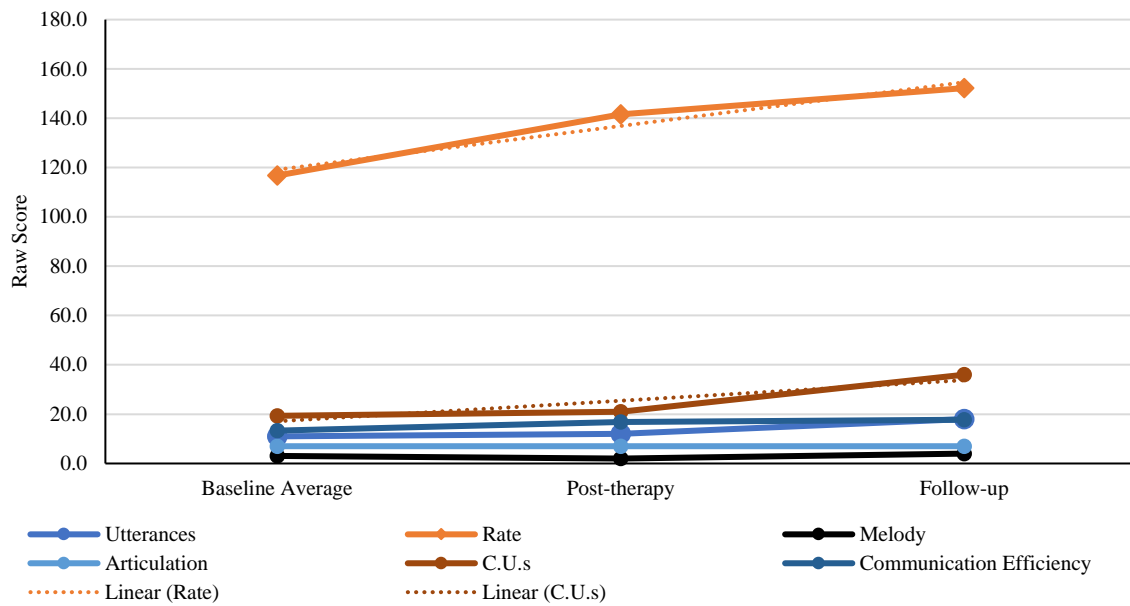
Figure 4.2.7a. Results of the personal stroke narrative analysis based on the SSLA showing the raw scores across baseline average, post-therapy, and follow-up phases.
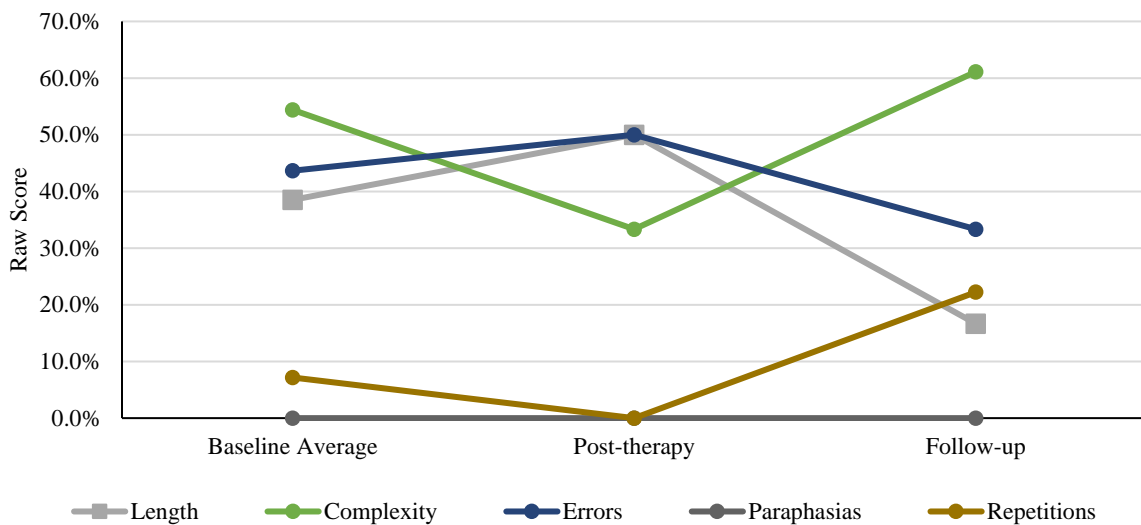
Figure 4.2.7.b. Results of the personal stroke narrative analysis based on the SSLA showing the raw percentage (%) scores between baseline average, post-therapy, and follow-up phases.

Table 4.2.7: Raw scores for personal stroke narrative analysis based on the *SSLA*.

	Baseline 1	Baseline 2	Baseline 3	Baseline Avg	Post-Therapy	Follow-up
Utterances	12.00	14.00	7.00	11.00	12.00	18.00
Rate	99.37	152.41	98.50	116.76	141.60	152.22
Length	58%	43%	14%	39%	50%	17%
Melody	3.00	3.00	3.00	3.00	2.00	4.00
Articulation	7.00	7.00	7.00	7.00	7.00	7.00
Complexity	42%	50.00%	72%	54%	33%	61%
Errors	17%	57%	57%	44%	50%	33%
C.U.s	19.00	22.00	17.00	19.33	21.00	36.00
Paraphasias	0%	0%	0%	0%	0%	0%
Repetitions	0%	21%	0%	7%	0%	22%
Communication Efficiency	12.03	15.17	12.78	13.33	16.80	17.73

4.2.8 *RehaCom WM*

The results of the *RehaCom WM* screening show a positive linear trend line (**Figure 4.2.8**) on all the tasks assessed with a more prominent trend for improvement in the correct responses task. **Table 4.2.8** shows the raw scores attained by participant C.S.
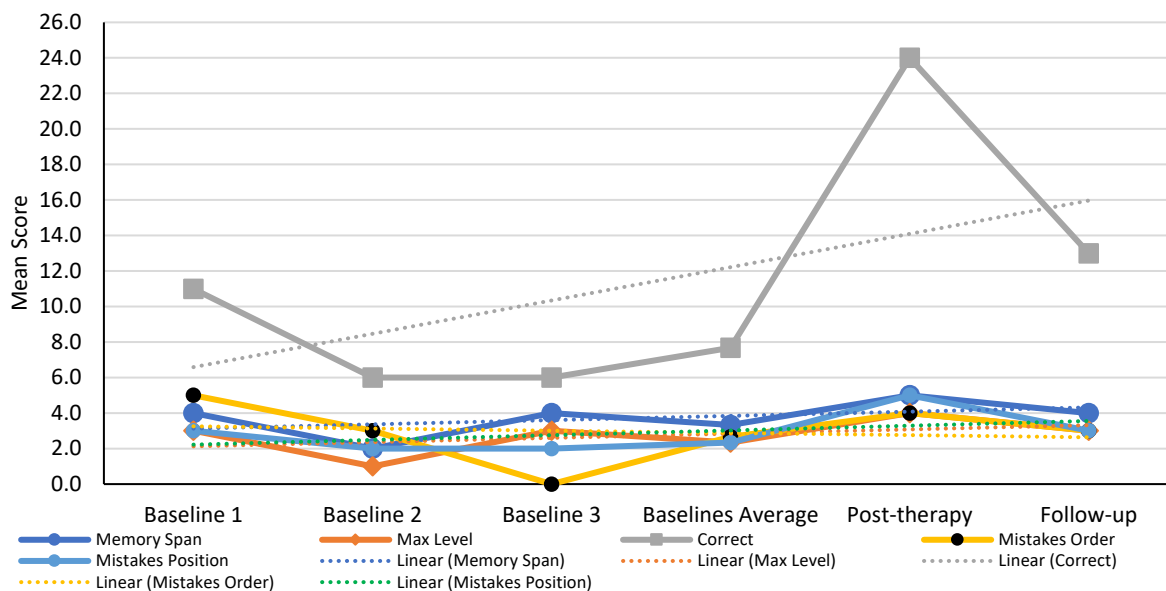
Figure 4.2.8: Schematic representation of C.S.'s raw scores on the *RehaCom* WM Screening task.

Based on the participant's scores, WM did not show improvement. Interestingly, all WM tasks measured showed a decrease in the scores attained between the baseline average and the post-therapy & follow-up periods.

Table 4.2.8: *RehaCom* WM Screening raw scores for C.S. by subcategory and study phase.

	Baseline 1	Baseline 2	Baseline 3	Baseline Average	Post-therapy	Follow-up
Memory Span	4	2	4	3	5	4
Max Level	3	1	3	2	4	3
Correct	11	6	6	8	24	13
Mistakes Order	5	3	0	3	4	3
Mistakes Position	3	2	2	2	5	3

4.2.9 *SAQOL-39*

With regards to investigating whether the overall QoL would improve after treatment, the self-rated SAQOL-39 was analysed by comparing the mean scores (**Figure 4.2.9.; Table 4.2.9.**). The participant's responses indicated that QoL based on the overall SAQOL-39 self-rated score improved between the baseline average (M = 3.63) and post-therapy (M = 4.51) by 18%, and it was maintained at follow-up (M = 4.23).
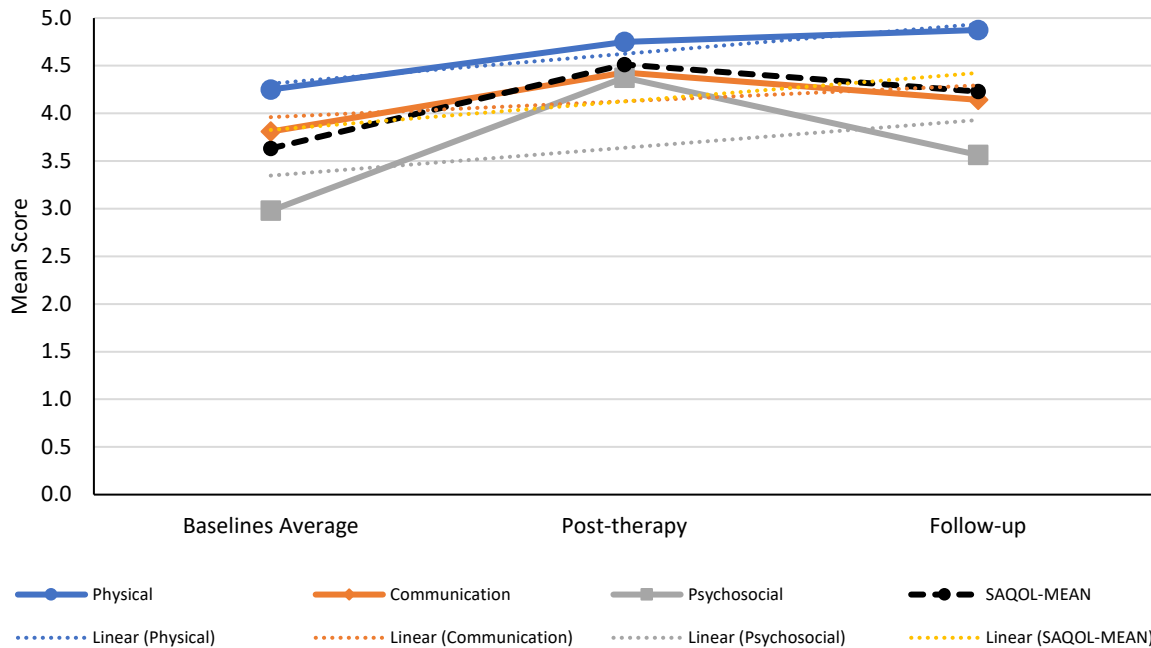
Figure 4.2.9: Schematic representation of the *SAQOL-39g* mean raw scores at baseline, post-therapy and follow-up (Participant C.S.).

The mean scores for the overall SAQOL-39 and for each subcategory are shown in **Table 4.2.9.** The Physical self-rated score improved from the baseline average (M = 4.25) to post-therapy (M = 4.75) by 10%, and it was maintained at follow-up (M = 4.88). The Communication self-rated score improved from the baseline average (M = 3.81) to post-therapy (M = 4.43) by 10%, and it was maintained at follow-up (M = 4.14). The Psychosocial self-rated score improved between the baseline average (M = 2.98) and post-therapy (M = 4.38) by 28%.

Table 4.2.9: Mean raw scores on the *SAQOL-39g* at baseline, post-therapy and follow-up (Participant C.S.).

	Baseline 1	Baseline 2	Baseline 3	Baseline average	Post-therapy	Follow-up
Physical	4.31	3.88	4.56	4.25	4.75	4.88
Communication	3.57	3.71	4.14	3.81	4.43	4.14
Psychosocial	2.50	2.88	3.56	2.98	4.38	3.56
Overall SAQOL-39	3.44	3.41	4.05	3.63	4.51	4.23

4.3   Participant #3 – S.H.

4.3.1   *BDAE Auditory Comprehension*

Statistical analysis of the *BDAE Auditory Comprehension* subtest (**Table 4.3.1**) showed that there was a significant overall trend for improvement in *Commands*, $t(9) = 2.47$, $p= .018$, but non-significant between the treated and untreated periods, $t(9) = 1.35$, $p=.105$. On the other hand the overall trend for improvement in *Word Comprehension* was not significant, $t(15) = 1.71$, $p=.054$, and the difference between the treated and untreated periods was also non-significant, $t(15) = -1.50$, $p=.078$. Similarly, there was non-significant overall trend for improvement in the *Complex Ideational Material*, $t(5) = -1.23$, $p=.136$, and non-significant difference between the treated and untreated periods, $t(5) = 0.69$, $p=.259$. Concluding, there was a non-significant overall trend for improvement in the overall *BDAE Auditory Comprehension* subtest, $t(2) = 0.32$, $p= .389$, and a non-significant difference between the treated and untreated periods, $t(2) = 1.25$, $p=.169$ (**Figure 4.3.1**).
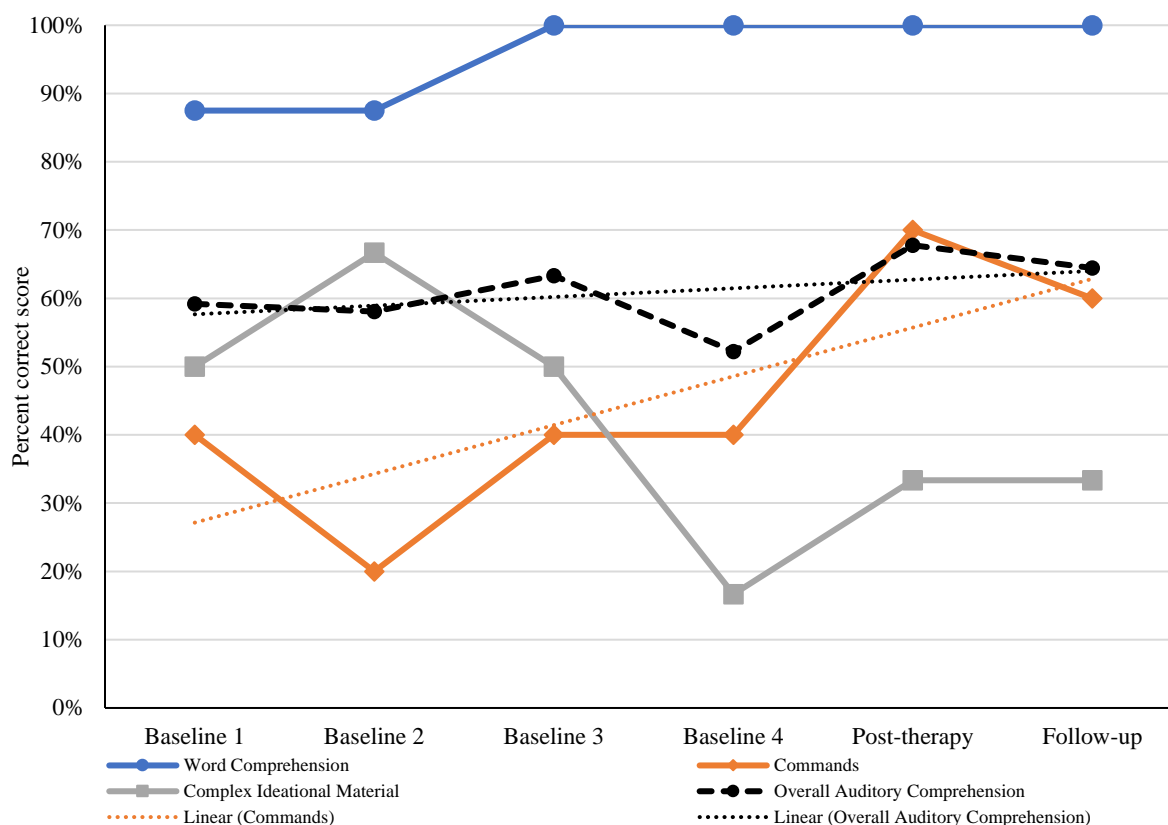

Figure 4.3.1: Percentage (%) correct for the *BDAE Auditory Comprehension subtests* and the overall *BDAE Auditory Comprehension* by study phase (Participant S.H.).

Table 4.3.1: WEST-Trend (sum of scores multiplied by −5, −3, −1, 1, 3, 5) and WEST-ROC (sum of scores multiplied by 25, 1, −23, -47, 34, 10) for the *BDAE Auditory Comprehension* (Participant S.H.)

		Baseline 1	Baseline 2	Baseline 3	Baseline 4	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Word Comprehension	Mean	0.88	0.88	1.00	1.00	1.00	1.00	1.00	-3.25
	S.D.	0.34	0.34	0.00	0.00	0.00	0.00	2.34	8.69
								t(15)= 1.71, p= 0.054	t(15)= -1.50, p= 0.078
Commands	Mean	0.40	0.20	0.40	0.40	0.70	0.60	2.50	12.00
	S.D.	0.52	0.42	0.52	0.52	0.48	0.52	3.21	28.07
								t(9)= 2.47, p= 0.018	t(9)= 1.35, p= 0.105
Complex Ideational Material	Mean	0.50	0.67	0.50	0.17	0.33	0.33	-2.17	8.50
	S.D.	0.55	0.52	0.55	0.41	0.52	0.52	4.31	29.98
								t(5)= -1.23, p= 0.136	t(5)= 0.69, p= 0.259
Overall BDAE Auditory Comprehension	Mean	0.59	0.58	0.63	0.52	0.68	0.64	0.44	5.75
	S.D.	0.25	0.35	0.32	0.43	0.33	0.34	2.38	7.99
								t(2)= 0.32, p= 0.389	t(2)= 1.25, p= 0.169

4.3.2 *BDAE Oral Expression*

Statistical analysis of the *BDAE Oral Expression* subtest (**Table 4.3.2**.) showed that overall improvement in the *Automated Sequences* was not significant, $t(1) = 0.33$, $p=.398$, and the difference was non-significant between the treated and untreated periods, $t(1) = 0.89$, $p=.268$. Also, there was a non-significant overall trend for improvement in *Responsive Naming*, $t(4) = -0.19$, $p= .431$, and the difference between the treated and untreated periods was non-significant, $t(4) = -0.46$, $p= .334$. Similarly, overall improvement in the *Boston Naming* was not significant, $t(14) =1.02$, $p= .164$, and the difference was non-significant between the treated and untreated periods, $t(14) = 0.66$, $p=.260$. Additionally, there was non-significant overall trend for improvement in the *Screening of Special Categories*, $t(11) = 1.58$, $p= .071$, and non-significant difference between the treated and untreated periods, $t(11) = 1.26$, $p= .117$. There were no differences in the responses between the six periods for the subtests of *Word Repetition* and *Sentence Repetition*. Concluding, there was a non-significant overall trend for improvement in the *overall BDAE Oral Expression* subtest, $t(5) = 1.40$, $p= .110$, and the difference was non-significant between the treated and untreated periods, $t(5) = 1.88$, $p=.059$.
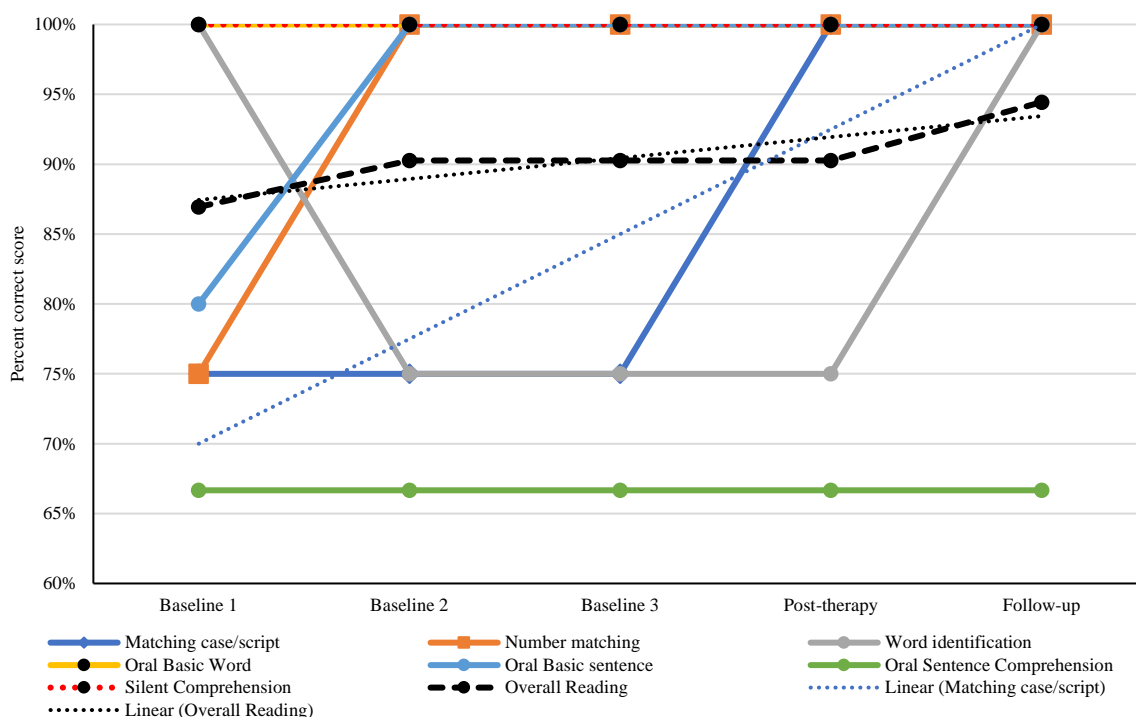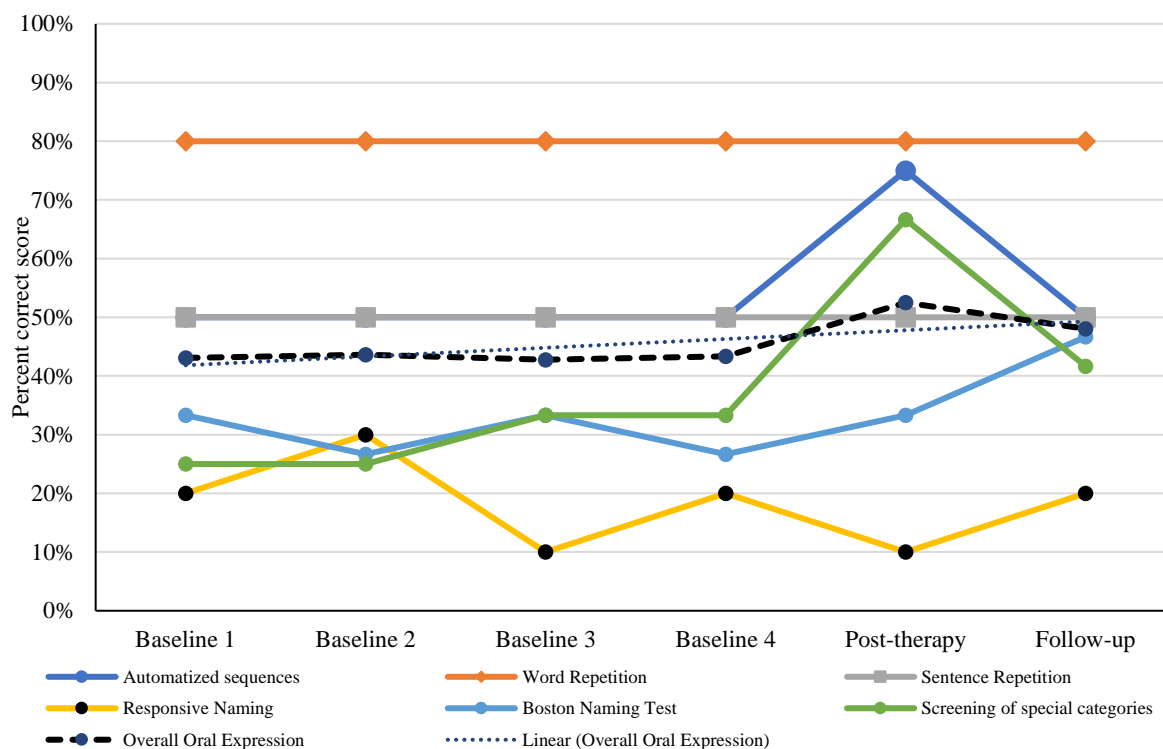

Figure 4.3.2: Percentage (%) correct on the *BDAE Oral Expression* subtests and the overall *BDAE Oral Expression* by study phase (Participant S.H.).

Table 4.3.2: WEST-Trend (sum of scores multiplied by −5, −3, −1, 1, 3, 5) and WEST-ROC (sum of scores multiplied by 25, 1, −23, -47, 34, 10) for the *BDAE Oral Expression* (Participant S.H.)

		Baseline 1	Baseline 2	Baseline 3	Baseline 4	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Automatized Sequences	Mean	0.50	0.50	0.50	0.50	0.75	0.50	1.50	17.00
	S.D.	0.71	0.00	0.71	0.00	0.35	0.00	6.36	26.87
								t(1)= 0.33, p= 0.398	t(1)= 0.89, p= 0.268
Word Repetition	Mean	0.80	0.80	0.80	0.80	0.80	0.80	0.00	0.00
	S.D.	0.45	0.45	0.45	0.45	0.45	0.45	0.00	0.00
Sentence Repetition	Mean	0.50	0.50	0.50	0.50	0.50	0.50	0.00	0.00
	S.D.	0.71	0.71	0.71	0.71	0.71	0.71	0.00	0.00
Responsive Naming	Mean	0.20	0.30	0.10	0.20	0.10	0.20	-1.00	-2.00
	S.D.	0.45	0.27	0.22	0.27	0.22	0.45	7.58	6.12
								t(4)= -0.19, p= 0.431	t(4)= -0.46, p= 0.334
Boston Naming Test	Mean	0.33	0.27	0.33	0.27	0.33	0.47	0.80	4.40
	S.D.	0.49	0.46	0.49	0.46	0.49	0.52	3.05	25.87
								t(14)= 1.02, p= 0.164	t(14)= 0.66, p= 0.260
Screening of Special Categories	Mean	0.25	0.25	0.33	0.33	0.67	0.42	2.08	10.00
	S.D.	0.45	0.45	0.49	0.49	0.49	0.51	4.56	27.51
								t(11)= 1.58, p= 0.071	t(11)= 1.26, p= 0.117
Overall BDAE Oral Expression	Mean	0.43	0.44	0.43	0.43	0.53	0.48	0.52	3.65
	S.D.	0.22	0.21	0.23	0.22	0.27	0.19	0.91	4.75
								t(5)= 1.40, p= 0.110	t(5)= 1.88, p= 0.059

168

4.3.3 *BDAE Reading*

Statistical analysis of the *BDAE Reading* subtest **(Table 4.3.3.)** showed that the overall trend for improvement in *Number Matching* was not significant, $t(3) = 1.00$, p= .196, and the difference between the treated and untreated periods was non-significant, $t(3)= -1.00$, p= .196. Also, there was non-significant overall trend for improvement in the *Word identification*, $t(3)= -1.57$, p= .108, and non-significant between the treated and untreated periods, $t(3)= -0.36$, p= .371. Similarly, the overall trend for improvement in in the *Oral Basic Word* task was not significant, $t(4) = 0.63$, p= .281, and non-significant between the treated and untreated periods, $t(4) = -0.27$, $p=.401$. Lastly, there was non-significant overall improvement in *Silent Comprehension*, $t(3) = 1.00$, p= .196, and the difference was non-significant between the treated and untreated periods, $t(3) = 1.00$, p= .196. There were no differences of the responses between the six periods for the subtests of *Matching case/script*, *Oral Basic Sentence* and *Oral Sentence Comprehension*. Concluding, there was a non-significant overall trend for improvement in the overall *BDAE Reading* subtest, $t(6) = 0.33$, $p= .378$, and a non-significant difference between the treated and untreated periods, $t(6) = -0.71$, $p=.251$ **(Figure 4.3.3.).**
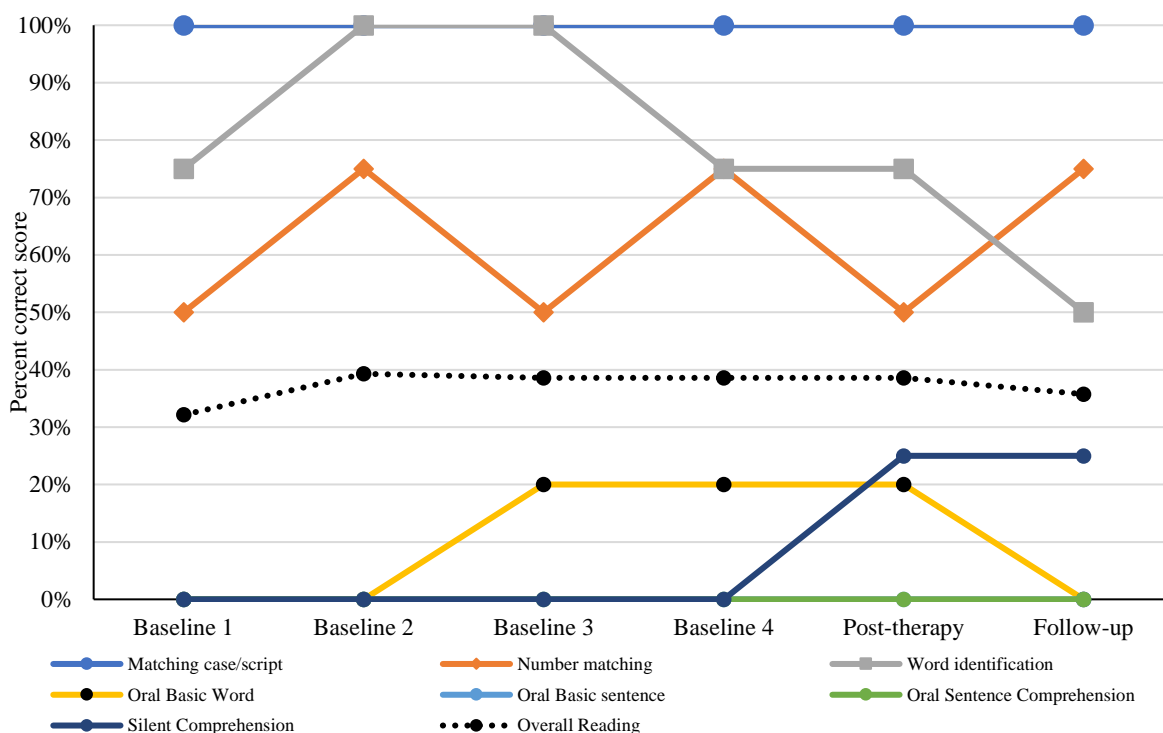
Figure 4.3.3: Percentage (%) correct on the *BDAE Reading* subtests and the overall *BDAE Reading* (Participant S.H.).

Table 4.3.3: WEST-Trend (sum of scores multiplied by −5, −3, −1, 1, 3, 5) and WEST-ROC (sum of scores multiplied by 25, 1, −23, -47, 34, 10) for the *BDAE Reading* (Participant S.H.)

		Baseline 1	Baseline 2	Baseline 3	Baseline 4	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Matching case/script	Mean	1.00	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Number Matching	Mean	0.50	0.75	0.50	0.75	0.50	0.75	0.75	-9.00
	S.D.	0.58	0.50	0.58	0.50	0.58	0.50	1.50	18.00
								t(3)= 1.00, p= 0.196	t(3)= -1.00, p= 0.196
Word identification	Mean	0.75	1.00	1.00	0.75	0.75	0.50	-2.25	-8.00
	S.D.	0.50	0.00	0.00	0.50	0.50	0.58	2.87	44.25
								t(3)= -1.57, p= 0.108	t(3)= -0.36, p= 0.371
Oral Basic Word	Mean	0.00	0.00	0.20	0.20	0.20	0.00	1.80	-21.60
	S.D.	0.00	0.00	0.45	0.45	0.45	0.00	4.02	114.21
								t(4)= 0.63, p= 0.281	t(4)= -0.27, p= 0.401
Oral Basic sentence	Mean	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Oral Sentence Comprehension	Mean	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Silent Comprehension	Mean	0.00	0.00	0.00	0.00	0.25	0.25	2.00	11.00
	S.D.	0.00	0.00	0.00	0.00	0.50	0.50	4.00	22.00
								t(3)= 1.00, p= 0.196	t(3)= 1.00, p= 0.196
Overall BDAE Reading	Mean	0.32	0.39	0.39	0.39	0.39	0.36	0.16	-1.89
	S.D.	0.43	0.50	0.46	0.43	0.38	0.40	1.28	6.99
								t(6)= 0.33, p= 0.378	t(6)= -0.71, p= 0.251

4.3.4 *RCPM*

Statistical analysis (**Table 4.3.4**) revealed a statistically significant overall trend for improvement in *Subtest AB*, $t(11) = 3.33$, $p= .003$, and significant difference between the treated and untreated periods, $t(11) = 2.61$, $p=.012$. Additionally, there was a significant overall trend for improvement in *Subtest B*, $t(11) = 2.63$, $p=.012$, but the difference was non-significant between the treated and untreated periods, $t(11) = 1.39$, $p= .096$. There was a non-significant overall trend for improvement in *Subtest A*, $t(11)= 0.00$, $p= .500$, and non-significant between the treated and untreated periods, $t(11)= 0.00$, $p= .500$. Overall, there was a significant trend for improvement in the *RCPM*, $t(35) = 3.25$, $p=.001$, and the difference between the treated and untreated periods was also significant, $t(35) = 2.19$, $p= .018$.
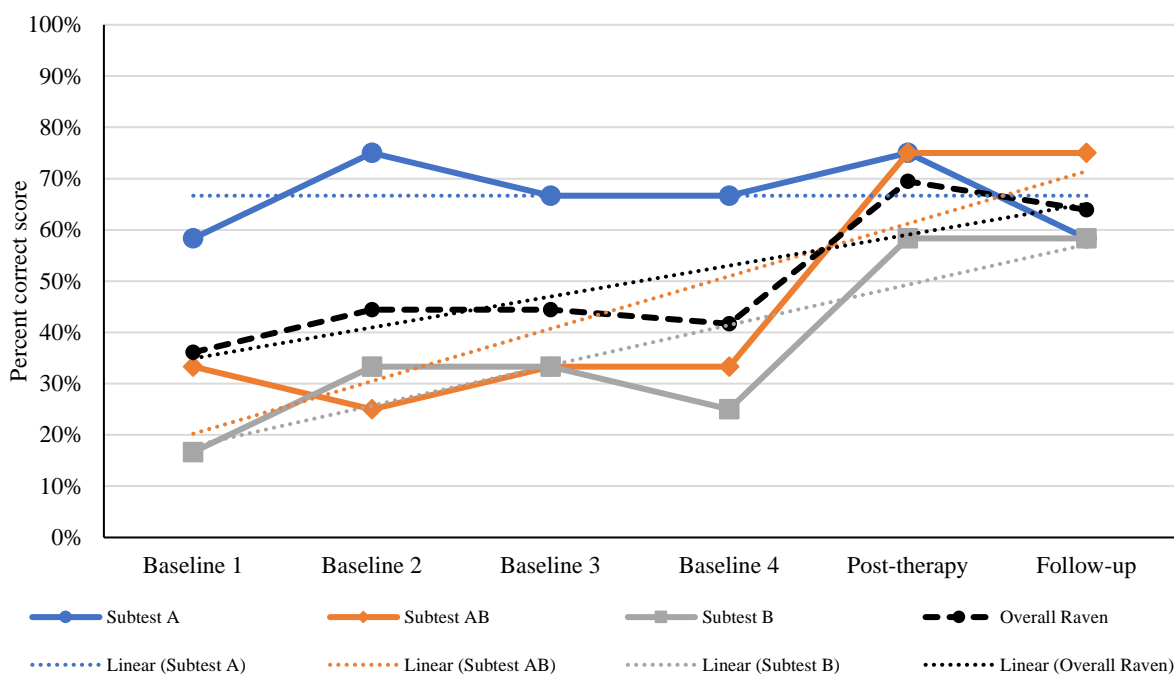
Figure 4.3.4: Percentage (%) correct on the *RCPM* subcategories and the overall *RCPM* (Participant S.H.).

Table 4.3.4: WEST-Trend (sum of scores multiplied by −5, −3, −1, 1, 3, 5) and WEST-ROC (sum of scores multiplied by 25, 1, −23, -47, 34, 10) for the *RCPM* (Participant S.H.).

		Baseline 1	Baseline 2	Baseline 3	Baseline 4	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
	Mean	0.58	0.75	0.67	0.67	0.75	0.58	0.00	0.00
Subtest A	S.D.	0.51	0.45	0.49	0.49	0.45	0.51	3.69	27.24
								t(11)= 0.00, p= 0.500	t(11)= 0.00, p= 0.500
	Mean	0.33	0.25	0.33	0.33	0.75	0.75	3.58	18.25
Subtest AB	S.D.	0.49	0.45	0.49	0.49	0.45	0.45	3.73	24.19
								t(11)= 3.33, p= 0.003	t(11)= 2.61, p= 0.012
	Mean	0.17	0.33	0.33	0.25	0.58	0.58	2.75	10.75
Subtest B	S.D.	0.39	0.49	0.49	0.45	0.51	0.51	3.62	26.83
								t(11)= 2.63, p= 0.012	t(11)= 1.39, p= 0.096
Overall RCPM	Mean	0.36	0.44	0.44	0.42	0.69	0.64	2.111	9.667
	S.D.	0.49	0.50	0.50	0.50	0.47	0.49	3.90	26.48
								t(35)= 3.25, p= 0.001	t(35)= 2.19, p= 0.018

4.3.5 *MAIN*

There was a non-significant overall trend for improvement on the MAIN, $t(16)= 1.59$, $p= .066$, and the difference between the treated and untreated periods was non-significant, $t(16)= 0.34$, $p= .370$ **(Figure 4.3.5; Table 4.3.5).**
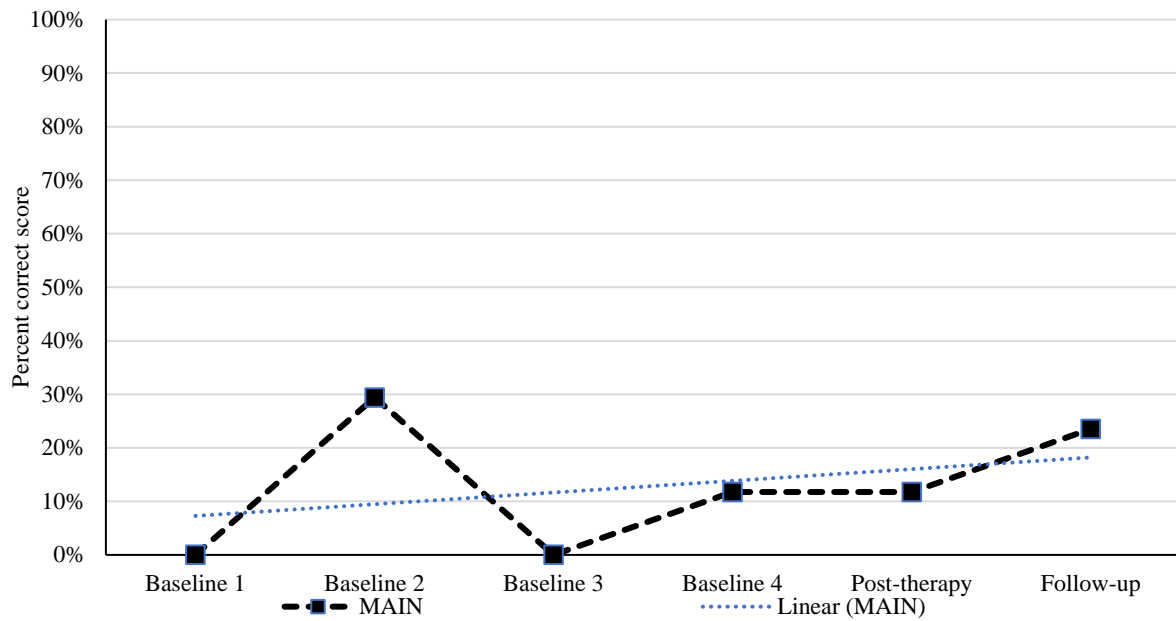
Figure 4.3.5: Percentage (%) correct on the *MAIN* across study phases (Participant S.H.).

Table 4.3.5: WEST-Trend (sum of scores multiplied by −5, −3, −1, 1, 3, 5) and WEST-ROC (sum of scores multiplied by 25, 1, −23, -47, 34, 10) for the *MAIN* (Participant S.H.).

		Baseline 1	Baseline 2	Baseline 3	Baseline 4	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
	Mean	0.00	0.29	0.00	0.12	0.12	0.24	0.76	1.12
MAIN	S.D.	0.00	0.47	0.00	0.33	0.33	0.44	1.99	13.61
								t(16)= 1.59, p= 0.066	t(16)= 0.34, p= 0.370

4.3.6 *Procedural Discourse*

There was a non-significant overall trend for improvement in the *Procedural Discourse* task, $t(9)= -0.13$, $p= .449$, and the difference between the treated and untreated periods was non-significant, $t(9)= -0.44$, $p= .334$.
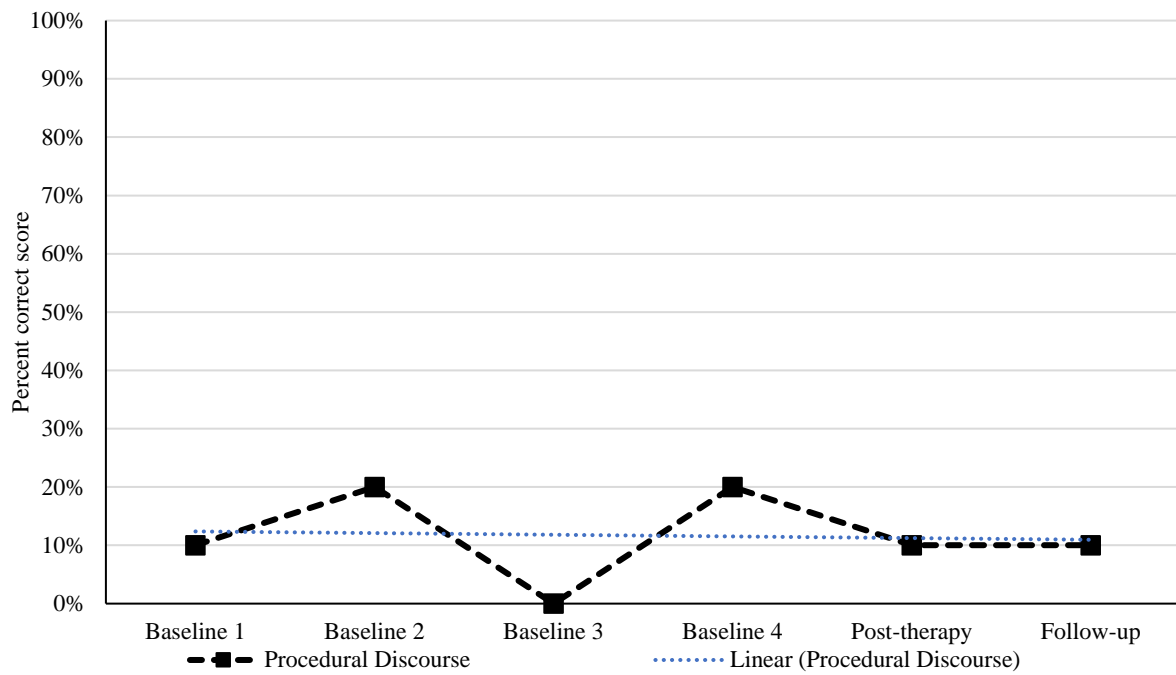
Figure 4.3.6: Percentage (%) correct on the *Procedural Discourse* across study phases (Participant S.H.).

Table 4.3.6: WEST-Trend (sum of scores multiplied by −5, −3, −1, 1, 3, 5) and WEST-ROC (sum of scores multiplied by 25, 1, −23, -47, 34, 10) for the *Procedural Discourse* (Participant S.H.).

		Baseline 1	Baseline 2	Baseline 3	Baseline 4	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Procedural Discourse	Mean	0.10	0.20	0.00	0.20	0.10	0.10	-0.10	-2.30
	S.D.	0.32	0.42	0.00	0.42	0.32	0.32	2.38	16.42
								t(9)= -0.13, p= 0.449	t(9)= -0.44, p= 0.334

4.3.7 *SSLA*

S.H..'s stroke narrative (spontaneous language sample) was analysed using the SSLA protocol (Shewan, 1988) designed to describe and quantify connected speech (**Table 4.3.7**). The language sample collected at each time point, was not sufficient in word length to undergo statistical analysis hence results were compared in raw scores. In this case the baseline average (avg) was compared with the post-testing and follow-up results. There was an increase in the rate of speech that improved from 20.62 syllables per minute to 29.31 at post-therapy but reverted to 17.49 at follow-up. Improvement was also noted between baseline avg and follow-up in the production of errors (from 68% to 57%). A small improvement in the number of content units was noted from 2.25 at baseline avg, to 3.00 at follow-up. A reduction in paraphasias was noted with a reduction from 30% at baseline avg to 25% at post-therapy and at 0% at follow-up. Improvement in the number of repetitions was noted with a reduction from 22% to 0% between baseline avg and post-therapy but reverted to 14% at follow-up. Finally, improvement in communication efficiency, which reflects the rate at which information is conveyed by the speaker (number of content units divided by time), was noted from 1.90 at baseline avg, to 3.45 post-therapy, but at follow-up, communication efficiency had reverted to baseline performance. Overall, based on the numerical values collected, there was no increase in the number of utterances, sentence length, melody, articulation, and sentence complexity after therapy (see **Table 4.3.7**).
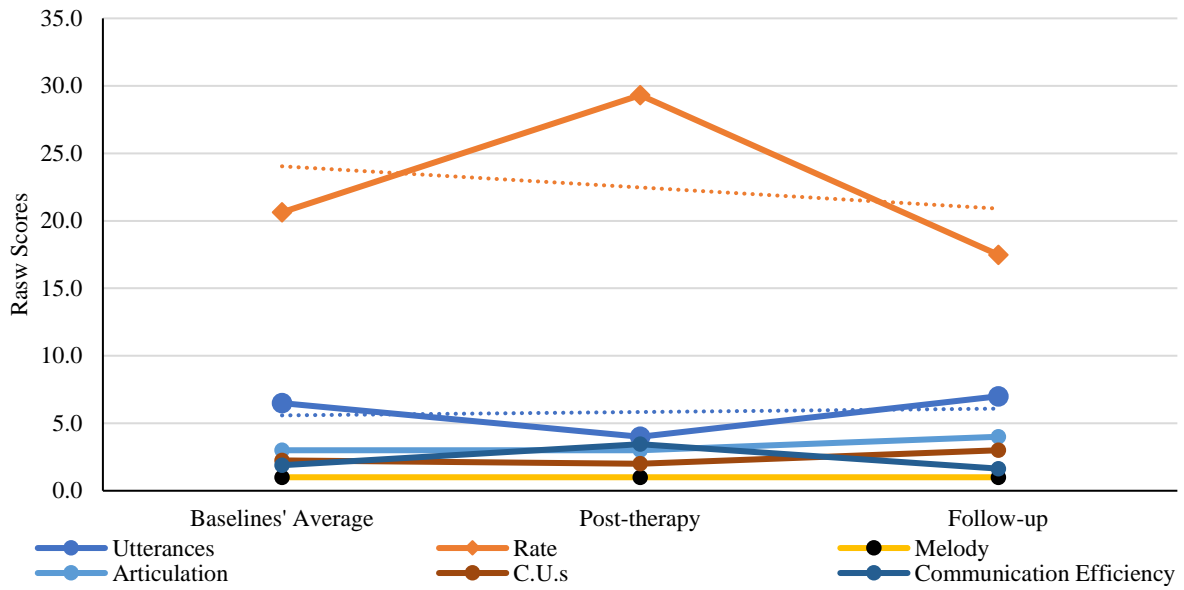
Figure 4.3.7.a. Results of S.H.'s personal stroke narrative analysis based on the *SSLA* showing the raw scores between baseline average, post-therapy, and follow-up phases.
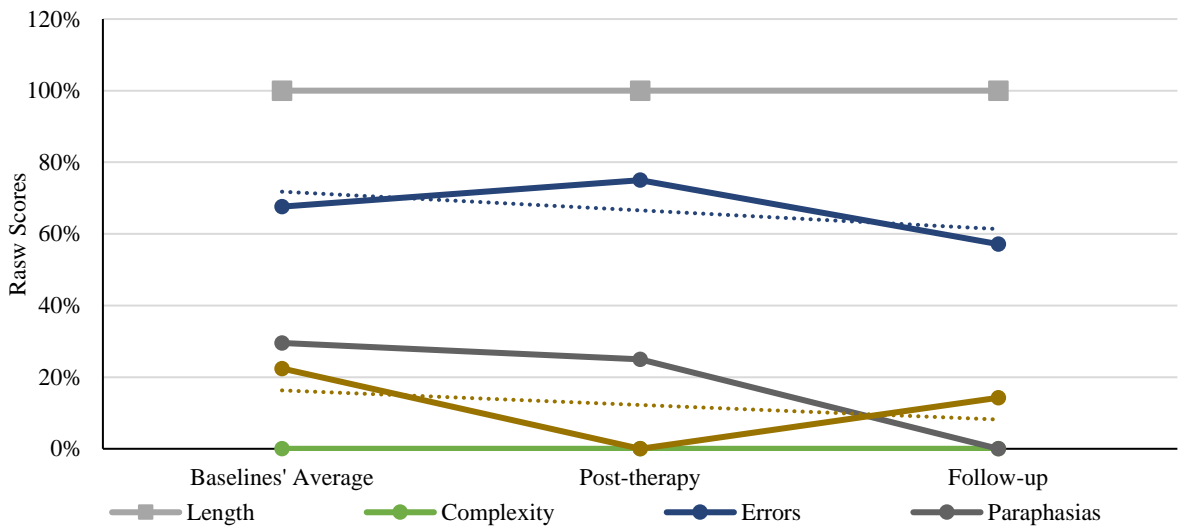
Figure 4.3.7.b. Results of S.H.'s personal stroke narrative analysis based on the *SSLA* showing the raw score percentages (%) between baseline average, post-therapy, and follow-up phases.

Table 4.3.7: Raw scores for S.H.'s personal stroke narrative analysis based on the *SSLA*.

	Baseline 1	Baseline 2	Baseline 3	Baseline 4	Baseline Average	Post-therapy	Follow-up
Utterances	11.00	9.00	1.00	5.00	6.50	4.00	7.00
Rate	20.26	38.04	8.96	15.22	20.62	29.31	17.49
Length	100%	100%	100%	100%	100%	100%	100%
Melody	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Articulation	3.00	3.00	3.00	3.00	3.00	3.00	4.00
Complexity	0%	0%	0%	0%	0%	0%	0%
Errors	64%	67%	100%	40%	68%	75%	57%
C.U.s	4.00	2.00	1.00	2.00	2.25	2.00	3.00
Paraphasias	18%	0%	100%	0%	30%	25%	0%
Repetitions	36%	33%	0%	20%	22%	0%	14%
Communication Efficiency	1.76	2.17	1.49	2.17	1.90	3.45	1.64

4.3.8 *RehaCom WM*

The results of the *RehaCom WM* screening show a positive linear trend on all the tasks assessed. **Table 4.3.8** shows the raw scores results for participant S.H. A graphic representation of the WM screening task results can be seen in **Figure 4.3.8**.
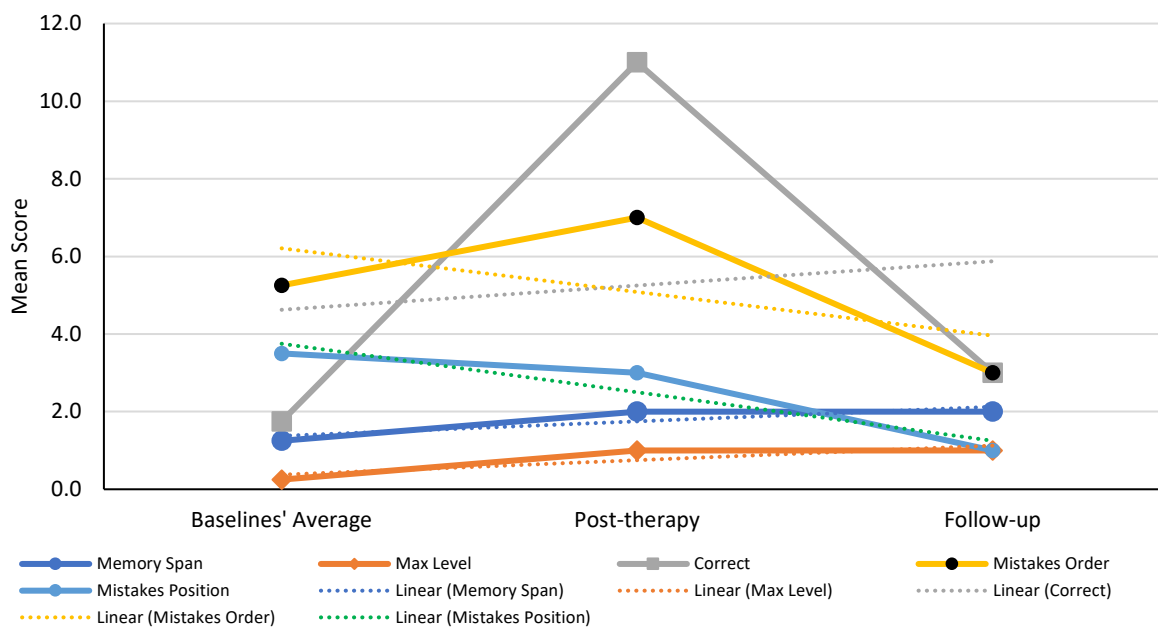
Figure 4.3.8: Schematic representation of the *RehaCom WM Screening* test results by study phase.

Table 4.3.8: *RehaCom WM Screening* raw scores for S.H. by subcategory and period of assessment

	Baseline 1	Baseline 2	Baseline 3	Baseline 4	Baseline Average	Post-therapy	Follow-up
Memory Span	2	1	1	1	1.25	2	2
Max Level	1	0	0	0	0.25	1	1
Correct	3	0	4	0	1.75	11	3
Mistakes Order	6	6	7	2	5.25	7	3
Mistakes Position	2	5	6	1	3.5	3	1

4.3.9 *SAQOL-39*

With regards to investigating whether the overall QoL would improve after treatment, the self-rated SAQOL-39 was analysed by comparing the mean scores (**Figure 4.3.9.; Table 4.3.9.**). The participant's responses indicated that the overall QoL improved between the baseline average (M = 2.57) and post-therapy (M = 3.67) by 22%, and it was maintained at follow-up (M = 3.46).
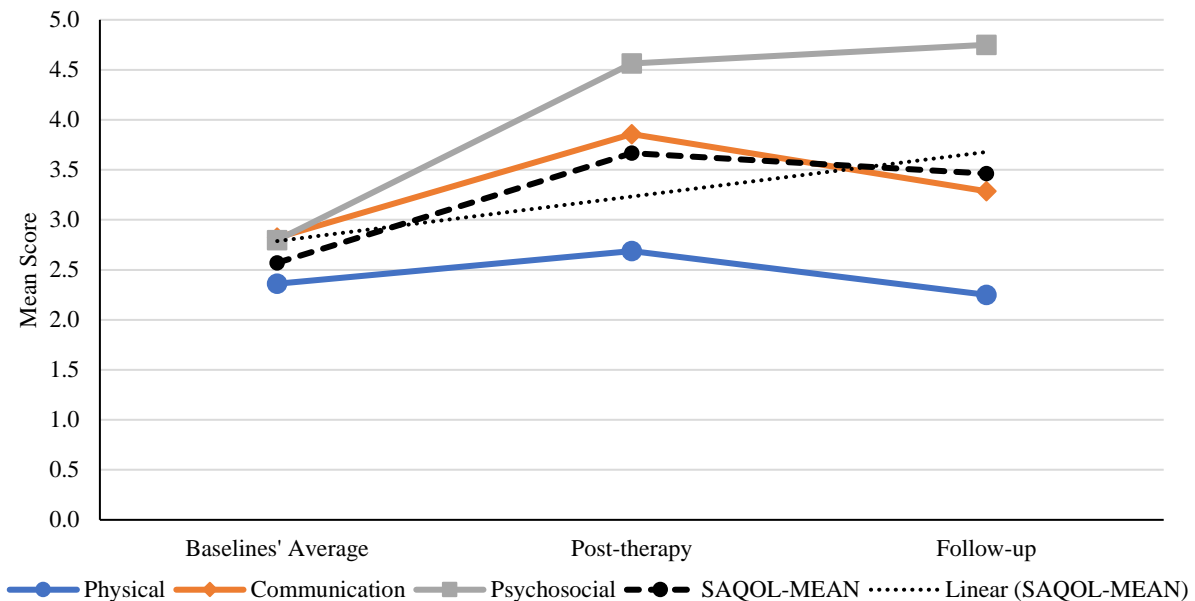
Figure 4.3.9: Schematic representation of the *SAQOL-39g* mean raw scores at baseline, post-therapy and follow-up (Participant S.H.).

The mean scores for the overall SAQOL-39 and for each subcategory are shown in **Table 4.3.9.** The Physical self-rated score improved from the baseline average (M = 2.36) to post-therapy (M = 2.69) by 7%. The Communication self-rated score improved from the baseline average (M = 2.82) to post-therapy (M = 3.86) by 21%, and it was maintained at follow-up (M = 3.29). The Psychosocial self-rated score improved between the baseline average (M = 2.80) and post-therapy (M = 4.56) by 35% and was maintained at follow-up (M = 4.75).

Table 4.3.9: Mean raw scores on *the SAQOL-39g* at baseline, post-therapy and follow-up (Participant S.H.).

	Baseline 1	Baseline 2	Baseline 3	Baseline 4	Baseline average	Post-therapy	Follow-up
Physical	2.31	1.88	2.63	2.63	2.36	2.69	2.25
Communication	2.57	3.29	3.00	2.43	2.82	3.86	3.29
Psychosocial	3.13	3.75	3.06	1.25	2.80	4.56	4.75
Overall SAQOL-39	2.62	2.82	2.79	2.05	2.57	3.67	3.46

4.4 Participant #4 – C.G.

4.4.1 BDAE Auditory Comprehension

Statistical analysis of the *BDAE Auditory Comprehension* subtest (**Table 4.4.1**) showed that the overall trend for improvement in *Word Comprehension* was significant, $t(15) = 0.88$, $p=.015$, and the improvement in the treated period was significantly lower than the untreated periods, $t(15) = -2.33$, $p=.017$. A significant overall trend for improvement was noted in *Commands*, $t(9) = 3.21$, $p= .005$, with a significant difference between the treated and untreated periods, $t(9) = 2.77$, $p=.011$. On the other hand, there was non-significant overall trend for improvement in *Complex Ideational Material*, $t(5) = 1.46$, $p=.102$, and non-significant difference between the treated and untreated periods, $t(5) = -1.54$, p=.093. Overall, there was a significant overall trend for improvement in the Auditory Comprehension subtest, $t(2) = 3.60$, $p= .035$, but the difference was non-significant between the treated and untreated periods, $t(2) =0.08$, $p=.473$ **(Figure 4.4.1)**.
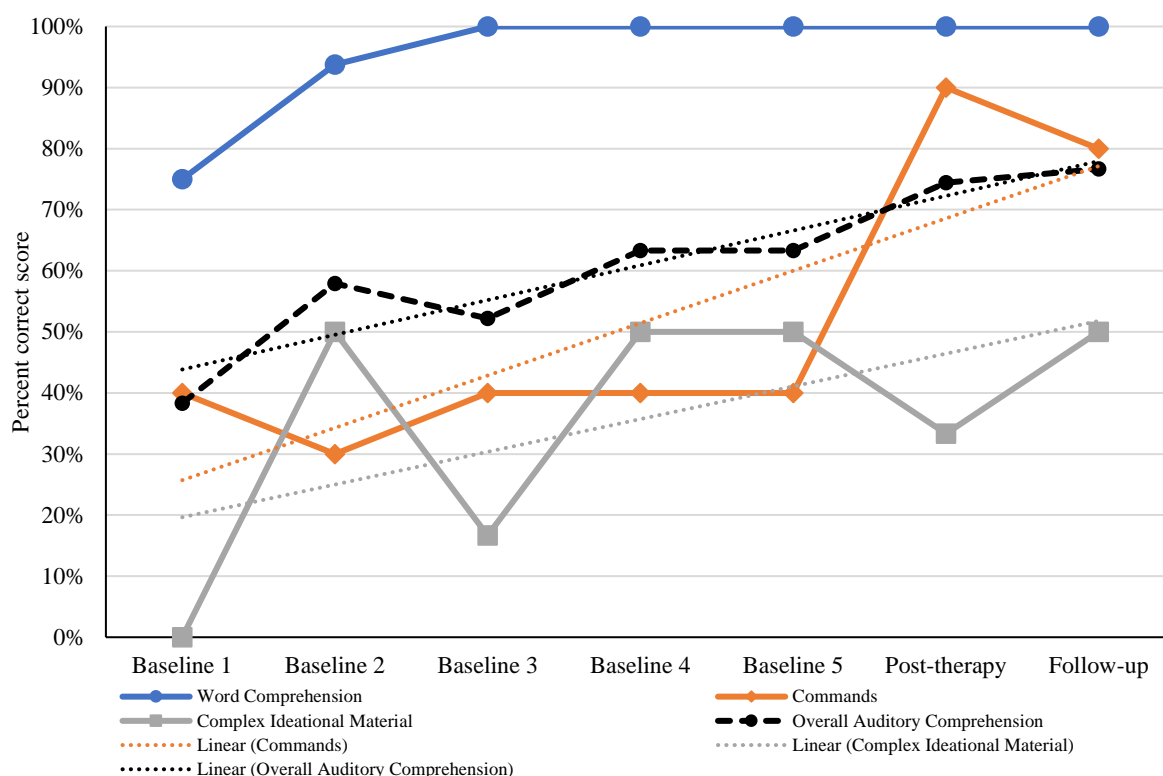
Figure 4.4.1: Percentage (%) correct on the *BDAE Auditory Comprehension* subtests and the overall *BDAE Auditory Comprehension* by phase (Participant C.G.).

Table 4.4.1: WEST-Trend (sum of scores multiplied by -3, −2, −1, 0, 1, 2, 3) and WEST-ROC (sum of scores multiplied by 7, 2, -3, −8, -13, 10, 5) for the *BDAE Auditory Comprehension* (Participant C.G.).

		Baseline 1	Baseline 2	Baseline 3	Baseline 4	Baseline 5	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Word Comprehension	Mean	0.75	0.94	1.00	1.00	1.00	1.00	1.00	0.88	-1.88
	S.D.	0.45	0.17	0.00	0.00	0.00	0.00	0.00	1.45	3.22
									t(15)= 2.41, p= 0.015	t(15)= -2.33, p= 0.017
Commands	Mean	0.40	0.30	0.40	0.40	0.40	0.90	0.80	2.40	6.80
	S.D.	0.52	0.48	0.52	0.52	0.52	0.32	0.42	2.37	7.76
									t(9)= 3.21, p= 0.005	t(9)= 2.77, p= 0.011
Complex Ideational Material	Mean	0.00	0.50	0.17	0.50	0.50	0.33	0.50	1.50	-4.17
	S.D.	0.00	0.55	0.41	0.55	0.55	0.52	0.55	2.51	6.65
									t(5)= 1.46, p= 0.102	t(5)= -1.54, p= 0.093
Overall BDAE Auditory Comprehension	Mean	0.38	0.58	0.52	0.63	0.63	0.74	0.77	1.59	0.25
	S.D.	0.38	0.33	0.43	0.32	0.32	0.36	0.25	0.77	5.78
									t(2)= 3.6, p= 0.035	t(2)= 0.08, p= 0.473

4.4.2 *BDAE Oral Expression*

Statistical analysis of the *BDAE Oral Expression* subtest showed that the overall trend for improvement in *Responsive Naming* was found to be significant, $t(4) = 3.32, p=.015$, with non-significant difference between the treated and untreated periods, $t(4) = 0.90, p=.209$. Similarly, the overall trend for improvement in *Boston Naming* was significant, $t(14) =4.28, p< .001$, and non-significant between the treated and untreated periods, $t(14) = 1.16, p=.133$. *Screening of Special Categories* was also found to be significant in the overall trend for improvement in $t(11) = 3.39, p=.003$, but improvement was not significant between the treated and untreated periods, $t(11)=1.40, p= .094$. On the other hand, the overall trend for improvement in *Automatized Sequences* was not significant, $t(1) = 1.00, p=.250$, and the difference between the treated and untreated periods was non-significant, $t(4) = -1.00, p=.250$. Also, the overall trend improvement in *Word Repetition* was not significant, $t(4) = 1.03, p=.180$, with non-significant difference between the treated and untreated periods, $t(4) = -1.03, p=.180$. Similarly, there was non-significant overall trend for improvement in *Sentence Repetition*, $t(1) = 1.00, p= .250$, and non-significant difference between the treated and untreated periods, $t(1) = 1.00, p= .250$. Overall, there was significant overall trend for improvement in the BDAE Oral Expression subtest, $t(5) =7.39, p < .001$, but with non-significant difference between the treated and untreated periods, $t(5) =1.02, p=.177$.
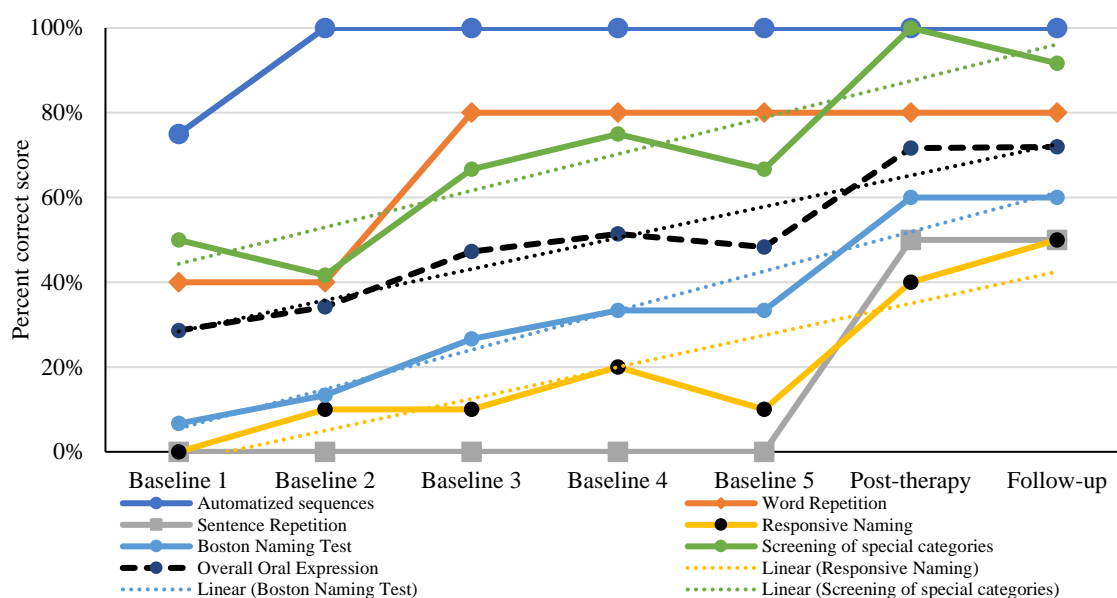
Figure 4.4.2: Percentage (%) correct on the *BDAE Oral Expression* subtests and the overall *BDAE Oral Expression* by stage (Participant C.G.).

Table 4.4.2: WEST-Trend (sum of scores multiplied by -3, −2, −1, 0, 1, 2, 3) and WEST-ROC (sum of scores multiplied by 7, 2, -3, −8, -13, 10, 5) for the *BDAE Oral Expression* (Participant C.G.).

		Baseline 1	Baseline 2	Baseline 3	Baseline 4	Baseline 5	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Automatized sequences	Mean	0.75	1.00	1.00	1.00	1.00	1.00	1.00	1.50	-3.50
	S.D.	0.35	0.00	0.00	0.00	0.00	0.00	0.00	2.12	4.95
									t(1)= 1.00, p= 0.250	t(1)= -1.00, p= 0.250
Word Repetition	Mean	0.40	0.40	0.80	0.80	0.80	0.80	0.80	2.00	-3.60
	S.D.	0.55	0.55	0.45	0.45	0.45	0.45	0.45	2.74	4.93
									t(4)= 1.03, p= 0.180	t(4)= -1.03, p= 0.180
Sentence Repetition	Mean	0.00	0.00	0.00	0.00	0.00	0.50	0.50	2.50	7.50
	S.D.	0.00	0.00	0.00	0.00	0.00	0.71	0.71	3.54	10.61
									t(1)= 1.00, p= 0.250	t(1)= 1.00, p= 0.250
Responsive Naming	Mean	0.00	0.10	0.10	0.20	0.10	0.40	0.50	4.20	7.00
	S.D.	0.00	0.22	0.22	0.45	0.22	0.55	0.00	1.79	10.95
									t(4)= 3.32, p= 0.015	t(4)= 0.90, p= 0.209
Boston Naming Test	Mean	0.07	0.13	0.27	0.33	0.33	0.60	0.60	2.60	1.93
	S.D.	0.26	0.35	0.46	0.49	0.49	0.51	0.51	2.35	6.47
									t(14)= 4.28, p< 0.001	t(14)= 1.16, p= 0.133
Screening of special categories	Mean	0.50	0.42	0.67	0.75	0.67	1.00	0.92	2.42	2.25
	S.D.	0.52	0.51	0.49	0.45	0.49	0.00	0.29	2.47	5.56
									t(11)= 3.39, p= 0.003	t(11)= 1.40, p= 0.094
Overall BDAE Oral Expression	Mean	0.29	0.34	0.47	0.51	0.48	0.72	0.72	2.06	1.64
	S.D.	0.31	0.36	0.41	0.39	0.40	0.26	0.22	0.68	3.93
									t(5)= 7.39, p< 0.001	t(5)= 1.02, p= 0.177

4.4.3 *BDAE Reading*

Statistical analysis of the *BDAE Reading* subtest (**Table 4.4.3)** showed that the overall trend for improvement in *Word Identification* was significant, $t(3)= 2.89$, p= .0326, and the improvement in the treated period was significantly lower that the untreated periods, $t(3)= -2.71$, p= .036. The overall trend for improvement in the *Oral Basic Word* task was not significant, $t(4) = 1.03$, p= .180, and the difference between the treated and untreated periods was non-significant, $t(4) = -1.03$, $p=.180$. Similarly, overall improvement in the *Oral Basic Sentence* task was not significant, $t(4) = 0.93$, p= .203, with non-significant difference between the treated and untreated periods, $t(4) = -1.17$, $p=.154$. Additionally, there was a non-significant overall trend for improvement in the *Oral Sentence Comprehension*, $t(2) = 1.00$, p= .211, and non-significant between the treated and untreated periods, $t(2) = -1.00$, p= .211. Lastly, there was a non-significant overall trend for improvement in the *Silent Comprehension*, $t(3) = 1.00$, p= .196, with a non-significant difference between the treated and untreated periods, $t(3) = 1.00$, p= .196. There was no difference in the responses between the seven periods for the *Matching case/script* and *Number Matching* tasks. Concluding, there was a significant overall trend for improvement in *the BDAE Reading subtest*, $t(6) = 3.19$, $p= .009$, and improvement was found to be significantly better in the untreated period, $t(6) = -3.19$, $p=.009$ (**Figure 4.4.3)**.
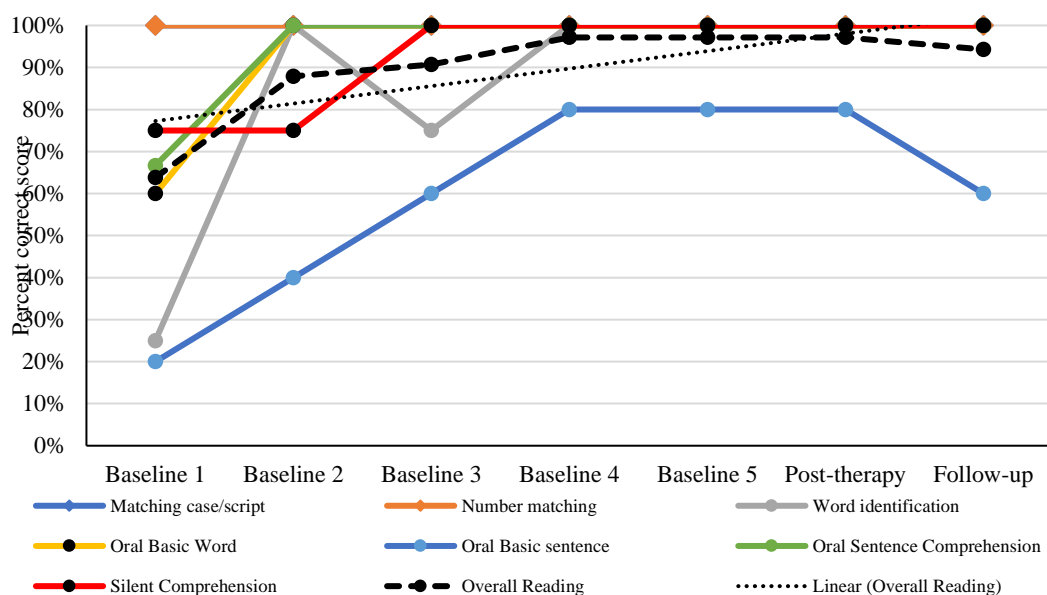
Figure 4.4.3: Percentage (%) correct on the *BDAE Reading* subtests and the overall *BDAE Reading* (Participant C.G.).

Table 4.4.3: WEST-Trend (sum of scores multiplied by -3, −2, −1, 0, 1, 2, 3) and WEST-ROC (sum of scores multiplied by 7, 2, -3, −8, -13, 10, 5) for the *BDAE Reading* (Participant C.G.).

		Baseline 1	Baseline 2	Baseline 3	Baseline 4	Baseline 5	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Matching Case/Script	Mean	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Number Matching	Mean	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Word Identification	Mean	0.25	1.00	0.75	1.00	1.00	1.00	1.00	2.50	-4.50
	S.D.	0.50	0.00	0.50	0.00	0.00	0.00	0.00	1.73	3.32
									t(3)= 2.89, p= 0.032	t(3)= -2.71, p= 0.036
Oral Basic Word	Mean	0.60	1.00	1.00	1.00	1.00	1.00	1.00	3.60	-8.40
	S.D.	0.55	0.00	0.00	0.00	0.00	0.00	0.00	4.93	11.50
									t(4)= 1.03, p= 0.180	t(4)= -1.03, p= 0.180
Oral Basic Sentence	Mean	0.20	0.40	0.60	0.80	0.80	0.80	0.60	2.20	-5.40
	S.D.	0.45	0.55	0.55	0.45	0.45	0.45	0.55	3.35	6.54
									t(4)= 0.93, p= 0.203	t(4)= -1.17, p= 0.154
Oral Sentence Comprehension	Mean	0.67	1.00	1.00	1.00	1.00	1.00	1.00	1.00	-2.33
	S.D.	0.58	0.00	0.00	0.00	0.00	0.00	0.00	1.73	4.04
									t(2)= 1.00, p= 0.211	t(2)= -1.00, p= 0.211
Silent Comprehension	Mean	0.75	0.75	1.00	1.00	1.00	1.00	1.00	1.25	-2.25
	S.D.	0.50	0.50	0.00	0.00	0.00	0.00	0.00	2.50	4.50
									t(3)= 1.00, p= 0.196	t(3)= -1.00, p= 0.196
Overall BDAE Reading	Mean	0.64	0.88	0.91	0.97	0.97	0.97	0.94	1.16	-2.47
	S.D.	0.32	0.23	0.16	0.08	0.08	0.08	0.15	0.97	2.04
									t(6)= 3.19, p= 0.009	t(6)= -3.19, p= 0.009

4.4.4 *RCPM*

Statistical analysis (**Table 4.4.4**) revealed that there was a non-significant overall trend for improvement in *Subtest A*, $t(11)= 1.00$, $p= .169$, and a non-significant difference between the treated and untreated periods, $t(11)= -1.00$, $p= .169$. There were no differences of the responses between the seven periods, regarding the *Subtest AB* and *Subtest B*. Concluding, there was a non-significant overall trend for improvement in the *RCPM*, $t(35) = 1.00$, $p=.162$, and also a non-significant difference between the treated and untreated periods, $t(35) = -1.00$, $p= .162$. (**Figure 4.4.4**).
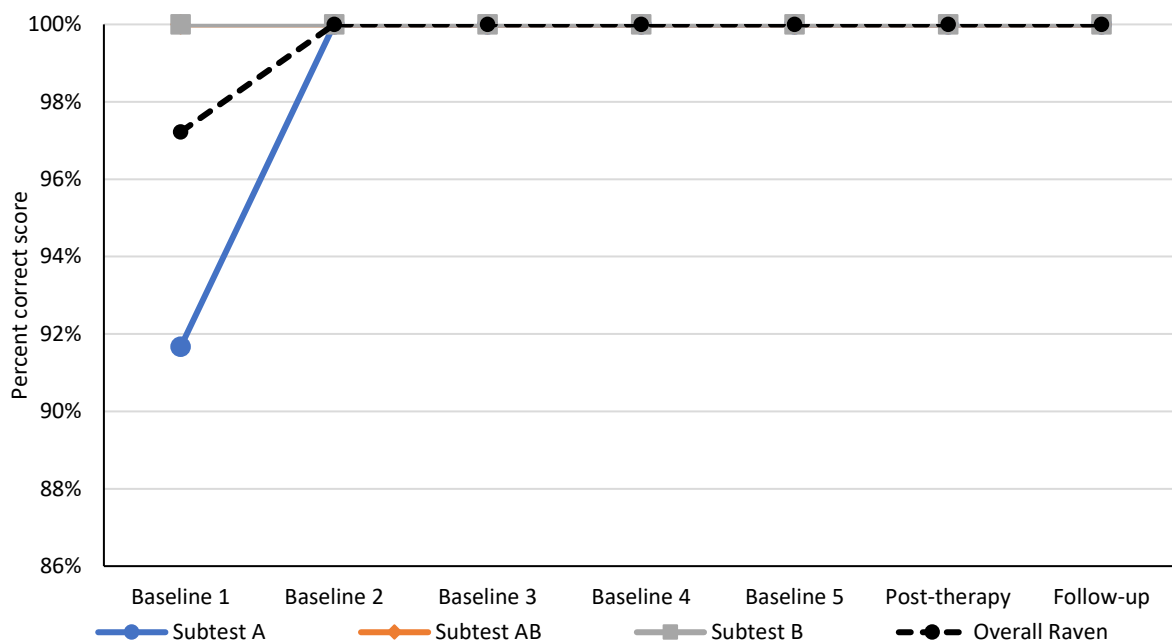
Figure 4.4.4: Percentage (%) correct on the *RCPM* subtests and the overall *RCPM* (Participant C.G.).

Table 4.4.4: WEST-Trend (sum of scores multiplied by -3, −2, −1, 0, 1, 2, 3) and WEST-ROC (sum of scores multiplied by 7, 2, -3, −8, -13, 10, 5) for the *RCPM* (Participant C.G.).

		Baseline 1	Baseline 2	Baseline 3	Baseline 4	Baseline 5	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
	Mean	0.92	1.00	1.00	1.00	1.00	1.00	1.00	0.25	-0.58
Subtest A	S.D.	0.29	0.00	0.00	0.00	0.00	0.00	0.00	0.87	2.02
									$t(11)= 1.00, p= 0.169$	$t(11)= -1.00, p= 0.169$
	Mean	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.00	0.00
Subtest AB	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Mean	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.00	0.00
Subtest B	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Mean	0.97	1.00	1.00	1.00	1.00	1.00	1.00	0.083	-0.194
Overall RCPM	S.D.	0.17	0.00	0.00	0.00	0.00	0.00	0.00	0.50	1.17
									$t(35)= 1.00, p= 0.162$	$t(35)= -1.00, p= 0.162$

4.4.5 *MAIN*

Statistical analysis revealed there was a significant overall trend for improvement in the *MAIN*, $t(16)= 2.84$, $p= .006$, but a non-significant difference between the treated and untreated periods, $t(16)= 1.55$, $p= .070$ **(Figure 4.4.5.; Table 4.4.5.).**
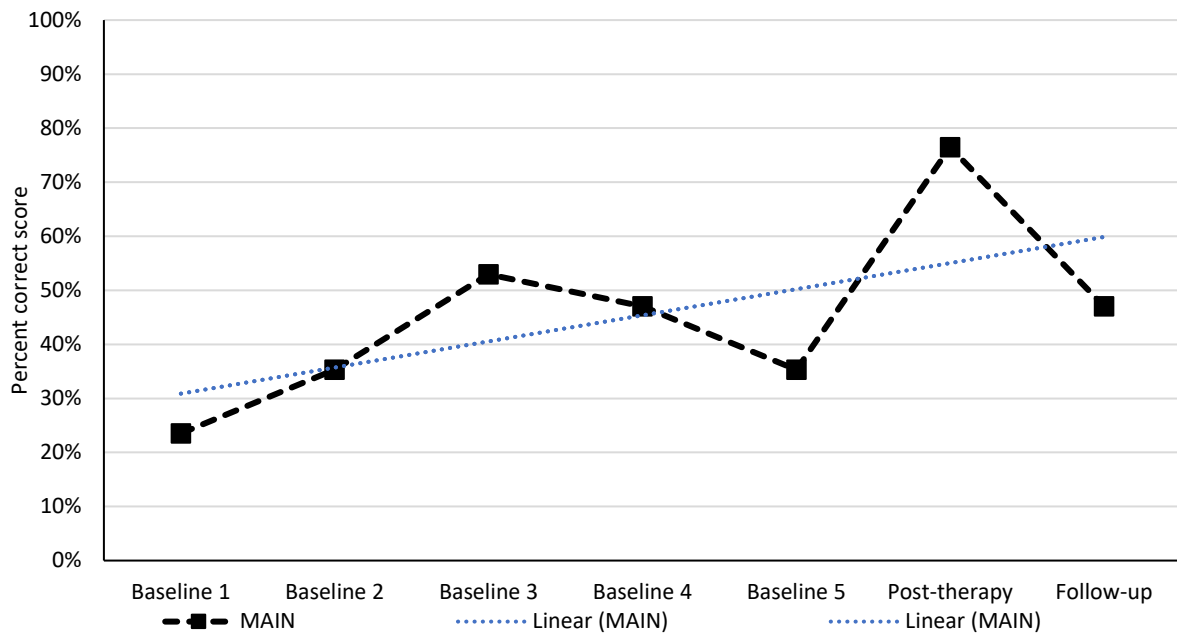
Figure 4.4.5: Percentage (%) correct on the *MAIN* across study phase (Participant C.G.).

Table 4.4.5: WEST-Trend (sum of scores multiplied by -3, −2, −1, 0, 1, 2, 3) and WEST-ROC (sum of scores multiplied by 7, 2, -3, −8, -13, 10, 5) for the *MAIN* (Participant C.G.).

		Baseline 1	Baseline 2	Baseline 3	Baseline 4	Baseline 5	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
	Mean	0.24	0.35	0.53	0.47	0.35	0.76	0.47	1.35	2.41
MAIN	S.D.	0.44	0.49	0.51	0.51	0.49	0.44	0.51	1.97	6.41
									t(16)= 2.84, p= 0.006	t(16)= 1.55, p= 0.070

4.4.6 *Procedural Discourse*

There was a non-significant overall trend for improvement in *Procedural Discourse*, $t(9)=$ 1.50, $p=.084$, and a non-significant difference between the treated and untreated periods, $t(9)=0.77$, $p= .232$.
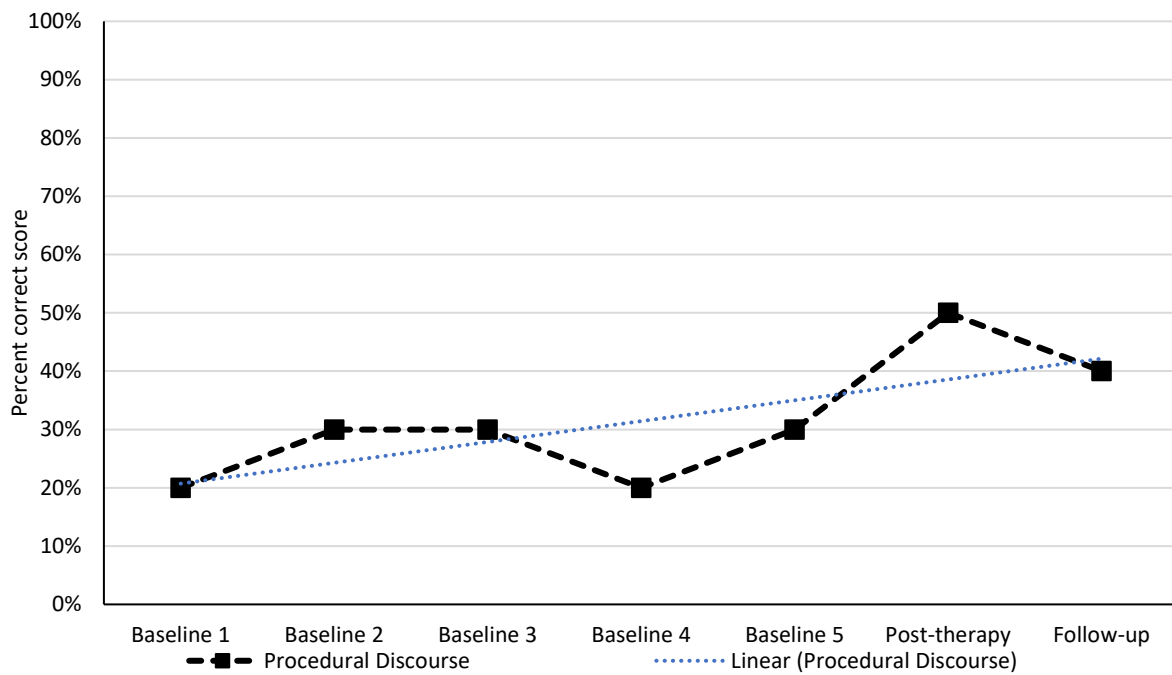
Figure 4.4.6: Percentage (%) correct on the *Procedural Discourse* task by phase (Participant C.G.).

Table 4.4.6: WEST-Trend (sum of scores multiplied by -3, −2, −1, 0, 1, 2, 3) and WEST-ROC (sum of scores multiplied by 7, 2, -3, −8, -13, 10, 5) for the Procedural Discourse (Participant C.G.).

		Baseline 1	Baseline 2	Baseline 3	Baseline 4	Baseline 5	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
	Mean	0.20	0.30	0.30	0.20	0.30	0.50	0.40	1.00	2.60
Procedural Discourse	S.D.	0.42	0.48	0.48	0.42	0.48	0.53	0.52	2.11	10.74
									$t(9)= 1.50, p= 0.084$	$t(9)= 0.77, p= 0.232$

4.4.7 *SSLA*

C.G..'s stroke narrative (spontaneous language sample) was analysed using the SSLA protocol (Shewan, 1988) designed to describe and quantify connected speech (**Table 4.4.7**). The language sample collected at each time point, was not sufficient in word length to undergo statistical analysis hence results were compared in raw scores. In this case the Baseline average (avg) was compared with the post-testing and follow-up results. There was an increase in the rate of speech from 163.30 syllables per minute to 203.20 at post-therapy but dropped to 124.04 at follow-up. The sentence length, which reflects the use of more than 5 words in the produced utterances, improved from 54% at baseline avg to 42% at post-therapy and was maintained at 47% at follow-up. Improvement was noted in sentence complexity between baseline avg and follow-up (from 18% to 26%). A small improvement was noted between baseline avg and follow-up in the production of errors (from 48% to 42%). The number of content units improved from 18.40 at baseline avg, to 23.00 at post-therapy, and was maintained at 24.00 at follow-up. Improvement in the number of repetitions was noted with a reduction from 76% to 68% between baseline avg and follow-up. A notable improvement in communication efficiency which reflects the rate at which information is conveyed by the speaker (number of content units divided by time), from 11.57 at baseline avg, to 18.40 post-therapy, but reverted to 13.11 at follow-up. Overall, based on the numerical values collected, there was no increase in the number of utterances after therapy and the overall melody and articulation were judged to be normal (see **Table 4.4.7**).
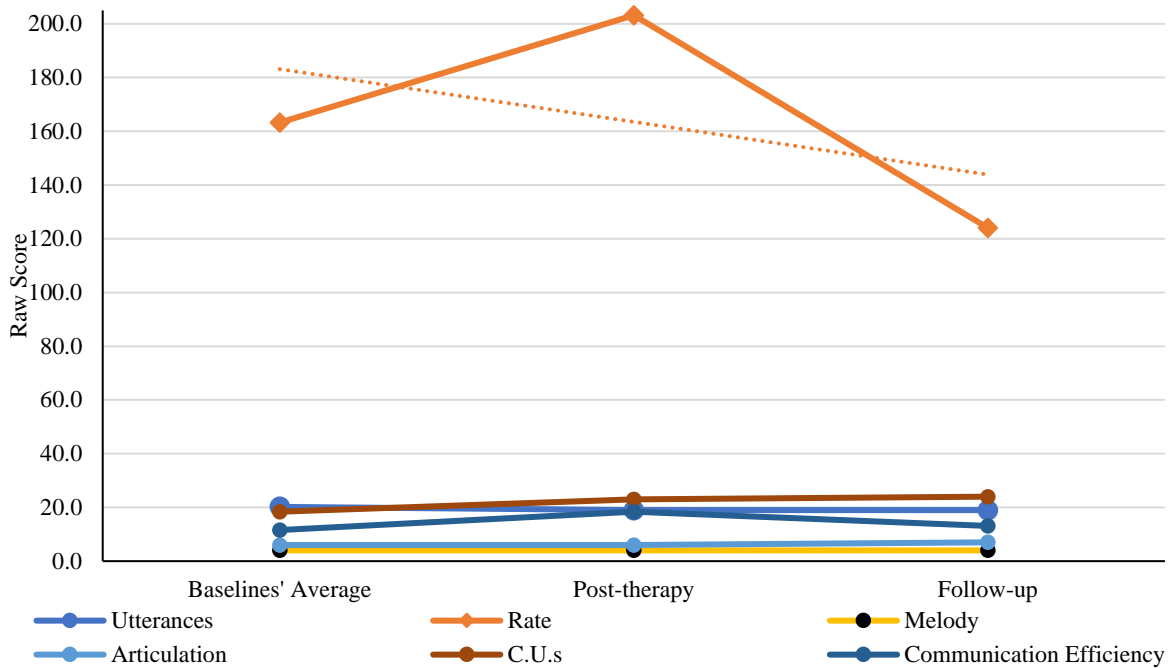
Figure 4.4.7 a. Results of C.G.'s personal stroke narrative analysis based on the *SSLA* showing the raw scores for baseline average, post-therapy, and follow-up phases.
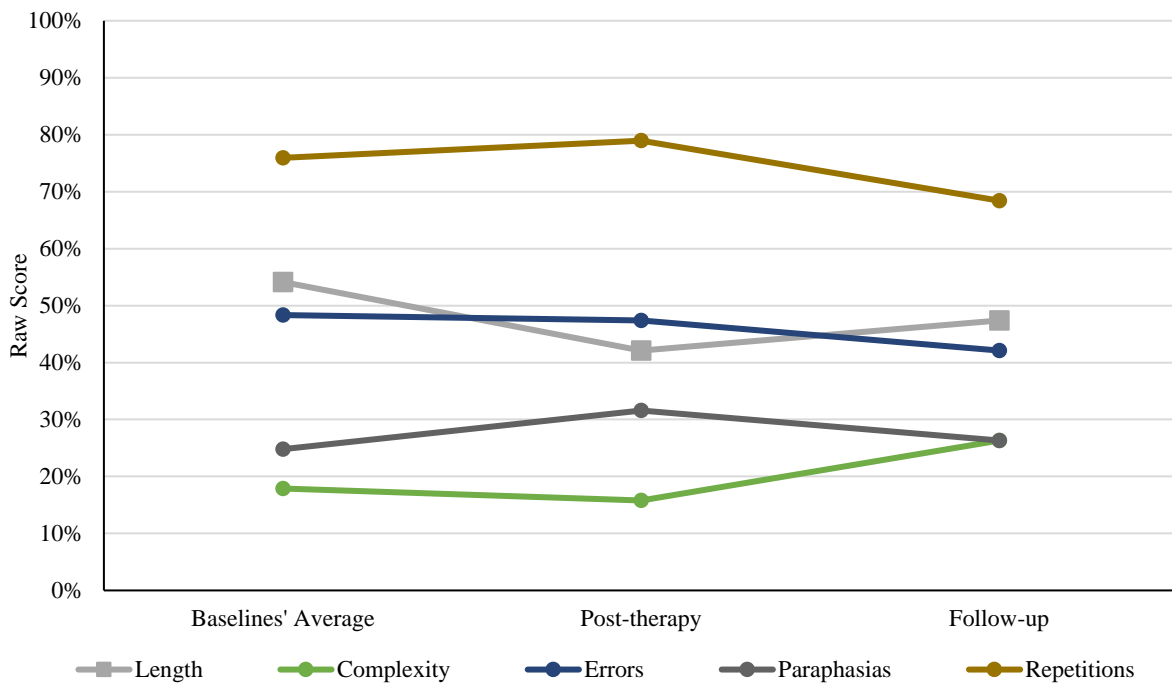
Figure 4.4.7.b. Results of C.G.'s personal stroke narrative analysis based on the *SSLA* showing the raw score percentages (%) for baseline average, post-therapy, and follow-up phases.

Table 4.4.7: Raw scores for C.G.'s personal stroke narrative analysis based on the *SSLA*.

	Baseline 1	Baseline 2	Baseline 3	Baseline 4	Baseline 5	Baseline Average	Post-therapy	Follow-up
Utterances	20.00	22.00	24.00	19.00	16.00	20.20	19.00	19.00
Rate	163.56	168.99	179.31	165.56	139.10	163.30	203.20	124.04
Length	65%	64%	54%	32%	56%	54%	42%	47%
Melody	4.00	4.00	4.00	4.00	4.00	4.00	4.00	4.00
Articulation	6.00	6.00	6.00	6.00	6.00	6.00	6.00	7.00
Complexity	15%	27%	13%	16%	19%	18%	16%	26%
Errors	35%	59%	17%	68%	63%	48%	47%	42%
C.U.s	12.00	19.00	22.00	23.00	16.00	18.40	23.00	24.00
Paraphasias	15%	41%	25%	37%	6%	25%	32%	26%
Repetitions	40%	64%	100%	95%	81%	76%	79%	68%
Communication Efficiency	10.17	12.03	10.84	12.78	12.03	11.57	18.40	13.11

4.4.8 *RehaCom WM*

The results of the *RehaCom WM* screening task show that there was no improvement in the tasks assessed. **Table 4.4.8** shows participant C.G.'s raw scores. A graphic representation of the WM screening results can be seen in **Figure 4.4.8**.
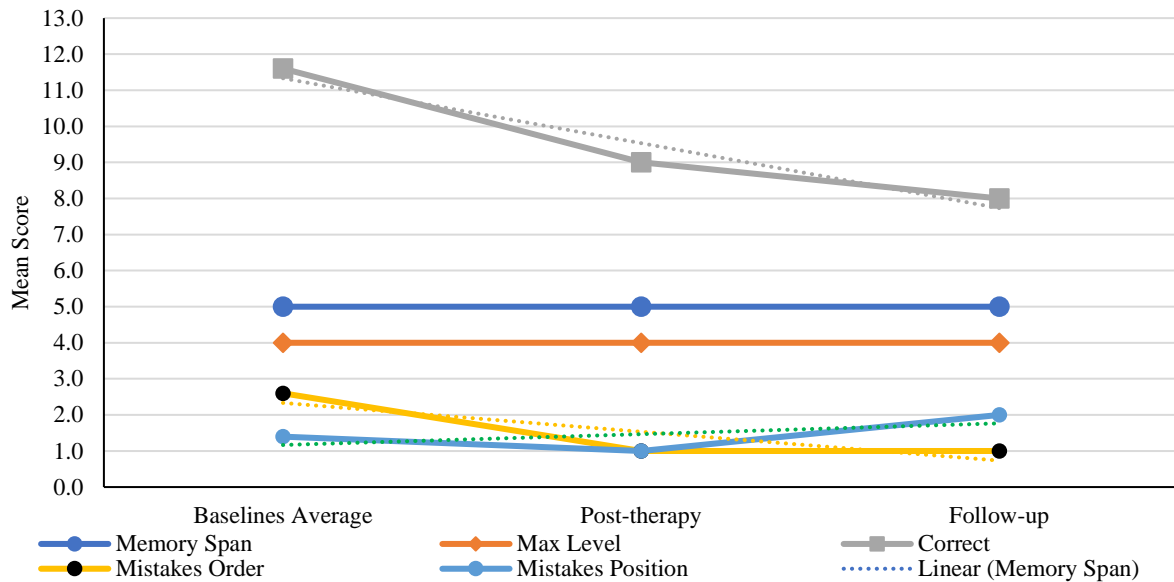
Table 4.4.8: Schematic representation of the *RehaCom WM Screening* test results

Table 4.4.9: *RehaCom WM Screening* raw scores for C.G. by subcategory and period of assessment

	Baseline 1	Baseline 2	Baseline 3	Baseline 4	Baseline 5	Baseline Average	Post-therapy	Follow-up
Memory Span	5	4	5	6	5	5	5	5
Max Level	4	3	4	5	4	4	4	4
Correct	8	7	21	12	10	12	9	8
Mistakes Order	1	1	6	2	3	3	1	1
Mistakes Position	2	1	1	2	1	1	1	2

4.4.9 SAQOL-39

With regards to investigating whether the overall QoL would improve after treatment, the self-rated SAQOL-39 was analysed by comparing the mean scores (**Figure 4.4.9.; Table 4.4.9.**). The participant's responses indicated that QoL improved between the baseline average (M = 4.01) and post-therapy (M = 4.41) by 8% and increased a further 3% at follow-up (M = 4.54).
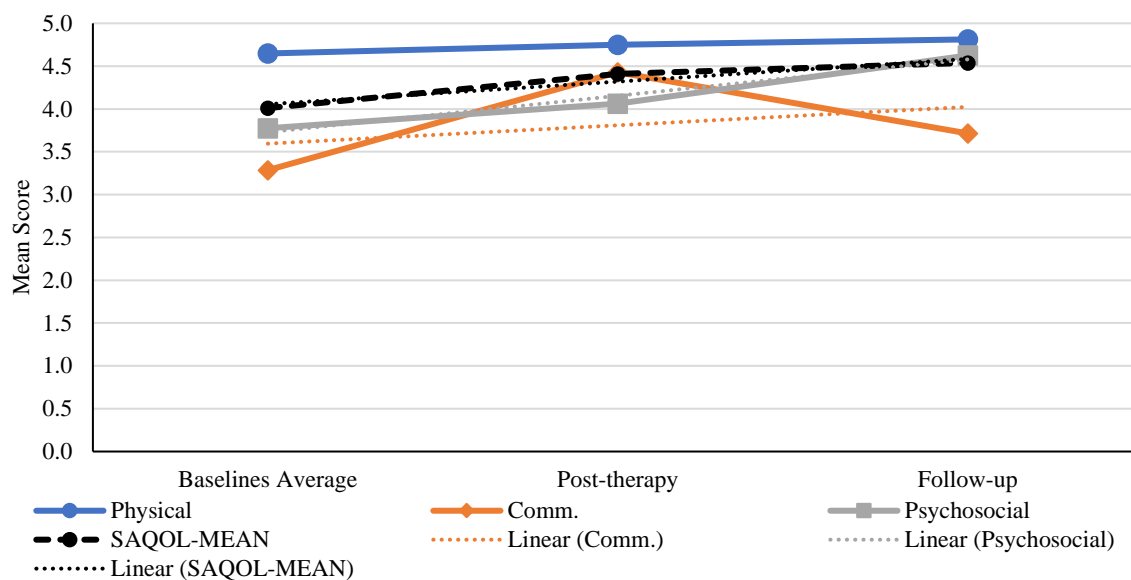
Figure 4.4.8: Schematic representation of the *SAQOL-39g* mean raw scores at baseline, post-therapy and follow-up (Participant C.G.).

The mean scores for the overall SAQOL-39 and for each subcategory are shown in **Table 4.4.9.** A small improvement was noted in the *Physical* self-rated score from the baseline average (M = 4.65) to post-therapy (M = 4.75) by 2%. The *Communication* self-rated score improved from the baseline average (M = 3.71) to post-therapy (M = 4.43) by 23%, but it reverted at follow-up (M = 3.29). The *Psychosocial* self-rated score improved between the baseline average (M = 4.06) and post-therapy (M = 4.63) by 6% and improved a further 11% at follow-up (M = 4.63).

Table 4.4.10: Mean raw scores on the *SAQOL-39g* at baseline, post-therapy and follow-up (Participant C.G.).

	Baseline 1	Baseline 2	Baseline 3	Baseline 4	Baseline 5	Baseline average	Post-therapy	Follow-up
Physical	4.60	4.67	4.60	4.69	4.69	4.65	4.75	4.81
Communication	3.00	3.57	3.57	3.14	3.14	3.29	4.43	3.71
Psychosocial	3.63	4.00	3.75	3.75	3.75	3.78	4.06	4.63
Overall SAQOL-39	3.82	4.16	4.05	4.03	4.00	4.01	4.41	4.54

4.5 Participant #5 – F.C.

4.5.1 *BDAE Auditory Comprehension*

Statistical analysis of the *BDAE Auditory Comprehension* subtest showed that there was a significant overall trend for improvement in *Commands*, $t(9) = 1.96$, $p= .041$, as well as significant difference between the treated and untreated periods, $t(9) = 2.45$, $p=.018$. On the other hand, the overall trend for improvement in *Word Comprehension* was not significant, $t(15) = 1.46$, $p=.082$, and the difference was non-significant between the treated and untreated periods, $t(15) = 1.46$, $p=.082$. Similarly, there was non-significant overall trend for improvement in *Complex Ideational Material* $t(5) = -0,79$, $p=.233$, and non-significant difference between the treated and untreated periods, $t(5) = 1.08$, $p=.164$. Concluding, there was a non-significant overall trend for improvement in the overall BDAE Auditory Comprehension, $t(2) = 0.48$, $p= .338$, but the difference between the treated and untreated periods was significant, $t(2) = 3.09$, $p=.045$.
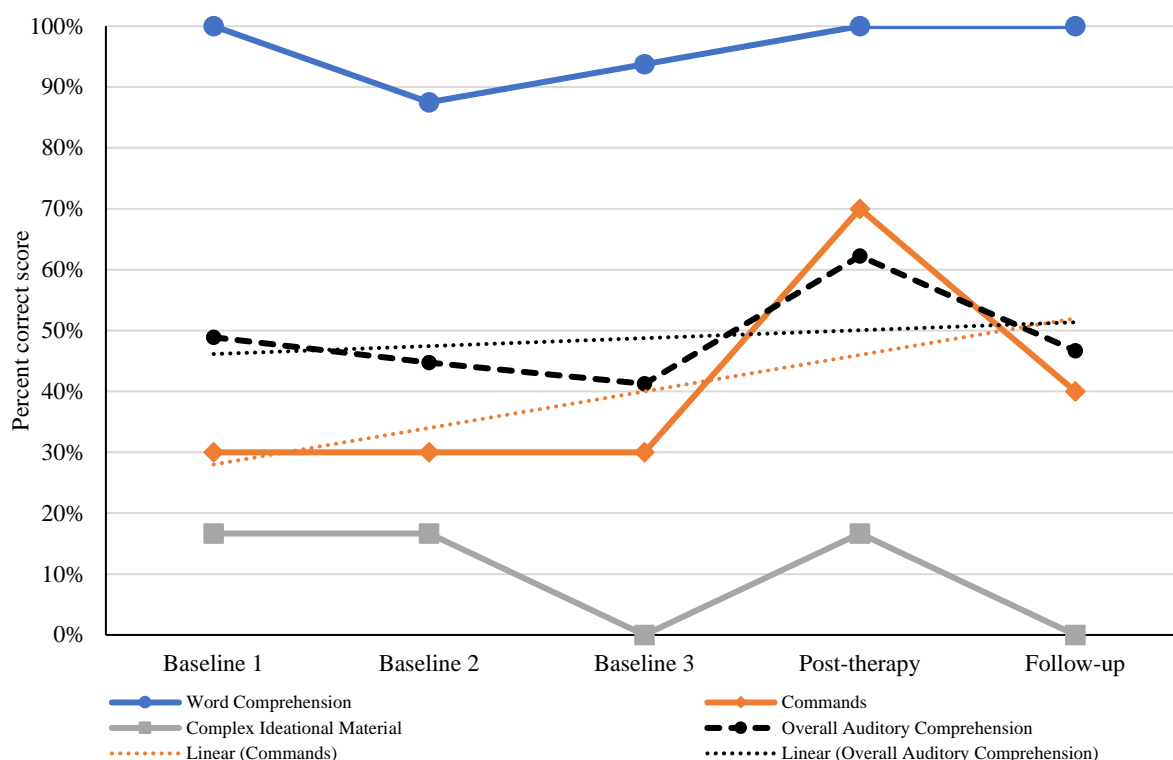
Figure 4.5.1: Percentage (%) correct on the *BDAE Auditory Comprehension* subtests and the overall *BDAE Auditory Comprehension* by phase (Participant F.C.).

Table 4.5.1: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) for the *BDAE Auditory Comprehension* (Participant F.C.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Word Comprehension	Mean	1.00	0.88	0.94	1.00	1.00	0.13	0.38
	S.D.	0.00	0.34	0.25	0.00	0.00	0.34	1.02
							t(15)= 1.46, p= 0.082	t(15)= 1.46, p= 0.082
Commands	Mean	0.30	0.30	0.30	0.70	0.40	0.60	1.20
	S.D.	0.48	0.48	0.48	0.48	0.52	0.97	1.55
							t(9)= 1.96, p= 0.041	t(9)= 2.45, p= 0.018
Complex Ideational Material	Mean	0.17	0.17	0.00	0.17	0.00	-0.33	0.67
	S.D.	0.41	0.41	0.00	0.41	0.00	1.03	1.51
							t(5)= -0.79, p= 0.233	t(5)= 1.08, p= 0.164
Overall BDAE Auditory Comprehension	Mean	0.49	0.45	0.41	0.62	0.47	0.13	0.75
	S.D.	0.45	0.38	0.48	0.42	0.50	0.47	0.42
							t(2)= 0.48, p= 0.338	t(2)= 3.09, p= 0.045

4.5.2 *BDAE Oral Expression*

Statistical analysis of the *BDAE Oral Expression* subtest (**Table 4.5.2**) showed that there was a significant overall trend for improvement in *Screening of Special Categories*, $t(11) = 3.19$, p= .004, but non-significant improvement between the treated and untreated periods, $t(11) = 0.46$, p= .329. The overall trend for improvement in *Word Repetition* was not significant, $t(4) = 0.63$, $p=.281$, with non-significant difference between the treated and untreated periods, $t(4) = -0.63$, $p=.281$. Also, there was non-significant overall trend for improvement in *Responsive Naming*, $t(4) = 0.95$, p= .198, and non-significant difference between the treated and untreated periods, $t(4) = 1.03$, p= .180. Similarly, the overall trend for improvement in *Boston Naming* was not significant, $t(14) =0.54$, p= .298, and non-significant between the treated and untreated periods, $t(14) = 0.59$, $p=.283$. For the tasks of *Automated Sequences* and *Sentence Repetition* there were no differences of the responses between the five periods. Concluding, there was a significant overall trend for improvement in the overall *BDAE Oral Expression*, $t(5) = 2.17$, $p = .041$, but with a non-significant difference between the treated and untreated periods, $t(5) = 0.98$, $p=.185$ **(Figure 4.5.2).**
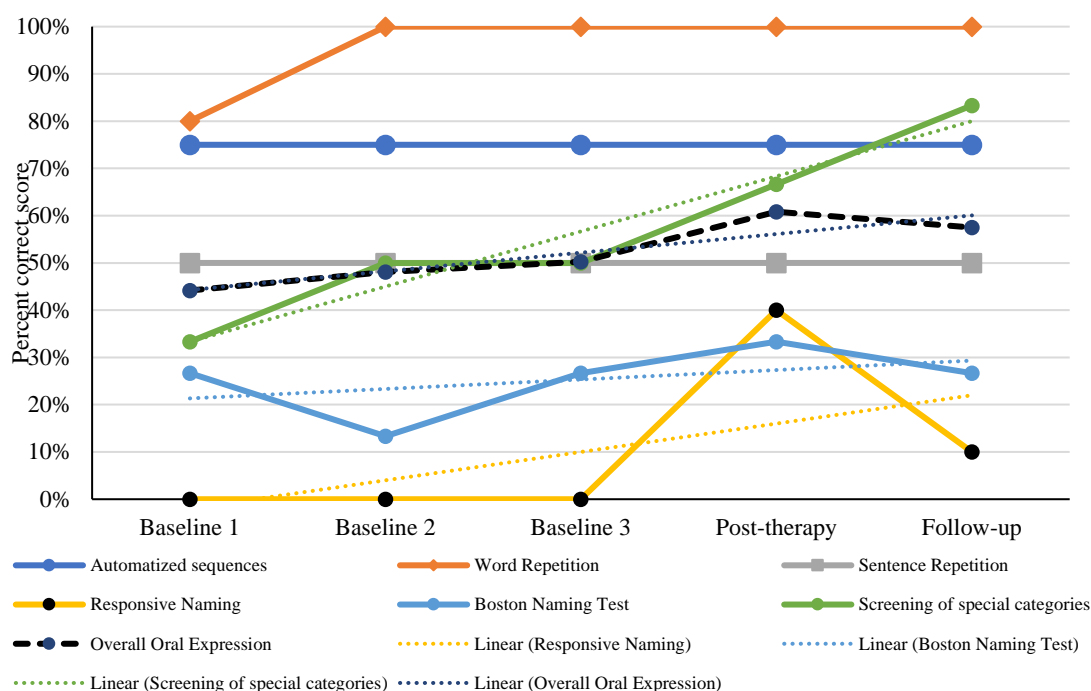
Figure 4.5.2: Percentage (%) correct on the *BDAE Oral Expression* subtests and the overall *BDAE Oral Expression* by phase (Participant F.C.).

Table 4.5.2: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) for the *BDAE Oral Expression* (Participant F.C.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Automatized Sequences	Mean	0.75	0.75	0.75	0.75	0.75	0.00	0.00
	S.D.	0.35	0.35	0.35	0.35	0.35	0.00	0.00
Word Repetition	Mean	0.80	1.00	1.00	1.00	1.00	0.40	-0.40
	S.D.	0.45	0.00	0.00	0.00	0.00	0.89	0.89
							$t(4)= 0.63, p= 0.281$	$t(4)= -0.63, p= 0.281$
Sentence Repetition	Mean	0.50	0.50	0.50	0.50	0.50	0.00	0.00
	S.D.	0.71	0.71	0.71	0.71	0.71	0.00	0.00
Responsive Naming	Mean	0.00	0.00	0.00	0.40	0.10	1.20	2.40
	S.D.	0.00	0.00	0.00	0.55	0.22	1.79	3.29
							$t(4)= 0.95, p= 0.198$	$t(4)= 1.03, p= 0.180$
Boston Naming Test	Mean	0.27	0.13	0.27	0.33	0.27	0.20	0.33
	S.D.	0.46	0.35	0.46	0.49	0.46	1.42	2.19
							$t(14)= 0.54, p= 0.298$	$t(14)= 0.59, p= 0.283$
Screening of Special Categories	Mean	0.33	0.50	0.50	0.67	0.83	1.17	0.17
	S.D.	0.49	0.52	0.52	0.49	0.39	1.27	1.27
							$t(11)= 3.19, p= 0.004$	$t(11)= 0.46, p= 0.329$
Overall BDAE Oral Expression	Mean	0.44	0.48	0.50	0.61	0.58	0.39	0.22
	S.D.	0.30	0.37	0.35	0.25	0.35	0.44	0.54
							$t(5)= 2.17, p= 0.041$	$t(5)= 0.98, p= 0.185$

4.5.3 *BDAE Reading*

Statistical analysis of the *BDAE Reading* subtest (**Table 4.5.3)** showed that the overall trend for improvement in *Word identification* was not significant, $t(3)= 0.19$, p= .431, and the difference between the treated and untreated periods was non-significant, $t(3)= 1.00$, p= .196. Similarly, the overall trend for improvement in *Oral Basic Sentence* was not significant, $t(4) = 0.37$, p= .364, and non-significant between the treated and untreated periods, $t(4) = 0.61$, $p=.287$. Additionally, there was a non-significant overall trend for improvement in *Oral Sentence Comprehension*, $t(2) = 0.00$, p= .500, with a non-significant difference between the treated and untreated periods, $t(2) = 0.72$, p= .274. Lastly, there was a non-significant overall trend for improvement in *Silent Comprehension*, $t(3) = -0.79$, p= .243, with a non-significant difference between the treated and untreated periods, $t(3) = -0.68$, p= .274. For the tasks of *Matching case/script, Number Matching* and *Oral Basic Sentence*, there was no differences in the number of responses between the five periods. In general, there was a non-significant overall trend for improvement in the *BDAE Reading* subtest, $t(6) = -0.10$, $p= .460$, and a non-significant difference between the treated and untreated periods, $t(6) = 1.27$, $p=.126$ (**Figure 4.5.3).**
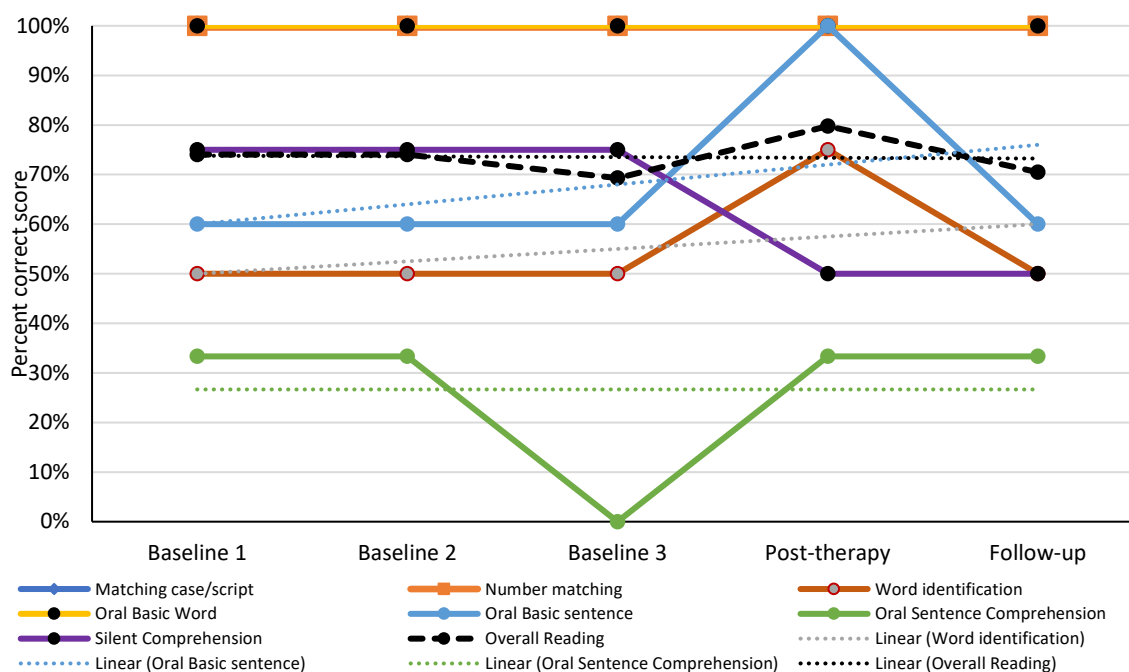
Figure 4.5.3: Percentage (%) correct on the *BDAE Reading* subtests and the overall *BDAE Reading* (Participant F.C.).

Table 4.5.3: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) for the *BDAE Reading* (Participant F.C.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Matching Case/Script	Mean	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Number Matching	Mean	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Word Identification	Mean	0.50	0.50	0.50	0.75	0.50	0.25	0.75
	S.D.	0.58	0.58	0.58	0.50	0.58	2.63	1.50
							$t(3)= 0.19, p= 0.431$	$t(3)= 1.00, p= 0.196$
Oral Basic Word	Mean	1.00	1.00	1.00	1.00	1.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Oral Basic Sentence	Mean	0.60	0.60	0.60	1.00	0.60	0.40	1.20
	S.D.	0.55	0.55	0.55	0.00	0.55	1.52	2.77
							$t(4)= 0.37, p= 0.364$	$t(4)= 0.61, p= 0.287$
Oral Sentence Comprehension	Mean	0.33	0.33	0.00	0.33	0.33	0.00	1.33
	S.D.	0.58	0.58	0.00	0.58	0.58	1.00	3.21
							$t(2)= 0.00, p= 0.500$	$t(2)= 0.72, p= 0.274$
Silent Comprehension	Mean	0.75	0.75	0.75	0.50	0.50	-0.75	-0.75
	S.D.	0.50	0.50	0.50	0.58	0.58	1.89	2.22
							$t(3)= -0.79, p= 0.243$	$t(3)= -0.68, p= 0.274$
Overall BDAE Reading	Mean	0.74	0.74	0.69	0.80	0.70	-0.01	0.36
	S.D.	0.27	0.27	0.37	0.28	0.29	0.36	0.76
							$t(6)= -0.10, p= 0.460$	$t(6)= 1.27, p= 0.126$

4.5.4 *RCPM*

Statistical analysis **(Table 4.5.4.)** revealed that there was a non-significant overall trend for improvement in *Subtest A*, $t(11)= 1.47$, $p= .085$, but a significant improvement between the treated and untreated periods, $t(11)= 2.28$, $p= .022$. On the other hand, overall improvement in *Subtest AB* was statistically significant, $t(11) = 2.03$, $p= .034$, but non-significant between the treated and untreated periods, $t(11) = 1.02$, $p=.164$. Lastly, there was a non-significant overall trend for improvement in *Subtest B*, $t(11)= -1.00$, $p= .169$, and a non-significant difference between the treated and untreated periods, $t(11) = 1.00$, p= .169. In general, there was a significant overall trend for improvement in the *RCPM,* $t(35) = 2.13$, $p=.020$, and also a significant difference between the treated and untreated periods, $t(35) = 2.15$, p= .019 **(Figure 4.5.4.).**
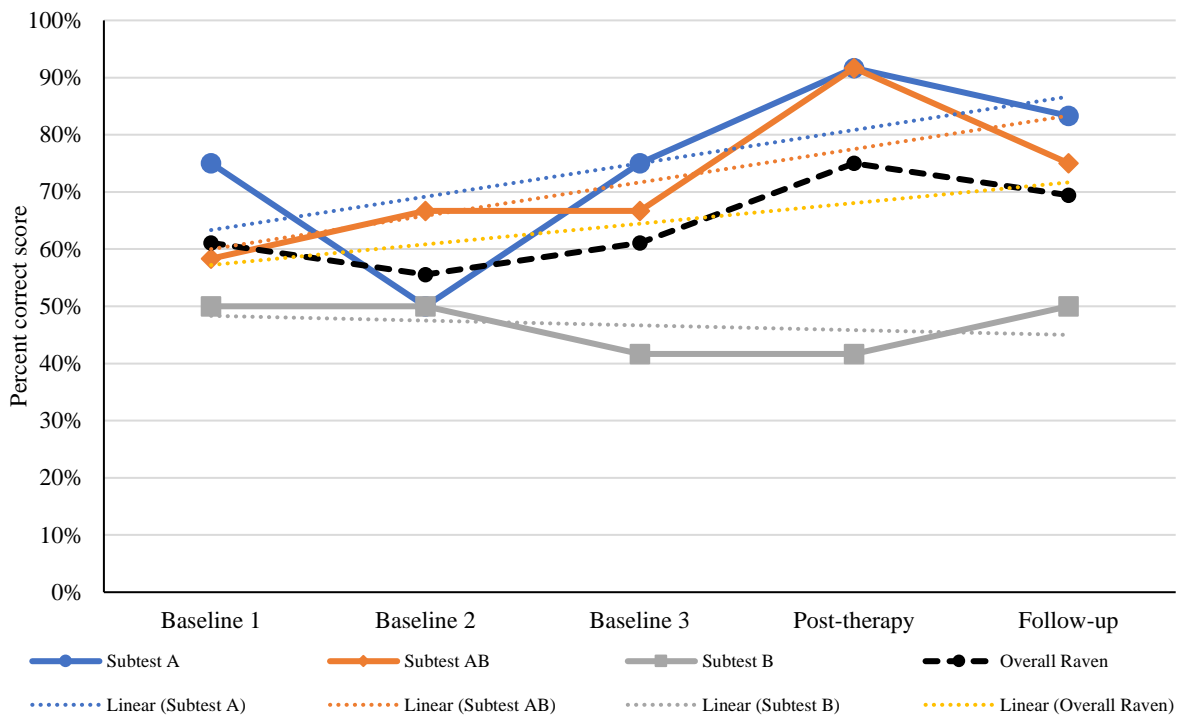
Figure 4.5.4: Percentage (%) correct on the subcategories and the overall *RCPM* (Participant F.C.).

Table 4.5.4: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) for the *RCPM* (Participant F.C.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
Subtest A	Mean	0.75	0.50	0.75	0.92	0.83	0.58	0.75
	S.D.	0.45	0.52	0.45	0.29	0.39	1.38	1.14
							t(11)= 1.47, p= 0.085	t(11)= 2.28, p= 0.022
Subtest AB	Mean	0.58	0.67	0.67	0.92	0.75	0.58	0.58
	S.D.	0.51	0.49	0.49	0.29	0.45	1.00	1.98
							t(11)= 2.03, p= 0.034	t(11)= 1.02, p= 0.164
Subtest B	Mean	0.50	0.50	0.42	0.42	0.50	-0.08	0.08
	S.D.	0.52	0.52	0.51	0.51	0.52	0.29	0.29
							t(11)= -1.00, p= 0.169	t(11)= 1.00, p= 0.169
Overall RCPM	Mean	0.61	0.56	0.61	0.75	0.69	0.361	0.472
	S.D.	0.49	0.50	0.49	0.44	0.47	1.02	1.32
							t(35)= 2.13, p= 0.02	t(35)= 2.15, p= 0.019

4.5.5 *MAIN*

There was a non-significant overall trend for improvement on the *MAIN*, $t(16)= 0.57$, $p= .290$, and non-significant between the treated and untreated periods, $t(16)= 1.43$, $p= .086$.
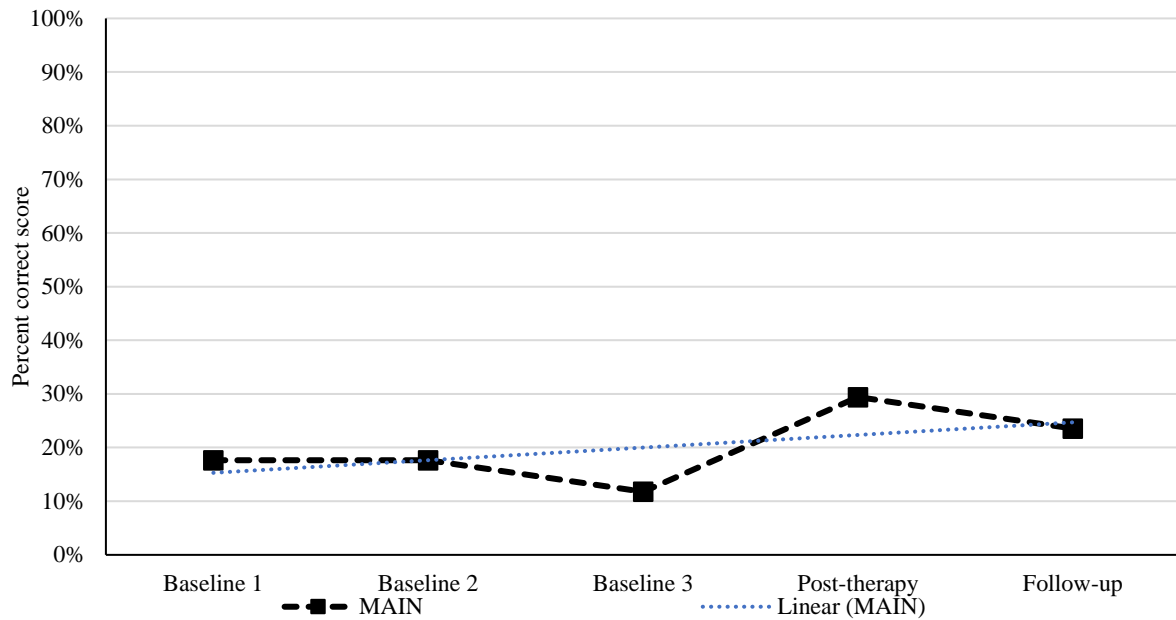
Figure 4.5.5: Percentage (%) correct on the *MAIN* by phase (Participant F.C.)

Table 4.5.5: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) for the *MAIN* (Participant F.C.).

		Baseline 1	Baseline 2	Baseline 3	Post-therapy	Follow-up	WEST-Trend	WEST-ROC
	Mean	0.18	0.18	0.12	0.29	0.24	0.24	0.59
MAIN	S.D.	0.39	0.39	0.33	0.47	0.44	1.71	1.70
							t(16)= 0.57, p= 0.290	t(16)= 1.43, p= 0.086

4.5.6 *Procedural Discourse*

The WEST-Trend could not be evaluated due the standard deviation being equal to zero. There was non-significant improvement in *Procedural Discourse* between the treated and untreated periods, $t(9)$= -1.00, p= .172.
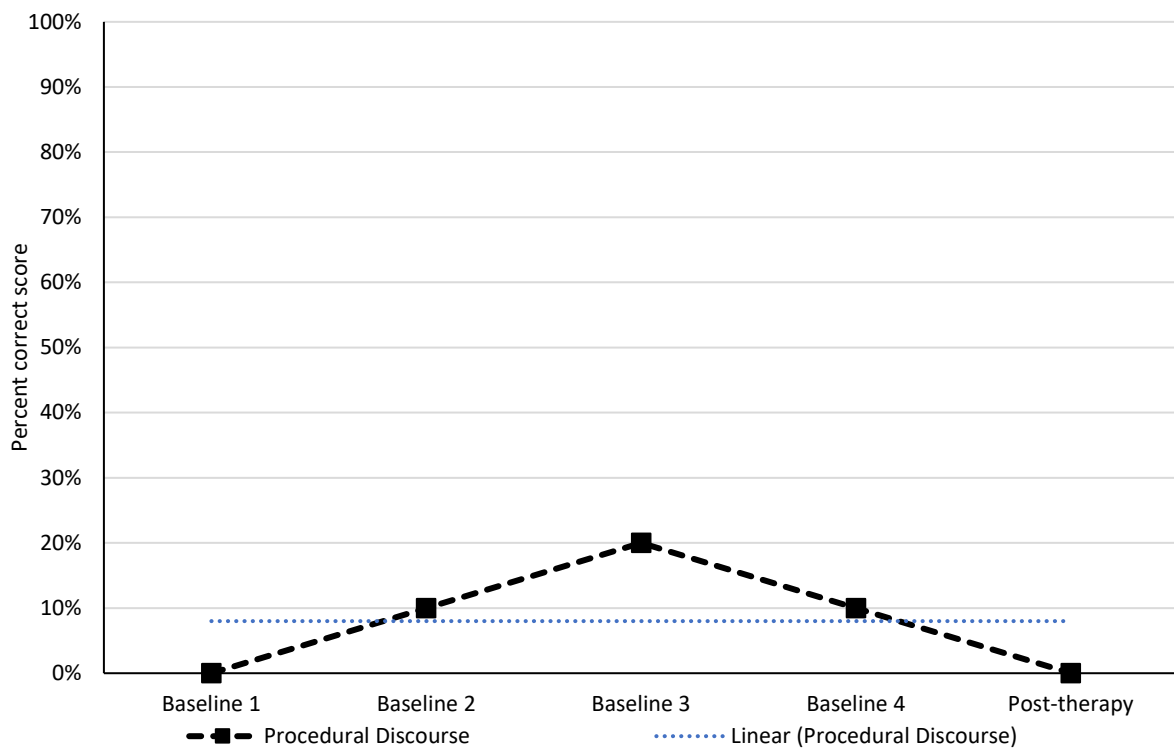
Figure 4.5.6: Percentage (%) correct on the *Procedural Discourse* by phase (Participant F.C.).

Table 4.5.6: WEST-Trend (sum of scores multiplied by −2, −1, 0, 1, 2) and WEST-ROC (sum of scores multiplied by 2, −1, −4, 3, 0) for the *Procedural Discourse* (Participant F.C.).

		Baseline 1	**Baseline 2**	**Baseline 3**	**Post-therapy**	**Follow-up**	**WEST-Trend**	**WEST-ROC**
	Mean	0.00	0.10	0.20	0.10	0.00	0.00	-0.60
Procedural Discourse	S.D.	0.00	0.32	0.42	0.32	0.00	0.00	1.90
							---	t(9)= -1.00, p= 0.172

4.5.7 *SSLA*

F.C..'s stroke narrative (spontaneous language sample) was analysed using the SSLA protocol (Shewan, 1988) designed to describe and quantify connected speech (**Table 4.5.7**). The language sample collected at each time point, was not sufficient in word length to undergo statistical analysis hence results were compared in raw scores. In this case the baseline average (avg) was compared with the post-testing and follow-up results. There was an increase in the sentence length, which reflects the use more than 5 words in the produced utterances, improved from 49% at baseline avg to 19% at post-therapy and was maintained at 27% at follow-up. Improvement was noted in sentence complexity between baseline avg and post-therapy (from 7% to 19%) but reverted back to baseline avg at follow-up. An improvement was noted between baseline avg and post-therapy in the production of errors (from 102% to 75%) and was maintained at follow-up (67%). Lastly, the number of content units improved from 11.30 at baseline avg, to 20.00 at post-therapy, and but reverted to 14.00 at follow-up. Overall, based on the numerical values collected, there was no increase in the number of utterances, melody, articulation, paraphasias, and repetitions after therapy (see **Table 4.5.7**).
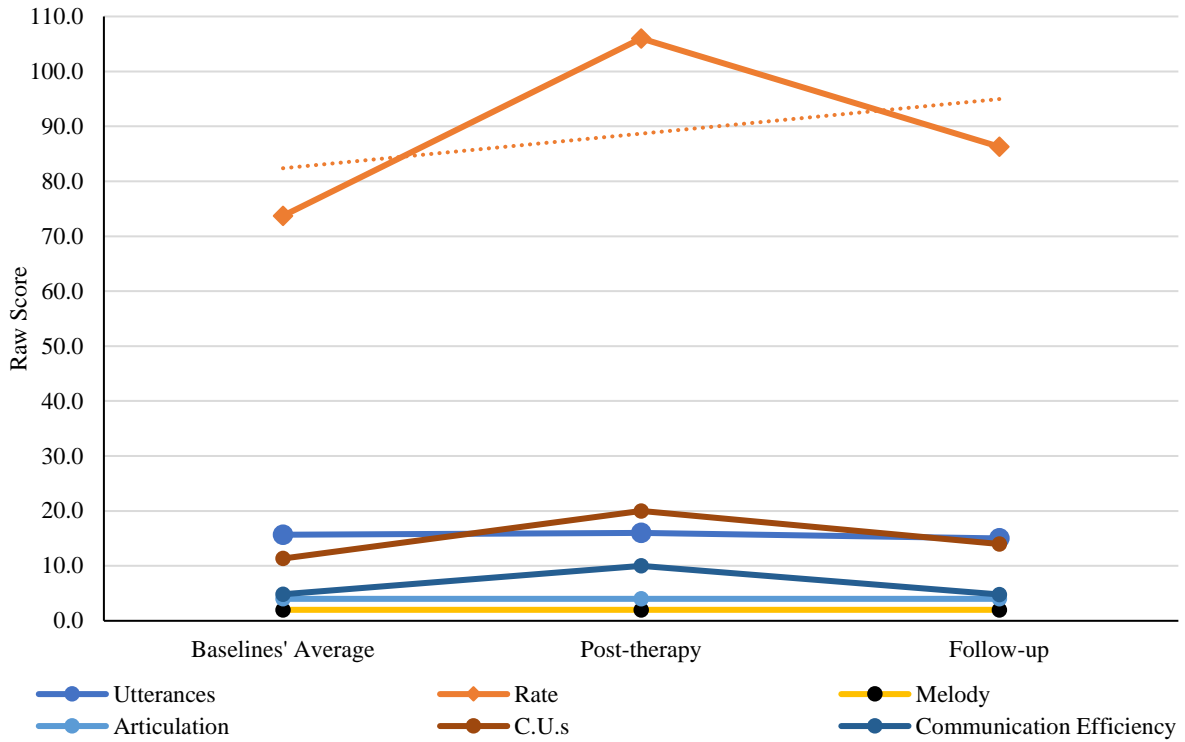
Figure 4.5.7.a. Results of F.C.'s personal stroke narrative analysis based on the *SSLA* showing the raw scores across baseline average, post-therapy, and follow-up phases.
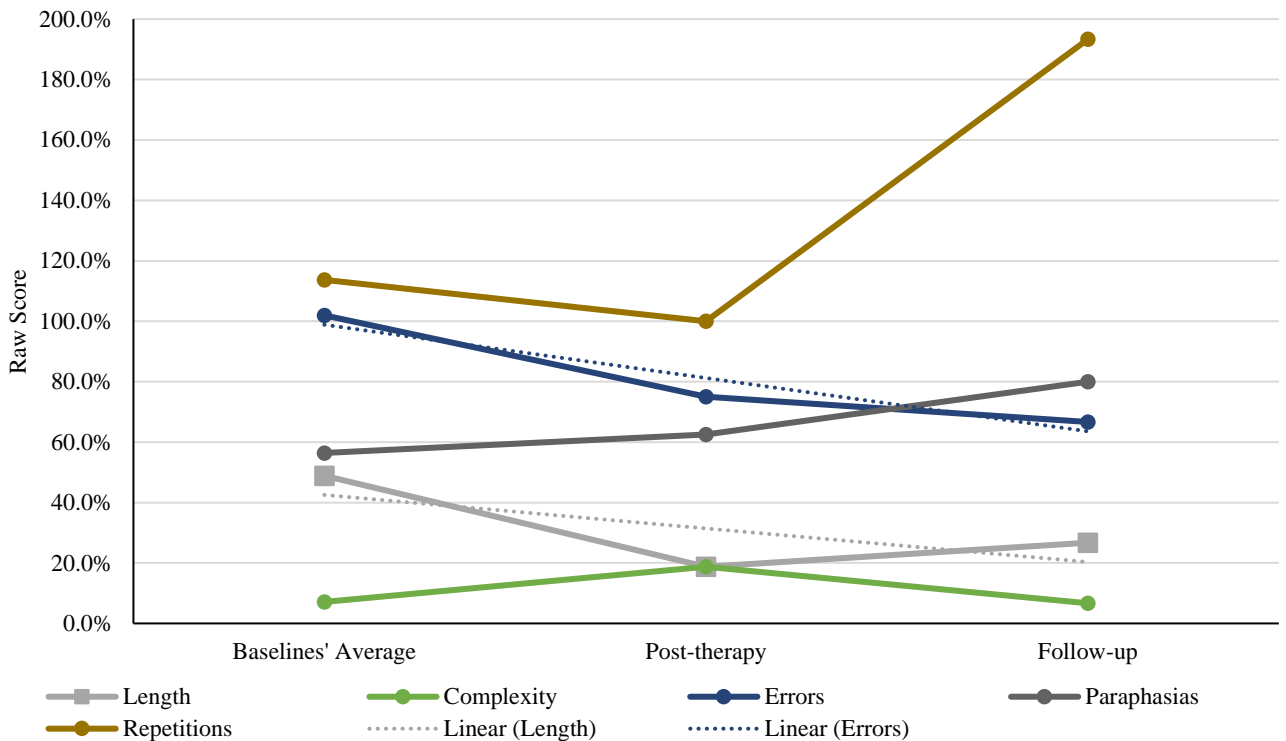
Figure 4.5.7.b. Results of F.C.'s personal stroke narrative analysis based on the *SSLA* showing the percentage (%) scores for baseline average, post-therapy, and follow-up phases.

Table 4.5.7: Raw scores for F.C.'s personal stroke narrative analysis based on the *SSLA*.

	Baseline 1	Baseline 2	Baseline 3	Baseline Average	Post-therapy	Follow-up
Utterances	13.00	17.00	17.00	15.67	16.00	15.00
Rate	84.14	62.75	74.25	73.71	106.00	86.30
Length	23%	59%	65%	49%	19%	27%
Melody	2.00	2.00	2.00	2.00	2.00	2.00
Articulation	4.00	4.00	4.00	4.00	4.00	4.00
Complexity	15%	0%	6%	7%	19%	7%
Errors	100%	100%	106%	102%	75%	67%
C.U.s	15.00	9.00	10.00	11.33	20.00	14.00
Paraphasias	69%	59%	41%	56%	63%	80%
Repetitions	100%	141%	100%	114%	100%	193%
Communication Efficiency	6.61	3.53	4.29	4.81	10.00	4.79

4.5.8   *RehaCom WM*

The results of the *RehaCom WM* screening show that there was no improvement in the tasks assessed. **Table 4.5.8** shows participant F.C.'s raw scores. A graphic representation of the WM screening results can be seen in **Figure 4.5.8**. Participant F.C. did not show an overall improvement in WM.
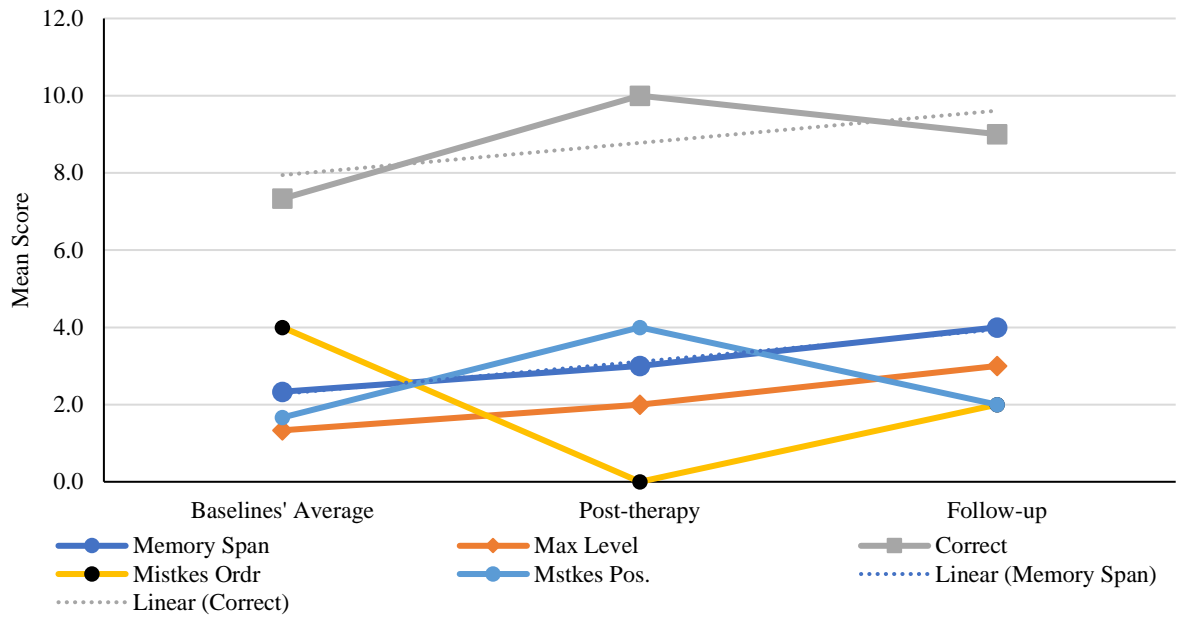
Figure 4.5.8: Schematic representation of the *RehaCom WM Screening* test results across phase.

Table 4.5.8: *RehaCom WM Screening* raw scores for F.C. by subcategory and period of assessment

	Baseline 1	Baseline 2	Baseline 3	Baseline Average	Post-therapy	Follow-up
Memory Span	1	3	3	2	3	4
Max Level	0	2	2	1	2	3
Correct	0	15	7	7	10	9
Mistakes Order	6	4	2	4	0	2
Mistakes Position	1	3	1	2	4	2

4.5.9   SAQOL-39

With regards to investigating whether the overall QoL would improve after treatment, the self-rated SAQOL-39 was analysed by comparing the mean scores (**Figure 4.5.9.; Table 4.5.9.**). The participant's responses indicated that overall QoL did not improve.
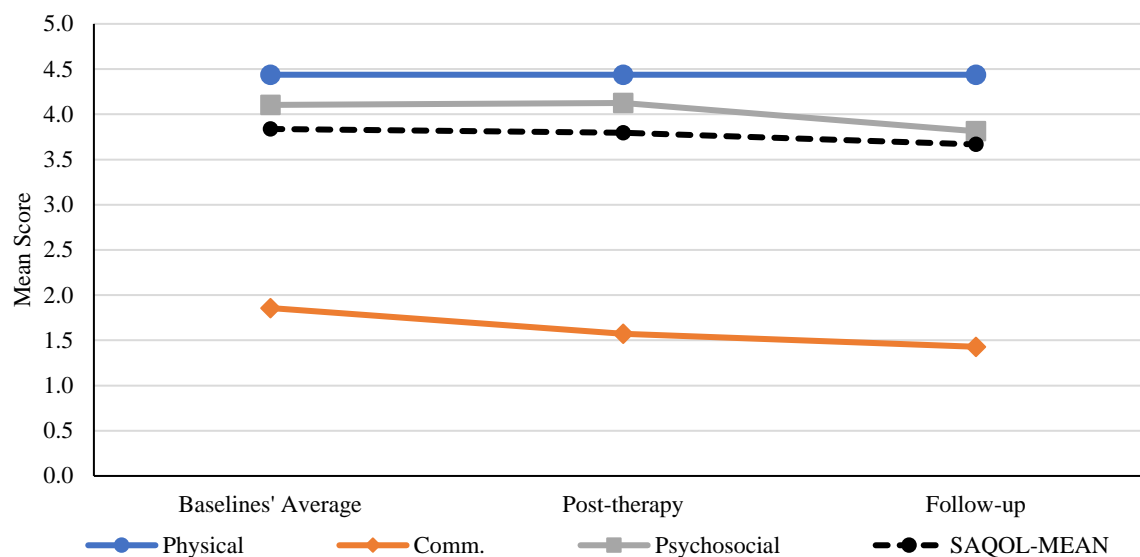
Figure 4.5.9: Schematic representation of the *SAQOL-39g* mean raw scores at baseline, post-therapy and follow-up (Participant F.C.).

Table 4.5.9: Mean raw scores on the *SAQOL-39g* at baseline, post-therapy and follow-up (Participant F.C.).

	Baseline 1	Baseline 2	Baseline 3	Baseline average	Post-therapy	Follow-up
Physical	4.44	4.44	4.44	4.44	4.44	4.44
Communication	2.14	1.71	1.71	1.86	1.57	1.43
Psychosocial	4.00	4.13	4.19	4.10	4.13	3.81
Overall SAQOL-39	3.85	3.82	3.85	3.84	3.79	3.67

4.6 Side effects and Dropouts

This study did not induce any adverse events and the participants did not report any side effects during and after treatment. All the participants completed the study in its entire duration as previously outlined (i.e. 3 months) and there were no dropouts.

4.7 Chapter Summary

This chapter reported the baseline and intervention outcomes, the statistical analyses of standardized language and cognitive measures, the reports of outcome summaries for working memory, procedural discourse, narratives produced, and QoL outcomes.

5 DISCUSSION

In the previous chapter all the results were analysed and compared between the untreated and post-treated periods of each participant. As previously mentioned, the main objective was to explore the potential domains of transfer effect after stimulating the left DLPFC and WM training, and also to measure how efficacious this treatment protocol was for PWA. Specifically, the purpose was to investigate the combined effects of iTBS and WM training on WM performance as a mediator to language generalization. The following sections of this chapter will address each of the research questions pertaining to each participant's results and indicate their supplementary significance to previous findings. To assess treatment efficacy the outcome measures were compared at the different time points, that is, between the repeated baselines, post-treatment, and follow-up (e.g. 3 months post-therapy). The findings from this study lend support to the evidence that (i) WM interacts with language abilities and deficits in WM influence language performance (i.e. Murray, 2012); (ii) applying iTBS to the LDLPFC results in improved WM performance (i.e. Hoy et al., 2015; Demeter et al., 2016); (iii) computerized WM training can have positive outcomes on WM tasks (i.e. Lundqvist et al., 2010); (iv) aphasia has a negative effect on QoL (i.e. Manning, MacFarlane, Hickey, & Franklin, 2019).

5.1 Question 1: Does WM training generalize to trained cognitive areas as measured by untrained WM (near-transfer effect) and fluid intelligence tasks (far-transfer effect)?

Previous research has shown that benefits resulting from WM training were not task specific, but instead, they extended beyond the trained task by affecting WM processes, including WM updating (Dahlin et al., 2008). Other studies have further demonstrated transfer of WM training to other assessments of cognition, including measures of fluid intelligence (Jaeggi et al., 2008). This study has revealed a trend for improvement in both WM tasks and *Gf* transfer and a statistically significance of *Gf* as measured with the RCPM after the 10-day iTBS application to the left DLPFC followed by 30-minute WM training.

5.1.1 *Short- and long-term near-transfer effects of iTBS to the LDLPFC combined with WM training to cognitive areas*

Three participants showed a positive linear trend for improvement only in the number of correct responses on the *RehaCom WM* screening task. The results are in agreement with previous research showing a non-significant improvement in WM post-training, despite a steady improvement over the duration of the training sessions in healthy ageing adults (Barbu et al., 2017). To this date, there is no research evidence signifying the possible improvement that could yield specifically from the *RehaCom* WM training program in PWA. Future research is needed to clarify how beneficial *RehaCom* as a CACR method is for aphasia recovery. In contrast to the expectation that WM would improve after the 10-day treatment, the effect was insignificant with minor improvements in the number of correct responses in three participants between baseline and post-therapy only. These results are in contrast with previous research indicating that computerized WM training improves WM abilities after acquired brain injury (e.g. Lundqvist et al., 2010; Westerberg et al., 2007), but this contradiction could be due to the short training period (10 days) and/or that only one outcome measure was used to measure WM improvement and multiple baselines were not obtained to provide sufficient information for comparative purposes.

Table 5.1.1 Summary of near-transfer effects of WM training to cognitive areas (*RehaCom*)

	Short-term effect	*Long-term Effect*
Participant 1 (I.A.)	No improvement.	No improvement.
Participant 2 (C.S)	Improved number of correct responses from 8 to 24.	Minor maintenance of correct responses improvement from 8 at 13 correct responses.
Participant 3 (S.H.)	Improved number of correct responses from 1.75 to 11.	No improvement.
Participant 4 (C.G.)	Improvement was noted within the untreated baselines period but it was inconsistent and was not maintained.	No improvement.
Participant 5 (F.C.)	Minor improvement in the number of correct responses from 7 to 10.	Improvement of correct responses was retained at 9 at follow-up.

5.1.2 *Short- and long-term far-transfer effects of iTBS to the LDLPFC combined with WM training to cognitive areas*

Table 5.1.2 Summary of far-transfer effects of WM training effect to cognitive areas (*RCPM*)

	Improvement between treated and untreated periods (WEST-ROC)	*Improvement across time (WEST-Trend)*
Participant 1 (I.A.)	Statistically significant improvement	Statistically significant trend for improvement across time
Participant 2 (C.S)	Non- significant improvement	Non-significant a trend of improvement
Participant 3 (S.H.)	Statistically significant improvement	Statistically significant trend for improvement across time
Participant 4 (C.G.)	N/A	N/A
Participant 5 (F.C.)	Statistically significant improvement	Statistically significant trend for improvement across time

It was also hypothesised that stimulation of the DLPFC combined with WM training would result in positive far transfer cognitive effects with subsequent improved scores on untreated cognitive areas. Significant treatment effects were found on the *RCPM,* a non-trained measure that indicates improvement and far-transfer effects of *Gf* (non-verbal intelligence). Specifically, three participants showed statistically significant trend for improvement with a statistically significant difference between the treated and untreated periods, and one participant showed improvement but it did not reach significance. This finding is in line with results from a study where significant improvements in *Gf* resulted following cognitive intervention combined with different transcranial electrical brain stimulation protocols (Brem et al., 2018). The findings support the notion that *Gf* can be improved with WM training (Engle et al., 1999; Friedman et al., 2006; Unsworth et al., 2014) and DLPFC stimulation (Brem et al., 2018). Considering the fact that a combination of treatments was used and it is still debateable that WM training leads to *Gf* improvement (Harrison et al., 2013) the findings are inconclusive as to whether improvement was due to the treatment combination or to the DLPFC stimulation. It is important to note that the two of the three participants who achieved significant

improvement in the overall *RCPM* were experiencing moderate to severe global aphasia. It might be worthwhile investigating further whether this association is significant in future research. *Participant 4 (C.G.)* had reached the maximum level of improvement during the baseline period. Therefore, there was no improvement to be measured.

5.2 Question 2: Does WM training generalize to untrained receptive and expressive language and functional communication tasks (far-transfer effect) in the short- and long-term?

The *BDAE-SF* results revealed statistically significant improvements in the language skills on the untrained tasks. All of the participants improved in the majority of the tasks in the subtests of *BDAE-SF Auditory Comprehension*, *Oral Expression*, and *Reading*.

Participant 1 (I.A.) who had mild expressive aphasia with severe dysarthria and unintelligible speech improved significantly in the *Screening of Special Categories* task of the *BDAE Oral Expression* subtest. *Participant 2 (C.S.)* who had been experiencing mild receptive aphasia with STM and auditory comprehension difficulties, showed a significant overall trend for improvement in the *Boston Naming Test* of the *BDAE Oral Expression* subtest. There was a significant trend for improvement in the *BDAE Reading* subtest, although when the individual tasks were analysed, they did not reach significance. *Participant 3 (S.H.)*, who was experiencing moderate to severe global aphasia, showed a significant overall trend for improvement in *Commands* of the *BDAE Auditory Comprehension* subtest. *Participant 4 (C.G.)* who was experiencing moderate expressive aphasia, was only one-month post-stroke when entering the study. Therefore, repeated weekly baselines were administered until the participant had demonstrated stable results in the assessment. A total of 5 baselines were administered, where the tests showed similar results during the last 2 baselines. A significant overall trend for improvement was noted in *Commands* of the *BDAE Auditory Comprehension* subtest. This participant had reached the maximum score in the W*ord Comprehension* task during the baseline period, and therefore, improvement in this task could be attributed to spontaneous recovery. The *Responsive Naming,* the *Boston Naming Test,* and the *Screening of Special Categories* of the *BDAE Oral Expression* were found to show a significant improvement individually, which also lead to the significant overall trend for improvement in the *BDAE Oral Expression* subtest. With regards to the overall *BDAE Reading* subtest there was a significant overall trend for improvement, but the improvement was found to be

significantly better in the untreated period. Based on the subtest results all the *Reading* tasks except the *Oral Basic Sentence* had reached the maximum possible score during the baseline period. Therefore, this participant's improvement in the *BDAE Reading* subtest could not be attributed to this study's treatment. *Participant 5 (F.C.)* who was experiencing moderate to severe global aphasia, reached a significant overall trend for improvement only in one task of the *BDAE Auditory Comprehension* (*Commands*) and the overall *BDAE Auditory Comprehension* subtest reached significance between the treated and untreated periods due to improvements in the other tasks, even though those did not reach significance. Similarly, there was a significant overall trend for improvement in the overall *BDAE Oral Expression*, although there was only significant trend for improvement in the *Screening of Special Categories of the BDAE Oral Expression.* In summary, three participants (S.H., C.G, F.C.) improved significantly in the *Commands*, three participants improved in the *Screening of Special Categories* (I.A., C.G., F.C.), two participants (C.S., C.G.) improved in the *Boston Naming Test*, and one participant (C.G.) improved in *Responsive Naming*. Improvement in the *Auditory Comprehension* subtest is consistent with results from previous studies that used WM training to improve receptive language abilities in PWA (Eom & Sung, 2016; Harris et al., 2014; Salis, 2012; Salis et al., 2017; Zakariás et al., 2018). These aforementioned studies reported improvements in commands tasks, naming tasks in language tests such as the Test for the Reception of Grammar (TROG) and the Token Test (TT). To the best of our knowledge, no other research so far has explored improvements following WM training with regards to responsive naming or sentence reading. *Participant 5 (C.G.)* improved in more language tasks than the other four participants. Clear conclusions pertaining to this participant cannot be drawn. This remarkable improvement could be attributed to a number of factors that could not be measured since each participant was treated as a case study and did not have a control group to compare to. One of the considered factors is neuroplasticity itself, since the participant started the treatment while in the subacute stage (i.e. 2 months post stroke). Similarly, *Participant 5 (F.C.)* also started the treatment while in the subacute stage (i.e. 3 months post-stroke) but did not improve to the same level as C.G. did. Their difference in improvement in this case could be attributed to the damaged size and location. Other differences between the two participants are age and education. Therefore, it cannot be concluded that neuroplasticity was the only factor ascribed in C.G.'s improvement. Post-TMS language improvement in the subacute stage is in line with evidence from aphasia literature showing favourable results of

the application of therapeutic rTMS or TBS early on, in the subacute stage (Kindler et al., 2012).

Narrative discourse was elicited with two types of tasks: the Baby-Goat story from the *MAIN* (Gagarina et al., 2012) and a personal stroke narrative (following Kambanaros, 2019). *Participant 1 (I.A.)* was unable to produce any narrative due to unintelligible connected speech. *Participant 2 (C.S.)* showed a non-significant trend for improvement in the narrative, specifically showing improvement in the IST Initiating structure of the story. *Participant 3 (S.H.)* also showed a non-significant overall trend for improvement in the *MAIN* with minor changes noted in *the IST Initiating, Attempt, Outcome*, and *IST Reaction* structures of the story. *Participant 4 (C.G.)* showed a significant overall trend for improvement in the *MAIN* with notable changes in the *Goal* and *Outcome* of the story's structure, which was not maintained at follw-up. *Participant 5 (F.C.)* presented with a non-significant trend for improvement in the *MAIN* with discerned changes in the *Outcome* structure of the story. A positive trend towards improvement in discourse was noted for both tasks in all participants, with a marked improvement at the post-therapy phase. There is evidence to support higher scores on WM measures are associated with better discourse production abilities in people with brain injury (Youse & Coelho, 2005).

The SSLA system (Shewan, 1988) was used in this study to examine the broad spectrum of language variables, in order to analyse and quantify the personal stroke narrative. *Participant 1 (I.A.)* did not produce an intelligible narrative, therefore quantification and analysis were not achieved in this case. *Participant 2 (C.S.)* showed a positive linear trend in the *Rate* of speech and *Sentence Complexity*, while there was a negative linear trend in *Errors* indicating improvement. *Participant 3 (S.H.)* demonstrated minor improvements based on the *SSLA*. A linear trend for improvement was noted in the reduction of *Repetitions*. *Participant 4 (C.G.)* showed a positive linear trend for improvement in the *Sentence Complexity* subtest accompanied by a negative linear trend in *Errors* and *Repetitions. Participant 5 (F.C.)* demonstrated a positive linear trend for improvement in the *Rate* of speech, as well as a negative linear trendline in the number of *Errors*, indicating improvement. Although linguistic analysis was not generally used in the aphasia treatment literature to evaluate changes in linguistic complexity, there is an increase in published research over the last few years (Bryant, Ferguson, & Spencer, 2016). Many researchers have examined verbal abilities by analysing language samples (e.g. Capilouto, Wright, & Wagovich, 2005; Shewan & Henderson, 1988)

226

although language sample analysis is usually used to evaluate linguistic development in children (e.g. Heilmann, Miller, Nockerts, & Dunaway, 2010). Few studies in the aging literature involving language analysis obtained oral language samples through prompts or through conversation as the means to obtain language samples for analysis (Kemper & Sumner, 2001).

Procedural Discourse analysis was based on the analysis developed by Richardson and Dalton (2016). *Participant 1 (I.A.)* did not produce a coherent sample to be able to undergo analysis. *Participant 2 (C.S.)* did not show any changes in the responses between the five periods in the *Procedural Discourse* task. *Participant 3 (S.H.)* and *Participant 4 (C.G.)* demonstrated a non-significant overall trend for improvement. Participant 5 (F.C.) did not show a trend for improvement. Although improvements in these tasks did not reach significance, findings are in agreement with research from the aphasia literature on discourse (Andreetta, Cantagallo, & Marini, 2012; Capilouto, Wright, & Wagovich, 2006; Ulatowska, Freedman-Stern, Doyel, Macaluso-Haynes, & North, 1983; Wright & Fergadiotis, 2012). From the aforementioned studies, only one study was specifically directed to procedural discourse (Ulatowska et al., 1981), with the more recent studies (Andreetta et al., 2012; Capilouto et al., 2006; Fergadiotis & Wright, 2011) exploring all aspects of discourse production, including narratives, revealing that as aphasia severity increases, quality and quantity of relevant discourse decreases. The reduction in sentence complexity experienced by PWA has also been shown to differ at a single word and semantic level, which is likely to affect procedural discourse, suggesting that PWA communicate less information in language in a context where spoken language may already be structurally less complex (Pritchard et al., 2015). PWA use fewer Correct Information Units (i.e. any single word, intelligible, informative, and relevant in context) in discourse than neurologically healthy people (NHP; Nicholas & Brookshire, 1993), as well as fewer types and tokens of spatial language in spatial tasks than NHP (Johnson, Cocks, & Dipper, 2013). Additionally, PWA use a high level of semantically "light" verbs containing little semantic information, such as come, go, make, take, get, give, do, have, be, and put (Berndt et al., 1997).

5.3 Does overall QoL improve after treatment?

In the present study the QoL of all participants was assessed using the self-reported SAQOL-39 questionnaire, which was administered in an interview format. *Participant 1 (I.A.), Participant 2 (C.S.), Participant 3 (S.H.), and Participant 4 (C.G.)* showed a positive linear

trend for improvement in the overall QoL across time, which was also maintained 3-months after the treatment, with prominent improvements noted in the Communication and Psychosocial fields. *Participant 5 (F.C.)* did not indicate improvements in QoL.

The fact that the participants did not rate their QoL as severely affected at the time of the study is in line with previous research reporting that PWA in the chronic stage often perceive their QoL as adequate, suggesting that with the passing of time individuals adapt to living with aphasia (Spaccavento et al., 2013). Nevertheless, improvement in the overall QoL in four participants was noted from baseline to post-therapy and maintained at follow-up. This is in agreement with the QoL literature that improvement in the severity of language deficits brings about an improvement in QoL (Spaccavento et al., 2013). Moreover, the results are consistent with what has been found in previous research, that non-verbal cognitive impairments may significantly affect QoL in PWA and are potentially important predictors to improvement (Nicholas et al., 2017). In addition to the measured results, *Participant 5*, who was in the subacute stage, was disappointed with his overall communication progress even though expectations were managed by his family from the beginning.

5.4 Summary of findings

A mixed pattern of training and transfer effects across participants was identified. While all participants showed improvements in cognitive and linguistic tasks, the most noteworthy observation was that the participants with global aphasia (S.H. and F.C.) significantly improved in non-verbal intelligence. Another remarkable observation was that all of the participants showed a modest improvement in the WM screening task. The transfer effects in this study did not result in a clear pattern. The inconsistent patterns detected are in line with the assumption that WM training-induced language improvements do not always occur in the presence of improvements on the trained WM task itself in aphasia (i.e. Minkina, Rosenberg, Kalinyak-Fliszar, & Martin, 2017). It may be possible that improvements detected in non-verbal intelligence, language abilities, functional communication, and QoL after training were not primarily induced by the WM training itself, but by the combination with the iTBS application to the LDLPFC.

6 CONCLUSION

The aim of this study was to investigate the relationship of WM and language abilities in aphasia. The specific goals were to investigate whether WM can be improved through the application of excitatory non-invasive brain stimulation (iTBS) followed by computerized WM training in aphasia, to examine whether WM improvements lead to near-transfer on unpractised WM tasks and non-verbal intelligence, and far-transfer effects on language tasks, narratives, functional communication and QoL. Overall, the findings of a significant trend for improvement and a significant difference between the treated and untreated periods in non-verbal intelligence, accompanied with the significant and non-significant trends for improvements in language abilities are indicative that computerized WM training and stimulation of the LDLPFC are areas that have a positive effect in neurorehabilitation of PWA after a stroke. This study has proved the safety and efficacy of this treatment while improvements were not only noted in PWA at the subacute stage, but also at the chronic stage. In the field of traditional language rehabilitation of PWA, it is well known among specialized professionals that improvements in the chronic stage are minor and slower to achieve at the chronic stage. In this study improvements were noted in only 10 days and even though not all the benefits were maintained at follow-up (i.e. 3 months), the positive linear trendlines signify that there is efficacious treatment potential, which requires further exploration towards facilitating language recovery in PWA. This study may provide insights towards directions for further investigation, and a guide to the design of a more rigorous research program with larger numbers of participants. Results of this investigation study provides evidence that stimulation of the LDLPFC combined with computerized WM training after left hemisphere stroke generalizes to language improvements as it was initially hypothesized. Improvements related to spontaneous recovery were seen during the repeated baseline measures, but thereafter any improvements could be attributed to this treatment. One can assume if improvement was spontaneous, then the improvement would sustain and manifest in the long-term. In this study improvements were more prominent at the immediate post-therapy assessments but fluctuated at follow-up. A larger number of participants would provide more reliable results. The treatment results are encouraging as this treatment protocol seems to be efficacious towards improvement in non-verbal intelligence that boosts language improvements. The findings are promising although the overall level of improvement is small, but this should not be discouraging as these results are based only on six cases. It is clinically and theoretically

important to investigate whether brain stimulation and WM training operate synergistically as an underlying treatment approach that enhance cognitive and language processing networks. It is critical to further investigate whether such combined treatment protocols will be taken on as new methods for post-stroke aphasia rehabilitation in the future.

6.1 Study limitations

This study had two major limitations: the small sample size and the fact there was only one WM assessment task available (*RehaCom* Screening). Initially this study, planned to recruit a large number of PWA in order to compare the effects of WM training alone, iTBS to the LDLPFC alone, the combination of the two treatments (i.e. the current study), and sham treatment. Due to the limited participation, all 6 participants (pilot and main study) were analysed as single cases, received the most potential treatment combination, and each participant was their own control to indicate improvement. It is important to note that WM results were based on a single WM outcome measure. Using additional WM measures would potentially increase the chances of identifying factors that modulate transfer effects. Nevertheless, the trend for improvement highlights a relationship worthy of continued investigation. Future research should incorporate a wider variety of WM measures, auditory comprehension, and discourse measures.

REFERENCES

Albert, M. L. (1973). A simple test of visual neglect. *Neurology*. Retrieved from
https://www.strokengine.ca/en/assess/at/

Allendorfer, J. B., Storrs, J. M., & Szaflarski, J. P. (2012). Changes in white matter integrity follow excitatory rTMS treatment of post-stroke aphasia. *Restorative Neurology and Neuroscience*, *30*(2), 103–113. https://doi.org/10.3233/RNN-2011-0627

Andreetta, S., Cantagallo, A., & Marini, A. (2012). Narrative discourse in anomic aphasia. *Neuropsychologia*, *50*(8), 1787–1793. https://doi.org/10.1016/j.neuropsychologia.2012.04.003

Arias-Carrión, O. (2008). Basic mechanisms of rTMS: Implications in Parkinson's disease. *International Archives of Medicine*, *1*(1), 2. https://doi.org/10.1186/1755-7682-1-2

Baddeley, A. (1992). Working Memory Alan Baddeley. *Science*, *255*(5044), 556–559. https://doi.org/10.1126/science.1736359

Baddeley, A. (1996). The fractionation of working memory. *Proceedings of the National Academy of Sciences of the United States of America*, *93*(24), 13468–13472. https://doi.org/10.1073/pnas.93.24.13468

Baddeley, A. (2003). Working memory and language: An overview. *Journal of Communication Disorders*, *36*(3), 189–208. https://doi.org/10.1016/S0021-9924(03)00019-4

Balconi, M. (2013). Dorsolateral prefrontal cortex, working memory and episodic memory processes: Insight through transcranial magnetic stimulation techniques. *Neuroscience Bulletin*, *29*(3), 381–389. https://doi.org/10.1007/s12264-013-1309-z

Barbey, A. K., Koenigs, M., & Grafman, J. (2013). Dorsolateral prefrontal contributions to human working memory. *Cortex*, *49*(5), 1195–1205. https://doi.org/10.1016/j.cortex.2012.05.022

Barnett-Page, E., & Thomas, J. (2009). Methods for the synthesis of qualitative research: A critical review. *BMC Medical Research Methodology*, *9*(1). https://doi.org/10.1186/1471-2288-9-59

Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry*. US: American Medical Association. https://doi.org/10.1001/archpsyc.1961.01710120031004

Berndt, R., Haendiges, A., Mitchum, C., & Sandson, J. (1997). Verb retrieval in aphasia. 2.

Relationship to sentence processing. *Brain & Language, 56*, 107–137. doi:10.1006/brln.1997.1728

Berube, S., Nonnemacher, J., Demsky, C., Glenn, S., Saxena, S., Wright, A., … Hillis, A. E. (2019). Stealing cookies in the twenty-first century: Measures of spoken narrative in healthy versus speakers with aphasia. *American Journal of Speech-Language Pathology*, *28*(1S), 321–329. https://doi.org/10.1044/2018_AJSLP-17-0131

Berzon, R., Hays, R. D., & Shumaker, S. A. (1993). International use, application and performance of health-related quality of life instruments. *Quality of Life Research*, *2*(6), 367–368. https://doi.org/10.1007/BF00422214

Bilker, W. B., Hansen, J. A., Brensinger, C. M., Richard, J., Gur, R. E., & Gur, R. C. (2012). Development of Abbreviated Nine-Item Forms of the Raven's Standard Progressive Matrices Test. *Assessment*, *19*(3), 354–369. https://doi.org/10.1177/1073191112446655

Boggio, P. S., Fregni, F., Bermpohl, F., Mansur, C. G., Rosa, M., Rumi, D. O., … Araujo Silva, M. T. (2005). Effect of repetitive TMS and fluoxetine on cognitive function in patients with Parkinson's disease and concurrent depression. *Movement Disorders*, *20*(9), 1178–1184. https://doi.org/10.1002/mds.20508

Bonini, M. V., & Radanovic, M. (2015). Déficits cognitivos na afasia pós-AVE. *Arquivos de Neuro-Psiquiatria*, *73*(10), 840–847. https://doi.org/10.1590/0004-282X20150133

Brem, A. K., Almquist, J. N. F., Mansfield, K., Plessow, F., Sella, F., Santarnecchi, E., … Erdogmus, D. (2018). Modulating fluid intelligence performance through combined cognitive training and brain stimulation. *Neuropsychologia*, *118*(March), 107–114. https://doi.org/10.1016/j.neuropsychologia.2018.04.008

Bryant, L., Ferguson, A., & Spencer, E. (2016). Linguistic analysis of discourse in aphasia: A review of the literature. *Clinical Linguistics and Phonetics*, *30*(7), 489–518. https://doi.org/10.3109/02699206.2016.1145740

Bullinger, M., Anderson, R., Cella, D., & Aaronson, N. (1993). Developing and evaluating cross-cultural instruments from minimum requirements to optimal models. *Quality of Life Research*, *2*(6), 451–459. https://doi.org/10.1007/BF00422219

Capilouto, G. J., Wright, H. H., & Wagovich, S. A. (2006). Reliability of main event measurement in the discourse of individuals with aphasia. *Aphasiology*, *20*(2–4), 205–216. https://doi.org/10.1080/02687030500473122

Capilouto, G., Wright, H. H., & Wagovich, S. A. (2005). CIU and main event analyses of the structured discourse of older and younger adults. *Journal of Communication Disorders*,

38(6), 431–444. https://doi.org/10.1016/j.jcomdis.2005.03.005

Caplan, D., Michaud, J., & Hufford, R. (2013). Short-term memory, working memory, and syntactic comprehension in aphasia. *Cognitive Neuropsychology*, *30*(2), 77–109. https://doi.org/10.1080/02643294.2013.803958

Carpenter, P. A., Just, M. A., & Reichle, E. D. (2000). Working memory and executive function: Evidence from neuroimaging. *Current Opinion in Neurobiology*, *10*(2), 195–199. https://doi.org/10.1016/S0959-4388(00)00074-X

Carpenter, P. A., Just, M. A., & Shell, P. (1990). What one intelligence test measures: A theoretical account of the processing in the Raven progressive matrices test. *Psychological Review*, *97*(3), 404–431. https://doi.org/10.1037/0033-295X.97.3.404

Carr, J. E. (2005). Multiple-Baseline Designs Across Participants. *Behavioral Interventions*, *20*, 219–224. https://doi.org/10.1002/bin.191

Chai, W. J., Abd Hamid, A. I., & Abdullah, J. M. (2018). Working memory from the psychological and neurosciences perspectives: A review. *Frontiers in Psychology*, *9*(MAR), 1–16. https://doi.org/10.3389/fpsyg.2018.00401

Chein, J. M., Moore, A. B., & Conway, A. R. A. (2011). Domain-general mechanisms of complex working memory span. *NeuroImage*, *54*(1), 550–559. https://doi.org/10.1016/j.neuroimage.2010.07.067

Cornelissen, K., Laine, M., Tarkiainen, A., Järvensivu, T., Martin, N., & Salmelin, R. (2003). Adult brain plasticity elicited by anomia treatment. *Journal of Cognitive Neuroscience*, *15*(3), 444–461. https://doi.org/10.1162/089892903321593153

Cotelli, M., Fertonani, A., Miozzo, A., Rosini, S., Manenti, R., Padovani, A., … Miniussi, C. (2011). Anomia training and brain stimulation in chronic aphasia. *Neuropsychological Rehabilitation*, *21*(5), 717–741. https://doi.org/10.1080/09602011.2011.621275

Courtney, S. M. (2004). Emergent Properties of Information Representation. *Cognitive, Affective & Behavioral Neuroscience*, *4*(4), 501–516. https://doi.org/10.3758/CABN.4.4.501

Cruice, M., Worrall, L., Hickson, L., & Murison, R. (2003). Finding a focus for quality of life with aphasia: Social and emotional health, and psychological well-being. *Aphasiology*, *17*(4), 333–353. https://doi.org/10.1080/02687030244000707

Cumming, T. B., Marshall, R. S., & Lazar, R. M. (2013). Stroke, cognitive deficits, and rehabilitation: Still an incomplete picture. *International Journal of Stroke*, *8*(1), 38–45. https://doi.org/10.1111/j.1747-4949.2012.00972.x

D'Esposito, M., & Postle, B. R. (2015). The Cognitive Neuroscience of Working Memory. *Annual Review of Psychology*, *66*(1), 115–142. https://doi.org/10.1146/annurev-psych-010814-015031

D'Esposito, M., Postle, B. R., & Rypma, B. (2000). Prefrontal cortical contributions to working memory: Evidence from event-related fMRI studies. *Experimental Brain Research*, *133*(1), 3–11. https://doi.org/10.1007/s002210000395

Demeter, E., Mirdamadi, J. L., Meehan, S. K., & Taylor, S. F. (2016). Short theta burst stimulation to left frontal cortex prior to encoding enhances subsequent recognition memory. *Cognitive, Affective and Behavioral Neuroscience*, *16*(4), 724–735. https://doi.org/10.3758/s13415-016-0426-3

Demirtas-Tatlidede, A., Vahabzadeh-Hagh, A. M., & Pascual-Leone, A. (2013). Can noninvasive brain stimulation enhance cognition in neuropsychiatric disorders? *Neuropharmacology*, *64*, 566–578. https://doi.org/10.1016/j.neuropharm.2012.06.020

Dronkers, N. F., & Baldo, J. (2009). Language: Aphasia. In L. Squire (Ed.). *Encyclopedia of neuroscience* (Vol. 5, pp. 343–348). Oxford: Academic Press.

Efstratiadou, E. A., Chelas, E. N., Ignatiou, M., Christaki, V., Papathanasiou, I., & Hilari, K. (2012). Quality of life after stroke: Evaluation of the Greek SAQOL-39g. *Folia Phoniatrica et Logopaedica*, *64*(4), 179–186. https://doi.org/10.1159/000340014

El Hachioui, H., Visch-Brink, E. G., Lingsma, H. F., Van De Sandt-Koenderman, M. W. M. E., Dippel, D. W. J., Koudstaal, P. J., & Middelkoop, H. A. M. (2014). Nonlinguistic cognitive impairment in poststroke aphasia: A prospective study. *Neurorehabilitation and Neural Repair*, *28*(3), 273–281. https://doi.org/10.1177/1545968313508467

Engle, R. W., Laughlin, J. E., Tuholski, S. W., & Conway, A. R. A. (1999). Working memory, short-term memory, and general fluid intelligence: A latent-variable approach. *Journal of Experimental Psychology: General*, *128*(3), 309–331. https://doi.org/10.1037/0096-3445.128.3.309

Eom, B., & Sung, J. E. (2016). The Effects of Sentence Repetition–Based Working Memory Treatment on Sentence Comprehension Abilities in Individuals With Aphasia. *American Journal of Speech-Language Pathology*, *25*(4S), 1–15. https://doi.org/10.1044/2016_AJSLP-15-0151

Eriksson, J., Vogel, E. K., Lansner, A., Bergström, F., & Nyberg, L. (2015). Neurocognitive Architecture of Working Memory. *Neuron*, *88*(1), 33–46. https://doi.org/10.1016/j.neuron.2015.09.020

Fedorenko, E. (2014). The role of domain-general cognitive control in language comprehension. *Frontiers in Psychology*, *5*(APR), 1–17. https://doi.org/10.3389/fpsyg.2014.00335

Feldman, H., Levy, A. R., Hsiung, G. Y., Peters, K. R., Donald, A., Black, S. E., … Rockwood, K. (2003). A Canadian Cohort Study of Cognitive Impairment and Related Dementias (ACCORD): Study methods and baseline results. *Neuroepidemiology*, *22*(5), 265–274. https://doi.org/10.1159/000071189

Fergadiotis, G., & Wright, H. H. (2011). Lexical diversity for adults with and without aphasia across discourse elicitation tasks. *Aphasiology*, *25*(11), 1414–1430. https://doi.org/10.1080/02687038.2011.603898

Ferguson, A. (1999). Learning in aphasia therapy: It's not so much what you do, but how you do it! *Aphasiology*, *13*(2), 125–150. https://doi.org/10.1080/026870399402244

Franklin, S. (1997). Designing single case treatment studies for aphasic patients. *Neuropsychological Rehabilitation*, *7*(4), 401–418. https://doi.org/10.1080/713755544

Fridriksson, J. (2010). Preservation and modulation of specific left hemisphere regions is vital for treated recovery from anomia in stroke. *Journal of Neuroscience*, *30*(35), 11558–11564. https://doi.org/10.1523/JNEUROSCI.2227-10.2010

Friedman, N. P., Miyake, A., Corley, R. P., Young, S. E., DeFries, J. C., & Hewitt, J. K. (2006). Not all executive functions are related to intelligence. *Psychological Science*, *17*(2), 172–179. https://doi.org/10.1111/j.1467-9280.2006.01681.x

Gagarina, N., Klop, D., Kunnari, S., Tantele, K., Välimaa, T., Balciuniene, I., … Walters, J. (2012). M ultilingual A ssessment I nstrument for N arratives, *56*, 1–13.

Georgiou, A., Konstantinou, N., Phinikettos, I., & Kambanaros, M. (2019). Neuronavigated theta burst stimulation for chronic aphasia: two exploratory case studies. *Clinical Linguistics and Phonetics*, *33*(6), 532–546. https://doi.org/10.1080/02699206.2018.1562496

Georgiou, A. M., Lada, E., & Kambanaros, M. (2019). Evaluating the quality of conduct of systematic reviews on the application of transcranial magnetic stimulation (TMS) for aphasia rehabilitation post-stroke. *Aphasiology*, *00*(00), 1–17. https://doi.org/10.1080/02687038.2019.1632786

Georgiou, A. M., Phinikettos, I., Giasafaki, C., & Kambanaros, M. (2020). Can transcranial magnetic stimulation (TMS) facilitate language recovery in chronic global aphasia post-stroke ? Evidence from a case study. *Journal of Neurolinguistics*, *55*(March),

100907. https://doi.org/doi.org/10.1016/j.jneuroling.2020.100907

Giannakou, M., Roussi, P., Kosmides, M. E., Kiosseoglou, G., Adamopoulou, A., & Garyfallos, G. (2013). Adaptation of the beck depression inventory-II to greek population. *Hellenic Journal of Psychology*, *10*(2), 120–146.

Gray, J. R., Chabris, C. F., & Braver, T. S. (2003). Neural mechanisms of general fluid intelligence. *Nature Neuroscience*, *6*(3), 316–322. https://doi.org/10.1038/nn1014

Gray, J. R., & Thompson, P. M. (2004). Neurobiology of intelligence: Science and ethics. *Nature Reviews Neuroscience*, *5*(6), 471–482. https://doi.org/10.1038/nrn1405

Griffis, J. C., Nenert, R., Allendorfer, J. B., & Szaflarski, J. P. (2016). Interhemispheric Plasticity following Intermittent Theta Burst Stimulation in Chronic Poststroke Aphasia. *Neural Plasticity*, *2016*, 20–23. https://doi.org/10.1155/2016/4796906

Groppa, S., Oliviero, A., Eisen, A., Quartarone, A., Cohen, L. G., Mall, V., … Siebner, H. R. (2012). A practical guide to diagnostic transcranial magnetic stimulation: Report of an IFCN committee. *Clinical Neurophysiology*, *123*(5), 858–882. https://doi.org/10.1016/j.clinph.2012.01.010

Guse, B., Falkai, P., & Wobrock, T. (2010). Cognitive effects of high-frequency repetitive transcranial magnetic stimulation: A systematic review. *Journal of Neural Transmission*, *117*(1), 105–122. https://doi.org/10.1007/s00702-009-0333-7

Hallett, M. (2000). Transcranial magnetic stimulation and the human brain. *Nature*, *406*(6792), 147–150. https://doi.org/10.1038/35018000

Hallett, M. (2007). Transcranial Magnetic Stimulation: A Primer. *Neuron*, *55*(2), 187–199. https://doi.org/10.1016/j.neuron.2007.06.026

Hanten, G., & Martin, R. C. (2000). Contributions of Phonological and Semantic Short-Term Memory to Sentence Processing: Evidence from Two Cases of Closed Head Injury in Children. *Journal of Memory and Language*, *43*(2), 335–361. https://doi.org/10.1006/jmla.2000.2731

Harris, L., Olson, A., & Humphreys, G. (2014). The link between STM and sentence comprehension: A neuropsychological rehabilitation study. *Neuropsychological Rehabilitation*, *24*(5), 678–720. https://doi.org/10.1080/09602011.2014.892885

Harrison, T. L., Shipstead, Z., Hicks, K. L., Hambrick, D. Z., Redick, T. S., & Engle, R. W. (2013). Working Memory Training May Increase Working Memory Capacity but Not Fluid Intelligence. *Psychological Science*, *24*(12), 2409–2419. https://doi.org/10.1177/0956797613492984

Hartley, A. A., Speer, N. K., Jonides, J., Reuter-Lorenz, P. A., & Smith, E. E. (2001). Is the dissociability of working memory systems for name identity, visual-object identity, and spatial location maintained in old age? *Neuropsychology*, *15*(1), 3–17. https://doi.org/10.1037/0894-4105.15.1.3

Heilmann, J., Miller, J. F., Nockerts, A., & Dunaway, C. (2010). Properties of the narrative scoring scheme using narrative retells in young school-Age children. *American Journal of Speech-Language Pathology*, *19*(2), 154–166. https://doi.org/10.1044/1058-0360(2009/08-0024)

Hilari, K., Lamping, D. L., Smith, S. C., Northcott, S., Lamb, A., & Marshall, J. (2009). Psychometric properties of the Stroke and Aphasia Quality of Life Scale (SAQOL-39) in a generic stroke population. *Clinical Rehabilitation*, *23*(6), 544–557. https://doi.org/10.1177/0269215508101729

Hilari, K., Needle, J. J., & Harrison, K. L. (2012). What are the important factors in health-related quality of life for people with aphasia? A systematic review. *Archives of Physical Medicine and Rehabilitation*, *93*(1 SUPPL.), S86-S95.e4. https://doi.org/10.1016/j.apmr.2011.05.028

Hoffmann, T. C., Glasziou, P. P., Boutron, I., Milne, R., Perera, R., Moher, D., … Michie, S. (2014). Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ*, *348*(mar07 3), g1687–g1687. https://doi.org/10.1136/bmj.g1687

Hoogendam, J. M., Ramakers, G. M. J., & Di Lazzaro, V. (2010). Physiology of repetitive transcranial magnetic stimulation of the human brain. *Brain Stimulation*, *3*(2), 95–118. https://doi.org/10.1016/j.brs.2009.10.005

Horvath, J. C., Perez, J. M., Forrow, L., Fregni, F., & Pascual-Leone, A. (2011). Transcranial magnetic stimulation: A historical evaluation and future prognosis of therapeutically relevant ethical concerns. *Journal of Medical Ethics*, *37*(3), 137–143. https://doi.org/10.1136/jme.2010.039966

Howard, D., Best, W., & Nickels, L. (2015). Optimising the design of intervention studies: critiques and ways forward. *Aphasiology*, *29*(5), 526–562. https://doi.org/10.1080/02687038.2014.985884

Howe, T. J., Worrall, L. E., & Hickson, L. M. H. (2008). Observing people with aphasia: Environmental factors that influence their community participation. *Aphasiology*, *22*(6), 618–643. https://doi.org/10.1080/02687030701536024

Hoy, K. E., Bailey, N., Michael, M., Fitzgibbon, B., Rogasch, N. C., Saeki, T., & Fitzgerald, P. B. (2016). Enhancement of Working Memory and Task-Related Oscillatory Activity Following Intermittent Theta Burst Stimulation in Healthy Controls. *Cerebral Cortex*, *26*(12), 4563–4573. https://doi.org/10.1093/cercor/bhv193

Huang, Y. Z., Edwards, M. J., Rounis, E., Bhatia, K. P., & Rothwell, J. C. (2005). Theta burst stimulation of the human motor cortex. *Neuron*, *45*(2), 201–206. https://doi.org/10.1016/j.neuron.2004.12.033

Ivanova, M. V., & Hallowell, B. (2014). A new modified listening span task to enhance validity of working memory assessment for people with and without aphasia. *Journal of Communication Disorders*, *52*, 78–98. https://doi.org/10.1016/j.jcomdis.2014.06.001

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Perrig, W. J. (2008). Improving fluid intelligence with training on working memory. *Proceedings of the National Academy of Sciences*, *105*(19), 6829–6833. https://doi.org/10.1073/pnas.0801268105

Johnson, S., Cocks, N., & Dipper, L. (2013). Use of spatial communication in aphasia. *International Journal of Language and Communication Disorders*, *48*(4), 469–476. https://doi.org/10.1111/1460-6984.12022

Jonides, J., Lewis, R. L., Nee, D. E., Lustig, C. A., Berman, M. G., & Moore, K. S. (2008). The Mind and Brain of Short-Term Memory. *Annual Review of Psychology*, *59*(1), 193–224. https://doi.org/10.1146/annurev.psych.59.103006.093615

Kambanaros, M. (2019). Evaluating Personal Stroke Narratives from Bilingual Greek-English Immigrants with Aphasia. *Folia Phoniatrica et Logopaedica*, *71*(2–3), 101–115. https://doi.org/10.1159/000493126

Kane, M. J., & Engle, R. W. (2002). The role of prefrontal cortex in working-memory capacity, executive attention, and general fluid intelligence: An individual-differences perspective. *Psychonomic Bulletin and Review*, *9*(4), 637–671. https://doi.org/10.3758/BF03196323

Karpathiou, N., Papatriantafyllou, J., & Kambanaros, M. (2018). Bilingualism in a Case of the Non-fluent/agrammatic Variant of Primary Progressive Aphasia. *Frontiers in Communication*, *3*(November), 1–16. https://doi.org/10.3389/fcomm.2018.00052

Kartsona, A., & Hilari, K. (2007). Quality of life in aphasia: Greek adaptation of the stroke and aphasia quality of life scale- 39 item (SAQOL-39). *Europa Medicophysica*, *43*(1), 27–35.

Kasselimis, D. (2015). Working Memory and Aphasia. *International Journal of Neurology*

Research, *1*(4), 188–190. https://doi.org/10.17554/j.issn.2313-5611.2015.01.27

Kazem, A. M., Alzubiadi, A. S., Yousif, Y. H., Aljamali, F. A., Al-Mashhdany, S. I.,
Alkharusi, H. A., … Al-Fori, S. M. (2007). Psychometric properties of Raven's Colored
progressive matrices for Omani children AGED 5 through 11 years. *Social Behavior and
Personality*, *35*(10), 1385–1398. https://doi.org/10.2224/sbp.2007.35.10.1385

Kemper, S., & Sumner, A. (2001). The structure of verbal abilities in young and older adults.
Psychology and Aging, *16*(2), 312–322. https://doi.org/10.1037/0882-7974.16.2.312

Keser, Z., & Francisco, G. E. (2016). Neuromodulation for Post-Stroke Aphasia. *Current
Physical Medicine and Rehabilitation Reports*, *4*(3), 171–181.
https://doi.org/10.1007/s40141-016-0123-8

Kim, C., Kroger, J. K., Calhoun, V. D., & Clark, V. P. (2015). The role of the frontopolar
cortex in manipulation of integrated information in working memory. *Neuroscience
Letters*, *595*, 25–29. https://doi.org/10.1016/j.neulet.2015.03.044

Kim, T. D., Hong, G., Kim, J., & Yoon, S. (2019). Cognitive enhancement in neurological
and psychiatric disorders using transcranial magnetic stimulation (TMS): A review of
modalities, potential mechanisms and future implications. *Experimental Neurobiology*.
Korean Society for Neurodegenerative Disease. https://doi.org/10.5607/en.2019.28.1.1

Kindler, J., Schumacher, R., Cazzoli, D., Gutbrod, K., Koenig, M., Nyffeler, T., … Müri, R.
M. (2012). Theta burst stimulation over the right brocaês homologue induces
improvement of naming in aphasic patients. *Stroke*, *43*(8), 2175–2179.
https://doi.org/10.1161/STROKEAHA.111.647503

Krakauer, J. W., Carmichael, S. T., Corbett, D., & Wittenberg, G. F. (2012). Getting
neurorehabilitation right: What can be learned from animal models? *Neurorehabilitation
and Neural Repair*, *26*(8), 923–931. https://doi.org/10.1177/1545968312440745

Kuroda, Y., Motohashi, N., Ito, H., Ito, S., Takano, A., Nishikawa, T., & Suhara, T. (2006).
Effects of repetitive transcranial magnetic stimulation on [11C]raclopride binding and
cognitive function in patients with depression. *Journal of Affective Disorders*, *95*(1–3),
35–42. https://doi.org/10.1016/j.jad.2006.03.029

Lam, J. M. C., & Wodchis, W. P. (2010). The relationship of 60 disease diagnoses and 15
conditions to preference-based health-related quality of life in ontario hospital-based
long-term care residents. *Medical Care*, *48*(4), 380–387.
https://doi.org/10.1097/MLR.0b013e3181ca2647

Lambon Ralph, M. A., Snell, C., Fillingham, J. K., Conroy, P., & Sage, K. (2010). Predicting

the outcome of anomia therapy for people with aphasia post CVA: Both language and cognitive status are key predictors. *Neuropsychological Rehabilitation*, *20*(2), 289–305. https://doi.org/10.1080/09602010903237875

Lefaucheur, J. P., André-Obadia, N., Antal, A., Ayache, S. S., Baeken, C., Benninger, D. H., … Garcia-Larrea, L. (2014). Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). *Clinical Neurophysiology*, *125*(11), 2150–2206. https://doi.org/10.1016/j.clinph.2014.05.021

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P. A., … Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Journal of Clinical Epidemiology*, *62*(10), e1–e34. https://doi.org/10.1016/j.jclinepi.2009.06.006

Łojek, E., & Bolewska, A. (2013). The effectiveness of computer-assisted cognitive rehabilitation in brain-damaged patients. *Polish Psychological Bulletin*, *44*(1), 31–39. https://doi.org/10.2478/ppb-2013-0004

Lundqvist, A., Grundstrm, K., Samuelsson, K., & Rönnberg, J. (2010). Computerized training of working memory in a group of patients suffering from acquired brain injury. *Brain Injury*, *24*(10), 1173–1183. https://doi.org/10.3109/02699052.2010.498007

Manning, M., MacFarlane, A., Hickey, A., & Franklin, S. (2019). Perspectives of people with aphasia post-stroke towards personal recovery and living successfully: A systematic review and thematic synthesis. *PLoS ONE*, *14*(3), 1–22. https://doi.org/10.1371/journal.pone.0214200

Marron, E. M., Viejo-Sobera, R., Palaus, M., Boixadós, M., Valero-Cabre, A., & Redolar-Ripoll, D. (2017). P237 Modulating executive functions and working memory performance on clinical neuropsychological tasks with theta burst transcranial magnetic stimulation. *Clinical Neurophysiology*, *128*(3), e130–e131. https://doi.org/10.1016/j.clinph.2016.10.353

Martin, N., Kohen, F., Kalinyak-Fliszar, M., Soveri, A., & Laine, M. (2012). Effects of working memory load on processing of sounds and meanings of words in aphasia. *Aphasiology*, *26*(3–4), 462–493. https://doi.org/10.1080/02687038.2011.619516

Martin, P. I., Naeser, M. A., Ho, M., Doron, K. W., Kurland, J., Kaplan, J., … Pascual-Leone, A. (2009). Overt naming fMRI pre- and post-TMS: Two nonfluent aphasia patients, with and without improved naming post-TMS. *Brain and Language*, *111*(1),

20–35. https://doi.org/10.1016/j.bandl.2009.07.007

Martis, B., Alam, D., Dowd, S. M., Hill, S. K., Sharma, R. P., Rosen, C., … Janicak, P. G. (2003). Neurocognitive effects of repetitive transcranial magnetic stimulation in severe major depression. *Clinical Neurophysiology*, *114*(6), 1125–1132. https://doi.org/10.1016/S1388-2457(03)00046-4

Mayer, J. F., & Murray, L. L. (2002). Approaches to the treatment of alexia in chronic aphasia. *Aphasiology*, *16*(7), 727–743. https://doi.org/10.1080/02687030143000870

Mays, N., Pope, C., & Popay, J. (2005). Systematically reviewing qualitative and quantitative evidence to inform management and policy-making in the health field. *Journal of Health Services Research and Policy*, *10*(SUPPL. 1), 6–20. https://doi.org/10.1258/1355819054308576

Meinzer, M., Flaisch, T., Breitenstein, C., Wienbruch, C., Elbert, T., & Rockstroh, B. (2008). Functional re-recruitment of dysfunctional brain areas predicts language recovery in chronic aphasia. *NeuroImage*, *39*(4), 2038–2046. https://doi.org/10.1016/j.neuroimage.2007.10.008

Merton, P. A., & Morton, H. B. (1980). Stimulation of the cerebral cortex in the intact human subject. *Nature*. https://doi.org/10.1038/285227a0

Mile, V. (2018). Communication Related Quality of Life with Different Types of Aphasia Following a Stroke: Preliminary Insights. *International Archives of Communication Disorder*, *1*(1). https://doi.org/10.23937/iacod-2017/1710004

Miniussi, C., Cappa, S. F., Cohen, L. G., Floel, A., Fregni, F., Nitsche, M. A., … Walsh, V. (2008). Efficacy of repetitive transcranial magnetic stimulation/transcranial direct current stimulation in cognitive neurorehabilitation. *Brain Stimulation*, *1*(4), 326–336. https://doi.org/10.1016/j.brs.2008.07.002

Miniussi, C., & Rossini, P. M. (2011). Transcranial magnetic stimulation in cognitive rehabilitation. *Neuropsychological Rehabilitation*, *21*(5), 579–601. https://doi.org/10.1080/09602011.2011.562689

Minkina, I., Rosenberg, S., Kalinyak-Fliszar, M., & Martin, N. (2017). Short-Term Memory and Aphasia: From Theory to Treatment. *Seminars in Speech and Language*, *38*(1), 17–28. https://doi.org/10.1055/s-0036-1597261

Murray, L. L. (2012). Direct and indirect treatment approaches for addressing short-term or working memory deficits in aphasia. *Aphasiology*, *26*(3–4), 317–337. https://doi.org/10.1080/02687038.2011.589894

Nicholas, L. E., & Brookshire, R. H. (1993). A system for quantifying the informativeness and efficiency of the connected speech of adults with aphasia. *Journal of Speech and Hearing Research*, *36*(2), 338–350. https://doi.org/10.1044/jshr.3602.338

Nicholas, M., Hunsaker, E., & Guarino, A. J. (2017). The relation between language, non-verbal cognition and quality of life in people with aphasia. *Aphasiology*, *31*(6), 688–702. https://doi.org/10.1080/02687038.2015.1076927

O'Connor, M., Brenninkmeyer, C., Morgan, A., Bloomingdale, K., Thall, M., Vasile, R., & Leone, A. P. (2003). Relative effects of repetitive transcranial magnetic stimulation and electroconvulsive therapy on mood and memory: A neurocognitive risk-benefit analysis. *Cognitive and Behavioral Neurology*, *16*(2), 118–127. https://doi.org/10.1097/00146965-200306000-00005

Olesen, P. J., Westerberg, H., & Klingberg, T. (2004). Increased prefrontal and parietal activity after training of working memory. *Nature Neuroscience*, *7*(1), 75–79. https://doi.org/10.1038/nn1165

Osaka, M., Osaka, N., Kondo, H., Morishita, M., Fukuyama, H., Aso, T., & Shibasaki, H. (2003). The neural basis of individual differences in working memory capacity: An fMRI study. *NeuroImage*, *18*(3), 789–797. https://doi.org/10.1016/S1053-8119(02)00032-0

Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. *Human Brain Mapping*, *25*(1), 46–59. https://doi.org/10.1002/hbm.20131

Papantoniou, G., Moraitou, D., Dinou, M., Katsadima, E., Savvidou, E., & Foutsitzi, E. (2016). Comparing the Latent Structure of the Children's Category Test-Level 1 among Young Children and Older Adults: A Preliminary Study. *Psychology*, *07*(11), 1352–1368. https://doi.org/10.4236/psych.2016.711137

Papazachariadis, O., Dante, V., Verschure, P. F. M. J., Giudice, P. Del, & Ferraina, S. (2014). ITBS-induced LTP-like plasticity parallels oscillatory activity changes in the primary sensory and motor areas of macaque monkeys. *PLoS ONE*, *9*(11), 1–10. https://doi.org/10.1371/journal.pone.0112504

Pascual-Leone, A., Freitas, C., Oberman, L., Horvath, J. C., Halko, M., Eldaief, M., … Rotenberg, A. (2011). Characterizing Brain Cortical Plasticity and Network Dynamics Across the Age-Span in Health and Disease with TMS-EEG and TMS-fMRI. *Brain Topography*, *24*(3–4), 302–315. https://doi.org/10.1007/s10548-011-0196-8

Pearce, A. J., Lum, J. A. G., Seth, S., Rafael, O., Hsu, C. M. K., Drury, H. G. K., & Tooley, G. A. (2014). Multiple bout rTMS on spatial working memory: A comparison study of two cortical areas. *Biological Psychology*, *100*(1), 56–59. https://doi.org/10.1016/j.biopsycho.2014.05.002

Pessoa, L., Gutierrez, E., Bandettini, P., & Ungerleider, L. (2002). Neural correlates of visual working memory: fMRI amplitude predicts task performance. *Neuron*, *35*(5), 975–987. https://doi.org/10.1016/S0896-6273(02)00817-6

Potagas, C., Kasselimis, D., & Evdokimidis, I. (2011). Short-term and working memory impairments in aphasia. *Neuropsychologia*, *49*(10), 2874–2878. https://doi.org/10.1016/j.neuropsychologia.2011.06.013

Pritchard, M., Dipper, L., Morgan, G., & Cocks, N. (2015). Language and iconic gesture use in procedural discourse by speakers with aphasia. *Aphasiology*, *29*(7), 826–844. https://doi.org/10.1080/02687038.2014.993912

Rektorova, I., Megova, S., Bares, M., & Rektor, I. (2005). Cognitive functioning after repetitive transcranial magnetic stimulation in patients with cerebrovascular disease without dementia: A pilot study of seven patients. *Journal of the Neurological Sciences*, *229–230*, 157–161. https://doi.org/10.1016/j.jns.2004.11.021

Richardson, J. D., & Dalton, S. G. (2016). Main concepts for three different discourse tasks in a large non-clinical sample. *Aphasiology*, *30*(1), 45–73. https://doi.org/10.1080/02687038.2015.1057891

Rossi, S., Hallett, M., Rossini, P. M., & Pascual-Leone, A. (2009). Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology*, *120*(12), 2008–2039. https://doi.org/10.1016/j.clinph.2009.08.016

Rossini, P. M., Burke, D., Chen, R., Cohen, L. G., Daskalakis, Z., Di Iorio, R., … Ziemann, U. (2015). Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: Basic principles and procedures for routine clinical and research application: An updated report from an I.F.C.N. Committee. *Clinical Neurophysiology*, *126*(6), 1071–1107. https://doi.org/10.1016/j.clinph.2015.02.001

Rothkegel, H., Sommer, M., & Paulus, W. (2010). Breaks during 5 Hz rTMS are essential for facilitatory after effects. *Clinical Neurophysiology*, *121*(3), 426–430. https://doi.org/10.1016/j.clinph.2009.11.016

Rubi-Fessen, I., Hartmann, A., Huber, W., Fimm, B., Rommel, T., Thiel, A., & Heiss, W. D.

(2015). Add-on Effects of Repetitive Transcranial Magnetic Stimulation on Subacute Aphasia Therapy: Enhanced Improvement of Functional Communication and Basic Linguistic Skills. A Randomized Controlled Study. *Archives of Physical Medicine and Rehabilitation*, *96*(11), 1935-1944.e2. https://doi.org/10.1016/j.apmr.2015.06.017

Sack, A. T., & Linden, D. E. J. (2003). Combining transcranial magnetic stimulation and functional imaging in cognitive brain research: Possibilities and limitations. *Brain Research Reviews*, *43*(1), 41–56. https://doi.org/10.1016/S0165-0173(03)00191-7

Salis, C. (2012). Short-term memory treatment: Patterns of learning and generalisation to sentence comprehension in a person with aphasia. *Neuropsychological Rehabilitation*, *22*(3), 428–448. https://doi.org/10.1080/09602011.2012.656460

Salis, C., Hwang, F., Howard, D., & Lallini, N. (2017). Short-Term and Working Memory Treatments for Improving Sentence Comprehension in Aphasia: A Review and a Replication Study. *Seminars in Speech and Language*, *38*(1), 29–39. https://doi.org/10.1055/s-0036-1597262

Salis, C., Kelly, H., & Code, C. (2015). Assessment and treatment of short-term and working memory impairments in stroke aphasia: A practical tutorial. *International Journal of Language and Communication Disorders*, *50*(6), 721–736. https://doi.org/10.1111/1460-6984.12172

Sandrini, M., Umiltà, C., & Rusconi, E. (2011). The use of transcranial magnetic stimulation in cognitive neuroscience: A new synthesis of methodological issues. *Neuroscience and Biobehavioral Reviews*, *35*(3), 516–536. https://doi.org/10.1016/j.neubiorev.2010.06.005

Schulze-Rauschenbach, S. C., Harms, U., Schlaepfer, T. E., Maier, W., Falkai, P., & Wagner, M. (2005). Distinctive neurocognitive effects of repetitive transcranial magnetic stimulation and electroconvulsive therapy in major depression. *British Journal of Psychiatry*, *186*(MAY), 410–416. https://doi.org/10.1192/bjp.186.5.410

Seniów, J., Litwin, M., & Leśniak, M. (2009). The relationship between non-linguistic cognitive deficits and language recovery in patients with aphasia. *Journal of the Neurological Sciences*, *283*(1–2), 91–94. https://doi.org/10.1016/j.jns.2009.02.315

Shewan, C. M. (1988). The Shewan Spontaneous Language Analysis (SSLA) system for aphasic adults: Description, reliability, and validity. *Journal of Communication Disorders*, *21*(2), 103–138. https://doi.org/10.1016/0021-9924(88)90001-9

Shewan, C. M., & Henderson, V. L. (1988). Analysis of spontaneous language in the older

normal population. *Journal of Communication Disorders*, *21*(2), 139–154. https://doi.org/10.1016/0021-9924(88)90002-0

Singal, A. G., Higgins, P. D. R., & Waljee, A. K. (2014). A primer on effectiveness and efficacy trials. *Clinical and Translational Gastroenterology*, *5*(2), e45-4. https://doi.org/10.1038/ctg.2013.13

Smith, E. E., Jonides, J., & Koeppe, R. A. (1996). Dissociating Verbal and Spatial Working Memory Using PET. *Cerebral Cortex*, *6*(1), 11–20. https://doi.org/10.1093/cercor/6.1.11

Spaccavento, S., Craca, A., Del Prete, M., Falcone, R., Colucci, A., Di Palma, A., & Loverre, A. (2013). Quality of life measurement and outcome in aphasia. *Neuropsychiatric Disease and Treatment*, *10*, 27. https://doi.org/10.2147/NDT.S52357

Sternberg, R. J. (2008). Increasing fluid intelligence is possible after all. *Proceedings of the National Academy of Sciences of the United States of America*, *105*(19), 6791–6792. https://doi.org/10.1073/pnas.0803396105

Stinear, C., Ackerley, S., & Byblow, W. (2013). Rehabilitation is initiated early after stroke, but most motor rehabilitation trials are not: A systematic review. *Stroke*, *44*(7), 2039–2045. https://doi.org/10.1161/STROKEAHA.113.000968

Stinear, C. M. (2016). Stroke rehabilitation research needs to be different to make a difference [version 1; referees: 2 approved]. *F1000Research*, *5*, 1–5. https://doi.org/10.12688/F1000RESEARCH.8722.1

Szaflarski, J. P., Vannest, J., Wu, S. W., Difrancesco, M. W., Banks, C., & Gilbert, D. L. (2011). Excitatory repetitive transcranial magnetic stimulation induces improvements in chronic post-stroke aphasia. *Medical Science Monitor*, *17*(3), 6. https://doi.org/10.12659/msm.881446

Takeuchi, H., Sekiguchi, A., Taki, Y., Yokoyama, S., Yomogida, Y., Komuro, N., … Kawashima, R. (2010). Training of working memory impacts structural connectivity. *Journal of Neuroscience*, *30*(9), 3297–3303. https://doi.org/10.1523/JNEUROSCI.4611-09.2010

Tatemichi, T. K., Desmond, D. W., Stern, Y., Paik, M., Sano, M., & Bagiella, E. (1994). Cognitive impairment after stroke: Frequency, patterns, and relationship to functional abilities. *Journal of Neurology Neurosurgery and Psychiatry*, *57*(2), 202–207. https://doi.org/10.1136/jnnp.57.2.202

Thiel, A., Hartmann, A., Rubi-Fessen, I., Anglade, C., Kracht, L., Weiduschat, N., … Heiss, W. D. (2013). Effects of noninvasive brain stimulation on language networks and

recovery in early poststroke aphasia. *Stroke*, *44*(8), 2240–2246. https://doi.org/10.1161/STROKEAHA.111.000574

Thielscher, A., & Kammer, T. (2004). Electric field properties of two commercial figure-8 coils in TMS: Calculation of focality and efficiency. *Clinical Neurophysiology*, *115*(7), 1697–1708. https://doi.org/10.1016/j.clinph.2004.02.019

Thompson, C. K. (2006). Single subject controlled experiments in aphasia: The science and the state of the science. *Journal of Communication Disorders*, *39*(4), 266–291. https://doi.org/10.1016/j.jcomdis.2006.02.003

Tippett, D. C., Niparko, J. K., & Hillis, A. E. (2014). Aphasia: Current Concepts in Theory and Practice. *Journal of Neurology & Translational Neuroscience*, *2*(1), 1042. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/24904925%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4041294

Tsapkini, K., Vlahou, C. H., & Potagas, C. (2009). Adaptation and validation of standardized aphasia tests in different languages: Lessons from the Boston diagnostic aphasia examination - Short form in Greek. *Behavioural Neurology*, *22*(3–4), 111–119. https://doi.org/10.3233/BEN-2009-0256

Turken, A. U., & Dronkers, N. F. (2011). The neural architecture of the language comprehension network: Converging evidence from lesion and connectivity analyses. *Frontiers in Systems Neuroscience*, *5*(FEBRUARY 2011), 1–20. https://doi.org/10.3389/fnsys.2011.00001

Turkstra, L. S., Norman, R., Whyte, J., Dijkers, M. P., & Hart, T. (2016). Knowing What We're Doing: Why Specification of Treatment Methods Is Critical for Evidence-Based Practice in Speech-Language Pathology. *American Journal of Speech-Language Pathology*, *25*(2), 164–171. https://doi.org/10.1044/2015_AJSLP-15-0060

Ulatowska, H. K., North, A. J., & Macaluso-Haynes, S. (1981). Production of narrative and procedural discourse in aphasia. *Brain and Language*, *13*(2), 345–371. https://doi.org/10.1016/0093-934X(81)90100-0

Unsworth, N., Fukuda, K., Awh, E., & Vogel, E. K. (2014). Working memory and fluid intelligence: Capacity, attention control, and secondary memory retrieval. *Cognitive Psychology*, *71*(3), 1–26. https://doi.org/10.1016/j.cogpsych.2014.01.003

Vallar, G., & Bolognini, N. (2011). Behavioural facilitation following brain stimulation: Implications for neurorehabilitation. *Neuropsychological Rehabilitation*, *21*(5), 618–

649. https://doi.org/10.1080/09602011.2011.574050

Vallat, C., Azouvi, P., Hardisson, H., Meffert, R., Tessier, C., & Pradat-Diehl, P. (2005). Rehabilitation of verbal working memory after left hemisphere stroke. *Brain Injury*, *19*(13), 1157–1164. https://doi.org/10.1080/02699050500110595

Vallila-Rohter, S., & Kiran, S. (2013). Non-linguistic learning and aphasia: Evidence from a paired associate and feedback-based task. *Neuropsychologia*, *51*(1), 79–90. https://doi.org/10.1016/j.neuropsychologia.2012.10.024

Wager, T. D., & Smith, E. E. (2003). Neuroimaging studies of working memory: A meta-analysis. *Cognitive, Affective and Behavioral Neuroscience*, *3*(4), 255–274. https://doi.org/10.3758/CABN.3.4.255

Westerberg, H., Jacobaeus, H., Hirvikoski, T., Clevberger, P., Östensson, M. L., Bartfai, A., & Klingberg, T. (2007). Computerized working memory training after stroke - A pilot study. *Brain Injury*, *21*(1), 21–29. https://doi.org/10.1080/02699050601148726

Wilson, B. (1987). Single-case experimental designs in neuropsychological rehabilitation. *Journal of Clinical and Experimental Neuropsychology : Official Journal of the International Neuropsychological Society*, *9*(5), 527–544. https://doi.org/10.1080/01688638708410767

Woolgar, A., Parr, A., Cusack, R., Thompson, R., Nimmo-Smith, I., Torralva, T., … Duncan, J. (2010). Fluid intelligence loss linked to restricted regions of damage within frontal and parietal cortex. *Proceedings of the National Academy of Sciences of the United States of America*, *107*(33), 14899–14902. https://doi.org/10.1073/pnas.1007928107

Worrall, L. E., & Holland, A. L. (2003). Editorial: Quality of life in aphasia. *Aphasiology*, *17*(4), 329–332. https://doi.org/10.1080/02687030244000699

Wright, H. H., & Fergadiotis, G. (2012). Conceptualising and measuring working memory and its relationship to aphasia. *Aphasiology*, *26*(3–4), 258–278. https://doi.org/10.1080/02687038.2011.604304

Wright, H. H., & Fergadiotis, G. (2013). Conceptualizing and Measuring Working Memory and its Relationship to Aphasia, *26*, 258–278. https://doi.org/10.1080/02687038.2011.604304.Conceptualizing

Yoo, C., Yong, M. H., Chung, J., & Yang, Y. (2015). Effect of computerized cognitive rehabilitation program on cognitive function and activities of living in stroke patients. *Journal of Physical Therapy Science*, *27*(8), 2487–2489. https://doi.org/10.1589/jpts.27.2487

Youse, K. M., & Coelho, C. A. (2005). Working memory and discourse production abilities following closed-head injury. *Brain Injury*, *19*(12), 1001–1009. https://doi.org/10.1080/02699050500109951

Zakariás, L., Keresztes, A., Marton, K., & Wartenburger, I. (2018). Positive effects of a computerised working memory and executive function training on sentence comprehension in aphasia. *Neuropsychological Rehabilitation*, *28*(3), 369–386. https://doi.org/10.1080/09602011.2016.1159579

Appendix I: Ethical Committee Approval

ΚΥΠΡΙΑΚΗ ΔΗΜΟΚΡΑΤΙΑ
ΕΘΝΙΚΗ ΕΠΙΤΡΟΠΗ ΒΙΟΗΘΙΚΗΣ ΚΥΠΡΟΥ

Αρ. Φακ.: ΕΕΒΚ/ΕΠ /2017/37
Αρ. Τηλ.: 22809038 / 22809039
Αρ. Φαξ: 22353878

07 Φεβρουαρίου 2018

Δρ Μαρία Καμπανάρου
Αναπληρώτρια Καθηγήτρια
Τμήμα Επιστημών Αποκατάστασης
Τεχνολογικό Πανεπιστήμιο Κύπρου
Βραγαδίνου 15
3041 Λεμεσός

<u>Ερευνητική πρόταση με τίτλο:</u>
<u>« Neurorehabilitation using transcranial magnetic stimulation- Νευρολογική
Αποκατάσταση με τη Χρήση Διακρανιακής Μαγνητικής Διέγερσης »</u>

Επιθυμώ να αναφερθώ στο πιο πάνω θέμα και να σας πληροφορήσω ότι η Επιτροπή Βιοηθικής Αξιολόγησης Βιοϊατρικής Έρευνας ενεργώντας με βάση την εκχωρηθείσα σ' αυτήν αρμοδιότητα από την Εθνική Επιτροπή Βιοηθικής Κύπρου, να αξιολογεί βιοηθικά ερευνητικές προτάσεις που αφορούν την βιοϊατρική έρευνα στον άνθρωπο, έχει πραγματοποιήσει την βιοηθική αξιολόγηση της πιο πάνω ερευνητικής σας πρότασης, η οποία σας αποστέλλεται συνημμένα.

2. Σε σχέση με την επισήμανσή σας κατά πόσον «ισχύει η δυνατότητα λήψης «ανοικτής συγκατάθεσης» -όπως αναφέρεται στην Γνώμη της Εθνικής Επιτροπής Βιοηθικής περί «Δημιουργίας και χρήσης βιοτραπεζών και αρχείων βιολογικών δειγμάτων ανθρώπινης προέλευσης για σκοπούς έρευνας» όπως αναφέρεται στην Παράγραφο 7 σελίδα 10/21 και στην Παράγραφο 8 (σελίδα 11/21), όπου «Ανοικτή» συγκατάθεση είναι εκείνη η οποία θα δίδεται για ένα συγκεκριμένο ερευνητικό πρόγραμμα αλλά οι δότες θα δίδουν και την άδεια τους για να χρησιμοποιηθούν τα δείγματα/ουσίες τους και σε άλλα μελλοντικά προγράμματα χωρίς κατ' ανάγκη να γνωρίζουν αρκετές πληροφορίες για αυτά, η Επιτροπή επιβεβαιώνει ότι αυτή η δυνατότητα ισχύει.

…../2….

Κέντρο Υγείας Έγκωμης, Νίκου Κρανιδιώτη, 2411 Έγκωμη, Λευκωσία
Ηλεκτρονικό Ταχυδρομείο: cnbc@bioethics.gov.cy Ιστοσελίδα: www.bioethics.gov.cy

3.   Ωστόσο, η «ανοικτή» συγκατάθεση δεν συνεπάγεται τη φύλαξη/επεξεργασία δεδομένων επ' αόριστον, αλλά για συγκεκριμένο χρονικό διάστημα. Επισημαίνουμε, σύμφωνα με τον Νόμο 138 (1) του 2001, τον πρόσφατο Κανονισμό (ΕΕ) 2016/679 για την προστασία των φυσικών προσώπων έναντι της επεξεργασίας των δεδομένων προσωπικού χαρακτήρα και την κατάργηση της οδηγίας 95/46/ΕΚ (Γενικός Κανονισμός για την Προστασία Δεδομένων), και σύμφωνα με τις γενικές αρχές που διέπουν την προστασία των προσωπικών δεδομένων: Ο υπεύθυνος επεξεργασίας, κατά τη λήψη των δεδομένων προσωπικού χαρακτήρα, παρέχει στο υποκείμενο των δεδομένων επιπλέον πληροφορίες που είναι αναγκαίες για την εξασφάλιση θεμιτής και διαφανούς επεξεργασίας, μεταξύ των οποίων, και για το χρονικό διάστημα για το οποίο θα αποθηκευτούν τα δεδομένα προσωπικού χαρακτήρα ή, όταν αυτό είναι αδύνατο, τα κριτήρια που καθορίζουν το εν λόγω διάστημα.

Με εκτίμηση,

Δρ Μαρία Καρεκλά
Πρόεδρος
Επιτροπής Βιοηθικής Αξιολόγησης
Βιοϊατρικής Έρευνας

ΑΠΟΦΑΣΗ
ΕΠΙΤΡΟΠΗΣ ΒΙΟΗΘΙΚΗΣ
ΓΙΑ
ΕΓΚΡΙΣΗ Ή ΑΠΟΡΡΙΨΗ
ΠΡΟΓΡΑΜΜΑΤΟΣ

Η απόφαση της Επιτροπής Βιοηθικής θα πρέπει να κοινοποιηθεί προς την Εθνική Επιτροπή Βιοηθικής Κύπρου μαζί με όλα τα υπόλοιπα έντυπα που αφορούν το πρόγραμμα για το οποίο λήφθηκε σχετική απόφαση.

<u>Συμπληρώνεται από την Επιτροπή Βιοηθικής</u>

Τίτλος Προγράμματος για το οποίο γίνεται η αίτηση
«Neurorehabilitation using transcranial magnetic stimulation- Νευρολογική Αποκατάσταση με τη Χρήση Διακρανιακής Μαγνητικής Διέγερσης »

Επιστημονικός Υπεύθυνος του Προγράμματος
Δρ. Μαρία Καμπανάρου

Όνομα Επιτροπής Βιοηθικής
Επιτροπή Βιοηθικής Αξιολόγησης Βιοϊατρικής Έρευνας στον Άνθρωπο

Μέλη της Επιτροπής Βιοηθικής	
Όνομα	Επίθετο
Ανδρέας	Ζαχαριάδης
Γιασεμίνα	Καραγιώργη
Καλυψώ	Ιορδάνους
Μαρία	Αγγελή
Μαρία	Καρεκλά
Παύλος	Πολυκάρπου
Χρίστια	Μίτλεττον
Χριστίνα	Θεράποντος
Χρίστος	Σιαμμάς

Σχόλια από την Επιτροπή Βιοηθικής με βάση τα οποία λήφθηκε η απόφαση για την αίτηση που υποβλήθηκε
Η Επιτροπή κατά τη σημερινή συνεδρίαση της ημερομηνίας 07/02/2018, πραγματοποίησε τη βιοηθική αξιολόγηση των πρόσθετων ή/και αναθεωρημένων εγγράφων που κατατέθηκαν στις 22/01/2018 σε συνέχεια απόφασης της Επιτροπής ημερομηνίας 18/12/2017. Τα σχόλια της Επιτροπής κατά τη σημερινή συνεδρίαση παρουσιάζονται με έντονα μαύρα γράμματα.   **Θερμή παράκληση της Επιτροπής όπως οι διορθώσεις/αλλαγές γίνονται με επισήμανση αλλαγών (track changes). Επίσης, να κατατίθεται καλυπτική επιστολή στην οποία θα επεξηγείται η διαχείριση του κάθε σχολίου της Επιτροπής με αναφορά στον αριθμό του σημείου στο οποίο αναφέρονται.**   <u>Έντυπο ΕΕΒΚ02:</u>   <u>Η Επιτροπή παρακαλεί όπως υποβληθεί το ΕΕΒΚ02, αναθεωρημένο, στη βάση των διευκρινήσεων της ερευνητικής ομάδας όπως παρέχονται στην καλυπτική επιστολή.</u> **Απαντήθηκε.**   1. Στη σελ. 6 στις πληροφορίες για τη στρατολόγηση των συμμετεχόντων γίνεται αναφορά σε διάφορα πλαίσια από τα οποία θα αντληθούν επιλέξιμα άτομα. Στο πρωτόκολλο της έρευνας αναφέρεται επίσης: «*In order to participate in this study patients must present with unilateral damage subsequent to one (only) cerebrovascular accident (CVA)/stroke and fulfill the criteria outlined below*». Το πρωτόκολλο παραθέτει κριτήρια συμπερίληψης/αποκλεισμού τα

οποία περιλαμβάνουν και στοιχεία ιατρικού ιστορικού. Συνεπώς, η ερευνητική ομάδα καλείται να παράσχει περισσότερες πληροφορίες για τον τρόπο στρατολόγησης. Πώς ακριβώς θα αντληθούν αυτές οι πληροφορίες; Πώς θα προσεγγιστούν αυτά τα άτομα; Πώς θα διασφαλιστεί η αξιοπιστία των πληροφοριών, ειδικά αν αυτές υποβληθούν από τους ίδιους τους συμμετέχοντες; Επίσης, να επισυναφθούν δηλώσεις για ενδιαφέρον για συμμετοχή από τα δημόσια νοσοκομεία και τα ιδιωτικά κέντρα αποκατάστασης κτλ.

Σχόλιο 18/12/2017: Η ερευνητική ομάδα παρακαλείται όπως προχωρήσει σε προσαρμογή του εντύπου ΕΕΒΚ 03, ούτως ώστε οι συμμετέχοντες να ενημερώνονται για τη διαδικασία αξιολόγησης με χρήση των ερωτηματολογίων 1-7, που αναφέρονται στο ερευνητικό πρωτόκολλο (σ.5). **Απαντήθηκε.**

2. Στη σελ. 10 αναφέρεται ότι θα ακολουθηθούν *«safety guidelines that are designed to minimize the risk of seizures (Wassermann, 1998). Moreover, all researchers employed in the study have been trained in First Aid and are fully capable of handling a seizure in the unlikely event that one might take place.».* Η ερευνητική ομάδα να καθορίσει ποια ακριβώς μέτρα ασφαλείας θα λάβει για να ελαχιστοποιήσει αυτή την πιθανότητα.

Σχόλιο 18/12/2017: Απαντήθηκε. Εφόσον η ερευνητική ομάδα στην καλυπτική επιστολή (σ. 3) διευκρινίζει ότι οι θεραπείες θα διενεργούνται στην παρουσία ατόμου με δίπλωμα πρώτων βοηθειών που θα μπορεί να διαχειρίζεται επιληπτικές κρίσεις, η ερευνητική ομάδα καλείται όπως προσδιορίσει αυτό το άτομο και προωθήσει σημείωμα από το εν λόγω άτομο ότι αποδέχεται να έχει αυτό το ρόλο σε όλες τις συνεδρίες που αφορούν στη ΔΜΔ. **Απαντήθηκε.**

3. Στη σελ. 12, στις προϋποθέσεις που αφορούν τη χρήση TMS (Trained in using the specific TMS equipment, In possession of a First Aid diploma) η ερευνητική ομάδα δηλώνει ότι τα μέλη της (*«all TMS investigators»*) έχουν το σχετικό υπόβαθρο που απαιτείται. Η Επιτροπή παρακαλεί όπως η ερευνητική ομάδα τεκμηριώσει τη θέση αυτή περαιτέρω, υποβάλλοντας σχετικά έγγραφα που πιστοποιούν αυτό το υπόβαθρο (π.χ. δίπλωμα πρώτων βοηθειών). Η ερευνητική ομάδα καλείται, επίσης, να καθορίσει ονομαστικά τα άτομα αυτά. Επισημαίνεται ότι στη σελ. 2 γίνεται αναφορά μόνο στον κ. Νίκο Κωνσταντίνου ως *«Neuroscientist, responsible for neuroimaging (brain MRI) and TMS sessions».*

Σχόλιο 18/12/2017: Απαντήθηκε. Εφόσον η ερευνήτρια στην καλυπτική επιστολή (σ. 3) αναφέρει ότι θα ενημερώσει την ΕΕΒΚ με τα ονόματα των ερευνητών που θα είναι κάτοχοι διπλώματος Πρώτων Βοηθειών παρακαλείται όπως προχωρήσει σε σχετική ενημέρωση της Επιτροπής πριν ξεκινήσει τη διαδικασία της παρέμβασης με ΔΜΔ. **Αναμένεται η σχετική ενημέρωση, όπως διευκρινίζει σχετικά η ερευνητική ομάδα.**

4. Στη σελ. 14 επισημαίνεται ότι *«Samples will be safely destroyed five years after collection unless participants consent to the use of their samples by future studies by the principal investigator of the current study, pending approval by the Cyprus National Bioethics Committee.»* Επισημαίνεται ότι η φύλαξη των δειγμάτων για περίοδο πάνω των 5 χρόνων για αόριστο χρονικό διάστημα δεν είναι αποδεκτή από την Επιτροπή. Η ερευνητική ομάδα πρέπει

253

να καθορίσει επακριβώς περίοδο φύλαξης και να περιορίσει την χρήση σε μελέτες συγκεκριμένου περιεχομένου/στόχευσης.

Σχόλιο 18/12/2017: Δεν απαντήθηκε. Η ερευνητική ομάδα παρακαλείται όπως καθορίσει χρονικό διάστημα για το οποίο θα ισχύει η μελλοντική χρήση των δεδομένων, καθώς η φύλαξη για «αόριστο χρονικό διάστημα» δεν μπορεί να γίνει αποδεκτή. Ζητείται η συναίνεση των συμμετεχόντων για χρήση των δεδομένων για περίοδο 10 ετών. **Απαντήθηκε.**

Έντυπο ΕΕΒΚ03:

5. Στα έντυπα γίνεται η εξής αναφορά: «*Τα βιολογικά μου δείγματα και όλες οι λοιπές πληροφορίες που θα συλλεγούν για τους σκοπούς του παρόντος ερευνητικού προγράμματος μπορούν να κρατηθούν πέραν των 5 χρόνων και να χρησιμοποιηθούν σε μελλοντικές μελέτες αφού πρώτα εγκριθεί κάτι τέτοιο από την Εθνική Επιτροπή Βιοηθικής Κύπρου μέσω νέας αίτησης ή μετά από σχετικό αίτημα ανανέωσης σε περίπτωση επέκτασης της παρούσας μελέτης από τον υπεύθυνο ερευνητή του προγράμματος*». Επισημαίνεται στην ερευνητική ομάδα ότι μία τέτοια γενικού τύπου συναίνεση για φύλαξη βιολογικών δειγμάτων πέραν των 5 χρόνων δεν είναι αποδεκτή (σημείο πιο πάνω).

   Σχόλιο 18/12/2017: Δεν απαντήθηκε. Η ερευνητική ομάδα παρακαλείται όπως καθορίσει χρονικό διάστημα για το οποίο θα ισχύει η μελλοντική χρήση των δεδομένων, καθώς η φύλαξη για «αόριστο χρονικό διάστημα» δεν μπορεί να γίνει αποδεκτή. Ζητείται η συναίνεση των συμμετεχόντων για χρήση των δεδομένων για περίοδο 10 ετών. **Απαντήθηκε.**

6. Να γίνει γλωσσικός έλεγχος στα εν λόγω έγγραφα και να γίνει διόρθωση των ορθογραφικών/συντακτικών λαθών.

   Σχόλιο 18/12/2017: Απαντήθηκε. Ωστόσο, σε κάποια έντυπα συναίνεσης που αφορούν σε παρέμβαση για κινητικά προβλήματα γίνεται αναφορά σε 'Γλωσσική Αξιολόγηση'. Η ερευνητική ομάδα καλείται όπως προβεί σε προσεκτικό έλεγχο όλων των εντύπων για να διασφαλιστεί η προσαρμογή του λεκτικού σε κάθε υπο-ομάδα πληθυσμού. **Απαντήθηκε.**

7. Στο πρωτόκολλο της έρευνας αναφέρεται: «*Patients will be informed in the consent form that they can be informed about the results of the study relevant to them following completion of the study.*». Στο έντυπο συναίνεσης, ωστόσο, οι συμμετέχοντες ερωτώνται κατά πόσον θα ήθελαν να ενημερωθούν για τα αποτελέσματα της έρευνας που τους αφορούν. Η ερευνητική ομάδα να παράσχει περισσότερες πληροφορίες ως προς το είδος των αποτελεσμάτων που θα είναι προσβάσιμα σε κάθε ομάδα και τον τρόπο ενημέρωσής των συμμετεχόντων για αυτά.

   Σχόλιο 18/12/2017: Η ερευνητική ομάδα έχει προβεί σε σχετικές διευκρινήσεις προς την Επιτροπή (στην επιστολή), οι οποίες θα πρέπει να ενσωματωθούν στο έντυπο ΕΕΒΚ03 για ενημέρωση των συμμετεχόντων. **Απαντήθηκε.**

Γενικά Σχόλια:

8. Η ερευνητική ομάδα να διευκρινίσει περαιτέρω ότι οι συμμετέχοντες δεν θα επιβαρυνθούν με οποιοδήποτε κόστος ως προς τη συμμετοχή τους, καθώς δεν είναι ξεκάθαρο κατά πόσον τα διαγνωστικά κέντρα θα καλύψουν με δικά τους

έξοδα το κόστος της μαγνητικής τομογραφίας.

Σχόλιο 18/12/2017: Η ερευνητική ομάδα παρακαλείται όπως προωθήσει στην Επιτροπή τον προϋπολογισμό του προγράμματος, εφόσον η κάλυψη των εξόδων θα γίνει από το ερευνητικό πρόγραμμα. **Έχει προωθηθεί σχετική βεβαίωση από την επιστημονική υπεύθυνη για την κάλυψη των εξόδων από εσωτερικά κονδύλια του ΤΕΠΑΚ. Απαντήθηκε.**

9. Η ερευνητική ομάδα παρακαλείται όπως διευκρινίσει πώς θα διαχειριστεί περιπτώσεις συμμετεχόντων, οι οποίοι θα παρουσιάζουν συμπτώματα κατάθλιψης ή άλλης ψυχοπαθολογίας (στη βάση των δηλώσεων τους στα ερωτηματολόγια).

   Σχόλιο 18/12/2017: Δεν απαντήθηκε. Η ερευνητική ομάδα διευκρινίζει στην καλυπτική επιστολή (σ. 5) ότι θα άτομα θα ενημερώνονται για τα ευρήματα από ψυχίατρο ή κλινικό ψυχολόγο και θα παραπέμπονται για σχετική στήριξη. Η ερευνητική ομάδα παρακαλείται όπως καθορίσει αυτό το άτομο και διευκρινίσει κατά πόσον θα είναι μέλος της ερευνητικής ομάδας. Σε περίπτωση που θα είναι μέλος της ερευνητικής ομάδας θα πρέπει να προστεθεί στο έντυπο ΕΕΒΚ02 (και να επισυναφθεί βιογραφικό σημείωμα). Σε αντίθετη περίπτωση, να επισυναφθεί επιστολή από το άτομο αυτό ότι αποδέχεται να αναλάβει αυτό το ρόλο. **Έχει προστεθεί στην ομάδα η ψυχίατρος Στυλιανή Σπυρίδη. Απαντήθηκε.**

255

<u>Συμπληρώνεται από την Επιτροπή Βιοηθικής</u>

Έχουν δοθεί λεπτομέρειες στην Επιτροπή Βιοηθικής ή/και η Επιτροπή Βιοηθικής *έκρινε ικανοποιητικά τα κάτωθι:		
Στοιχεία	ΝΑΙ	ΟΧΙ
Βιογραφικά Στοιχεία ΟΛΩΝ των ερευνητών και των συνεργατών τους	Σχόλια	
Δήλωση μη συγκρουόμενων συμφερόντων	√	
Περιγραφή του είδους του Προγράμματος	√	
Περιγραφή του πληθυσμού που θα μελετηθεί	√	
Ο τρόπος με τον οποίο θα στρατολογηθούν άτομα για το Πρόγραμμα	√	
Μελετήθηκαν προσεκτικά τα έντυπα συγκατάθεσης (ΕΕΒΚ03);	√	
Τα έντυπα που θα χρησιμοποιηθούν για την στρατολόγηση ατόμων	√	
Ολόκληρο το πρωτόκολλο του Προγράμματος	√	
Δικαιολόγηση για την χρήση εικονικής φαρμακευτικής αγωγής	ΔΙ	
Υπεύθυνη δήλωση από όλους τους ερευνητές και συνεργάτες τους ότι τα έντυπα πληροφόρησης και συναίνεσης τους δεσμεύουν	√	
Διασφάλιση της προστασίας των δεδομένων που αφορούν τα άτομα που θα λάβουν μέρος στο Πρόγραμμα	√	
Λεπτομέρειες για την χρηματοδότηση του Προγράμματος	√	
Έχουν εκδοθεί ειδικά συμβόλαια σε σχέση με αμοιβές ;		√
Θα δίδονται αμοιβές στα άτομα που θα συμμετάσχουν στο Πρόγραμμα ;		√
Θα υπάρξουν οποιεσδήποτε οικονομικές επιβαρύνσεις για τα άτομα που θα συμμετάσχουν στο Πρόγραμμα ;		√
Οι ερευνητές ή/και συνεργάτες τους θα παίρνουν αμοιβές ;		√
Έχουν περιγραφεί τα αναμενόμενα οφέλη του Προγράμματος ;	√	
Έχει διαφανεί ότι προκύπτουν οποιαδήποτε οφέλη προς τον χρηματοδότη, τους ερευνητές και τους συνεργάτες τους από το Πρόγραμμα;	√	
Εάν πιο πάνω είναι ΝΑΙ, να εξηγηθεί:		
Έχουν τεκμηριωθεί όλες οι διευθετήσεις που έγιναν σε σχέση με τις υπηρεσίες που τυχόν θα παρασχεθούν για το Πρόγραμμα ;	√	
Θα υπάρχει συνεχής ενημέρωση για την ασφάλεια των ατόμων που θα λαμβάνουν μέρος στο Πρόγραμμα ;	√	
Υπάρχουν διαδικασίες για την υποβολή παραπόνων/καταγγελιών;	√	
Διασφαλίζονται επαρκώς τα δικαιώματα των ερευνητών για τις δημοσιεύσεις των αποτελεσμάτων ;	√	
Έχει δεσμευθεί ο/η Επιστημονικός Υπεύθυνος ότι δεν θα γίνουν οποιεσδήποτε αλλαγές στο Πρόγραμμα από την ημέρα που θα εγκριθεί από την Επιτροπή Βιοηθικής ;	√	

*Αποτελεί ευθύνη της Επιτροπής Βιοηθικής να σταθμίσει όλα τα στοιχεία που έχουν δοθεί, να δώσει την απαραίτητη βαρύτητα εκεί που χρειάζεται και να λάβει απόφαση ως προς το κατά πόσον έχουν δοθεί ικανοποιητικές επεξηγήσεις σε σχέση με το προτεινόμενο Πρόγραμμα.

Δήλωση για «μη συγκρουόμενα συμφέροντα» από την Επιτροπή Βιοηθικής		
Εμείς τα μέλη της Επιτροπής Βιοηθικής που λάβαμε μέρος στις συνεδρίες σε σχέση με την παρούσα αίτηση, υπογράφοντας πιο κάτω δηλώνουμε υπεύθυνα ότι δεν έχουμε οποιαδήποτε άμεσα ή έμμεσα συγκρουόμενα συμφέροντα σε σχέση με το Πρόγραμμα που μελετήσαμε και εκδώσαμε σχετική απόφαση.		
Ονοματεπώνυμο	Υπογραφή	Ημερομηνία
Δρ Ανδρέας Ζαχαριάδης		07/02/2018
Δρ Γιασεμίνα Καραγιώργη		07/02/2018
Δρ Καλυψώ Ιορδάνους		07/02/2018
κα Μαρία Αγγελή		07/02/2018
Δρ Μαρία Καρεκλά		07/02/2018
κος Παύλος Πολυκάρπου		07/02/2018
κα Χρίστια Μίτλεττον		07/02/2018
Δρ Χριστίνα Θεράποντος		07/02/2018
Δρ Χρίστος Σιαμμάς		07/02/2018

Τίτλος Προγράμματος
«Neurorehabilitation using transcranial magnetic stimulation- Νευρολογική Αποκατάσταση με τη Χρήση Διακρανιακής Μαγνητικής Διέγερσης »

Αριθμός Πρωτοκόλλου Επιτροπής Βιοηθικής
ΕΕΒΚ/ΕΠ/2017/37

Απόφαση της Επιτροπής Βιοηθικής (Εγκρίνεται, Ζητούνται επιπρόσθετα στοιχεία, Απορρίπτεται)
Εγκρίνεται 1. Νοείται ότι την νομική ευθύνη της επιστημονικής εγκυρότητας, αναγκαιότητας, πληρότητας και της συνολικής επιστημονικής αξίας της προτεινομένης έρευνας έχουν οι επιστημονικοί υπεύθυνοι της έρευνας και ο Φορέας του επιστημονικού υπεύθυνου. Όλοι οι πιο πάνω έχουν επίσης την νομική ευθύνη της διεξαγωγής της έρευνας με τη δέουσα επιστημονική επιμέλεια και φροντίδα. 2.Από 01/08/2012 η Εθνική Επιτροπή Βιοηθικής Κύπρου διενεργεί δειγματοληπτικό έλεγχο σε ερευνητικές προτάσεις που λαμβάνουν έγκριση. Περισσότερες λεπτομέρειες είναι διαθέσιμες στην ιστοσελίδα της Επιτροπής σε σχετική ανακοίνωση. 3.Το παρόν έντυπο απόφασης κοινοποιείται και στον χρηματοδότη της ερευνητικής πρότασης. 4. Οι ερευνητές υποχρεούνται να υποβάλλουν προς την Επιτροπή ανά εξάμηνο από σήμερα έκθεση για την εξέλιξη της έρευνας μέσα του εντύπου ΕΕΒΚ05. 5. Με το πέρας της έρευνας, οι ερευνητές υποχρεούνται όπως υποβάλουν στην Επιτροπή αναφορά μέσω του Εντύπου ΕΕΒΚ06. 6. Τονίζεται στους ερευνητές η υποχρέωσή τους να τηρούν τις εκάστοτε υποχρεώσεις τους με βάση την κείμενη νομοθεσία και κανονισμούς και ιδιαιτέρως η υποχρέωσή τους να ενημερώνουν άμεσα την Επιτροπή για οποιοδήποτε έκτακτο συμβάν ή οποιαδήποτε τροποποίηση στην πρόταση ως εγκρίθηκε, με την υποβολή των προνοουμένων εντύπων.

Μέλη που ήταν παρόντα στην λήψη απόφασης/Αποτέλεσμα Ψηφοφορίας
Ως αναφέρεται στην σελίδα 7 ανωτέρω και η απόφαση ήταν ομόφωνη.

Ημερομηνία έκδοσης απόφασης
Ημέρα: ………..…07…. Μήνας: ……Φεβρουαρίου….. Έτος: ……2017………

Υπογράφει ο Πρόεδρος της Επιτροπής Βιοηθικής και ο Αναπληρωτής Πρόεδρος			
Αξίωμα	Όνομα	Επίθετο	Υπογραφή
Πρόεδρος	Μαρία	Καρεκλά	
Αντιπρόεδρος	Παύλος	Πολυκάρπου	

Appendix II: Participation Consent Form

ΕΝΤΥΠΑ ΣΥΓΚΑΤΑΘΕΣΗΣ
για συμμετοχή σε πρόγραμμα έρευνας
(Τα έντυπα αποτελούνται συνολικά από 7σελίδες)

Καλείστε να συμμετάσχετε σε ένα ερευνητικό πρόγραμμα. Πιο κάτω (βλ. **«Πληροφορίες για Ασθενείς ή/και Εθελοντές»**) θα σας δοθούν εξηγήσεις σε απλή γλώσσα σχετικά με το τι θα ζητηθεί από εσάς ή/και τι θα συμβεί σε εσάς, εάν συμφωνήσετε να συμμετάσχετε στο πρόγραμμα. Θα σας περιγραφούν οποιοιδήποτε κίνδυνοι μπορεί να υπάρξουν ή ταλαιπωρία που τυχόν θα υποστείτε από την συμμετοχή σας στο πρόγραμμα. Θα σας επεξηγηθεί με κάθε λεπτομέρεια τι θα ζητηθεί από εσάς και ποιος ή ποιοι θα έχουν πρόσβαση στις πληροφορίες ή/και άλλο υλικό που εθελοντικά θα δώσετε για το πρόγραμμα. Θα σας δοθεί η χρονική περίοδος για την οποία οι υπεύθυνοι του προγράμματος θα έχουν πρόσβαση στις πληροφορίες ή/και υλικό που θα δώσετε. Θα σας επεξηγηθεί τι ελπίζουμε να μάθουμε από το πρόγραμμα σαν αποτέλεσμα και της δικής σας συμμετοχής. Επίσης, θα σας δοθεί μία εκτίμηση για το όφελος που μπορεί να υπάρξει για τους ερευνητές ή/και χρηματοδότες αυτού του προγράμματος. Δεν πρέπει να συμμετάσχετε, εάν δεν επιθυμείτε ή εάν έχετε οποιουσδήποτε ενδοιασμούς που αφορούν την συμμετοχή σας στο πρόγραμμα. Εάν αποφασίσετε να συμμετάσχετε, πρέπει να αναφέρετε εάν είχατε συμμετάσχει σε οποιοδήποτε άλλο πρόγραμμα έρευνας μέσα στους τελευταίους 12 μήνες. Εάν αποφασίσετε να μην συμμετάσχετε και είστε ασθενής, η θεραπεία σας δεν θα επηρεαστεί από την απόφασή σας. Είστε ελεύθεροι να αποσύρετε οποιαδήποτε στιγμή εσείς επιθυμείτε την συγκατάθεση για την συμμετοχή σας στο πρόγραμμα. Εάν είστε ασθενής, η απόφασή σας να αποσύρετε την συγκατάθεση σας, δεν θα έχει οποιεσδήποτε επιπτώσεις στην θεραπεία σας. Έχετε το δικαίωμα να υποβάλετε τυχόν παράπονα ή καταγγελίες, που αφορούν το πρόγραμμα στο οποίο συμμετέχετε, προς την Επιτροπή Βιοηθικής που ενέκρινε το πρόγραμμα ή ακόμη και στην Εθνική Επιτροπή Βιοηθικής Κύπρου.

Πρέπει όλες οι σελίδες των εντύπων συγκατάθεσης να φέρουν το ονοματεπώνυμο και την υπογραφή σας.

Σύντομος Τίτλος του Προγράμματος στο οποίο καλείστε να συμμετάσχετε
«Νευρολογική Αποκατάσταση με τη Χρήση Διακρανιακής Μαγνητικής Διέγερσης»
Υπεύθυνος του Προγράμματος στο οποίο καλείστε να συμμετάσχετε
Δρ. Μαρία Καμπανάρου, Αναπληρώτρια Καθηγήτρια, Τμήμα Επιστημών Αποκατάστασης, Τεχνολογικό Πανεπιστήμιο Κύπρου, Βραγαδίνου 15, Λεμεσός, 3041, τηλέφωνο: +35725002098, ηλεκτρονικό ταχυδρομείο (email) maria.kambanaros@cut.ac.cy

Επίθετο:		Όνομα:	
Υπογραφή:		Ημερομηνία	

ΕΝΤΥΠΑ ΣΥΓΚΑΤΑΘΕΣΗΣ

για συμμετοχή σε πρόγραμμα έρευνας

(Τα έντυπα αποτελούνται συνολικά από 5 σελίδες)

Σύντομος Τίτλος του Προγράμματος στο οποίο καλείστε να συμμετάσχετε
«Νευρολογική Αποκατάσταση με τη Χρήση Διακρανιακής Μαγνητικής Διέγερσης»

Δίδετε συγκατάθεση για τον εαυτό σας ή για κάποιο άλλο άτομο;	
Εάν πιο πάνω απαντήσατε για κάποιον άλλο, τότε δώσετε λεπτομέρειες και το όνομα του.	

Ερώτηση	ΝΑΙ ή ΟΧΙ
Συμπληρώσατε τα έντυπα συγκατάθεσης εσείς προσωπικά;	
Τους τελευταίους 12 μήνες έχετε συμμετάσχει σε οποιοδήποτε άλλο ερευνητικό πρόγραμμα;	
Διαβάσατε και καταλάβατε τις πληροφορίες για ασθενείς ή/και εθελοντές;	
Είχατε την ευκαιρία να ρωτήσετε ερωτήσεις και να συζητήσετε το Πρόγραμμα;	
Δόθηκαν ικανοποιητικές απαντήσεις και εξηγήσεις στα τυχόν ερωτήματά σας;	
Καταλαβαίνετε ότι μπορείτε να αποσυρθείτε από το πρόγραμμα, όποτε θέλετε;	
Καταλαβαίνετε ότι, εάν αποσυρθείτε, δεν είναι αναγκαίο να δώσετε οποιεσδήποτε εξηγήσεις για την απόφαση που πήρατε;	
(Για ασθενείς) καταλαβαίνετε ότι, εάν αποσυρθείτε, δεν θα υπάρξουν επιπτώσεις στην τυχόν θεραπεία που παίρνετε ή που μπορεί να πάρετε μελλοντικά;	
Συμφωνείτε να συμμετάσχετε στο πρόγραμμα;	
Με ποιόν υπεύθυνο μιλήσατε;	

Επίθετο:	....	Όνομα:	....
Υπογραφή:		Ημερομηνία:	

ΕΝΤΥΠΑ ΣΥΓΚΑΤΑΘΕΣΗΣ
για συμμετοχή σε πρόγραμμα έρευνας
(Τα έντυπα αποτελούνται συνολικά από 5 σελίδες)
Σύντομος Τίτλος του Προγράμματος στο οποίο καλείστε να συμμετάσχετε
«Νευρολογική Αποκατάσταση με τη Χρήση Διακρανιακής Μαγνητικής Διέγερσης»

ΠΛΗΡΟΦΟΡΙΕΣ ΓΙΑ ΑΣΘΕΝΕΙΣ ή/και ΕΘΕΛΟΝΤΕΣ

Κύριος Ερευνητής. Δρ. Μαρία Καμπανάρου, Αναπληρώτρια Καθηγήτρια, Τμήμα Επιστημών Αποκατάστασης, Τεχνολογικό Πανεπιστήμιο Κύπρου, Βραγαδίνου 15, Λεμεσός, 3041, τηλέφωνο: +35725002098, ηλεκτρονικό ταχυδρομείο: maria.kambanaros@cut.ac.cy

Θα θέλαμε να σας προσκαλέσουμε να συμμετάσχετε στο πιο πάνω αναφερόμενο ερευνητικό πρόγραμμα. Ο σκοπός του ερευνητικού προγράμματος είναι να ανιχνεύσουμε και να κατανοήσουμε τις πιθανές θετικές επιπτώσεις της Διακρανιακής Μαγνητικής Διέγερσης (ΔΜΔ) στη νευρολογική αποκατάσταση. Στο ερευνητικό αυτό πρόγραμμα συμμετέχουν ασθενείς με νευρολογικά προβλήματα λόγω εγκεφαλικού επεισοδίου. Το έντυπο αυτό αφορά άτομα με γλωσσικά προβλήματα. Ενδέχεται σε κάποιους ασθενείς με παρόμοια γλωσσικά προβλήματα να δοθεί διαφορετική παρέμβαση (λογοθεραπεία & TMS, εκπαίδευση μνήμης & TMS, μόνο TMS), για σκοπούς σύγκρισης των διαφόρων παρεμβάσεων. Ο τρόπος κατανομής σας σε μία από τις παραπάνω ομάδες θα είναι εντελώς τυχαίος (random assignment).

Είναι σημαντικό να γνωρίζετε ότι αν επιλέξετε να συμμετάσχετε, η συμμετοχή σας στο ερευνητικό πρόγραμμα δεν εγγυάται κάποιο άμεσο όφελος στην υγεία σας, αφού σε κάποιους από τους συμμετέχοντες θα δωθεί η πραγματική ΔΜΔ ενώ σε κάποιους άλλους συμμετέχοντες θα δωθεί εικονική ΔΜΔ. Η εικονική ΔΜΔ μοιάζει με την αληθινή ΔΜΔ, αλλά δεν είναι. Δεν έχει καμία επίδραση, επειδή δεν ενεργοποιεί τον εγκέφαλο σας. Μερικές φορές, όταν θέλουμε να μάθουμε αν μια καινούργια θεραπεία είναι αποτελεσματική, δίνουμε σε μερικούς ασθενείς τη νέα αυτή θεραπεία και σε μερικούς ασθενείς την εικονική θεραπεία. Για να είναι έγκυρη η έρευνα, είναι σημαντικό να μην ξέρετε εάν σας έχει δοθεί η πραγματική θεραπεία ή η εικονική θεραπεία. Αυτός είναι ένας από τους καλύτερους τρόπους που έχουμε για να μάθουμε εάν μια θεραπεία είναι αποτελεσματική. Τονίζεται ότι εάν η θεραπεία οδηγήσει σε σημαντική βελτίωση της αποκατάστασής σας, εάν το επιθυμείτε μπορείτε να συνεχίσετε να λαμβάνεται τη θεραπεία για μέχρι ακόμη 10 ημέρες δωρεάν. Περαιτέρω συνέχιση της θεραπείας δεν συνίσταται προς το παρόν αφού οι αρνητικές επιπτώσεις της συνεχόμενης μακροχρόνιας θεραπείας με ΔΜΔ είναι άγνωστες προς το παρόν.

Η συμμετοχή σας είναι εντελώς εθελοντική και θα πρέπει να συμμετάσχετε μόνο εάν εσείς το επιθυμείτε. Επιλέγοντας να μην λάβετε μέρος ή να αποχωρήσετε κατά τη διάρκεια του ερευνητικού προγράμματος δε θα έχει αρνητικές επιπτώσεις σε σας, δε θα σας κοστίσει οτιδήποτε και ούτε θα επηρεάσει με οποιονδήποτε τρόπο οποιαδήποτε άλλη μορφή θεραπείας λαμβάνετε. Σε περίπτωση αποχώρησής σας από το ερευνητικό πρόγραμμα τα δεδομένα σας σβήνονται από το σύστημα του ερευνητή (εκτός και αν επιθυμείτε την ανωνυμοποιησή τους) και το βιολογικό υλικό που έχετε δώσει θα καταστρέφεται. Πριν αποφασίσετε αν θέλετε να πάρετε μέρος, είναι σημαντικό για εσάς να διαβάσετε τις παρακάτω πληροφορίες προσεκτικά και να τις συζητήσετε με όποιο άλλο άτομο επιθυμείτε. Ρωτήστε μας αν υπάρχει κάτι που δεν είναι σαφές ή για το οποίο θα θέλατε περισσότερες πληροφορίες. Εάν συμφωνήσετε να συμμετάσχετε στο πείραμα, θα σας ζητήσουμε τα εξής:

Επίθετο:		Όνομα:	
Υπογραφή:		Ημερομηνία:	

Ιατρικό Ιστορικό και Γλωσσική Αξιολόγηση

Θα σας ζητηθεί να δώσετε στους ερευνητές πρόσβαση **με τη χρήση ερωτηματολογίων** στο προσωπικό ιατρικό σας ιστορικό, καθώς και ένα λεπτομερές ιστορικό το οποίο θα περιλαμβάνει δημογραφικά στοιχεία, την τρέχουσα κατάσταση της υγείας σας, χρήση φαρμάκων, την εκπαίδευση, την ποιότητα της ζωής σας και της καθημερινές σας δραστηριότητες, την επαγγελματική σας απασχόληση, **καθώς και άλλες πληροφορίες που αφορούν τις επιπτώσεις του εγκεφαλικού επεισοδίου στις καθημερινές σας δραστηριότητες, αν είστε αριστερόχειρας ή δεξιόχειρας, αξιολόγηση της πιθανότητας ύπαρξης άνοιας, αξιολόγηση της χρήσης της γλώσσας καθώς και της πιθανότητας ύπαρξης κατάθλιψης.**

Στη συνέχεια θα σας ζητηθεί να συμπληρώσετε κάποια εργαλεία αξιολόγησης της γλώσσας με σκοπό την αξιολόγηση της όποιας προόδου λόγω της συμμετοχής σας στο πρόγραμμα. Συγκεκριμένα, η πρώτη αξιολόγηση θα γίνει μία μέρα πριν από την έναρξη της θεραπείας με τη Διακρανιακή Μαγνητική Διέγερση. Η δεύτερη αξιολόγηση θα γίνει μία ήμερα μετά το τέλος της θεραπείας (10 ημέρες μετά). Η τρίτη αξιολόγηση θα γίνει περίπου 6 μήνες μετά το τέλος της θεραπείας. Κάθε συνάντηση θα διαρκέσει περίπου 60 λεπτά. Τα εργαλεία αξιολόγησης της γλώσσας θα σας ζητήσουν να απαντήσετε σε διάφορες ερωτήσεις καθημερινής φύσης, να κάνετε μία ελεύθεση συζήτηση με τον εξεταστή, να περιγράψετε διάφορες εικόνες, να ακούσετε κάποιες λέξεις και να δείξετε αυτές τις λέξεις σε εικόνες που θα σας δωθούν, καθώς και να επαναλάβετε κάποιες λέξεις και προτάσεις. Όλες οι αξιολογήσεις θα γίνουν από λογοπαθολόγο ο οποίος είναι εγγεγραμμένος στον Σύνδεσμο Λογοπαθολόγων Κύπρου.

Συλλογή Αίματος

Θα σας ζητηθεί να δώσετε περίπου 10mL. αίματος που θα αντληθούν από μια φλέβα του βραχίονα σας. Η συλλογή του αίματος θα γίνει τρεις φορές (μία πριν από τη θεραπευτική παρέμβαση, μία φορά μετά το πέρας της θεραπευτικής παρέμβασης και μία φορά περίπου 6 μήνες μετά) από έμπειρο νοσηλευτικό προσωπικό με εξειδίκευση σε αυτή τη διαδικασία. Η συλλογή του αίματος με σύριγγα πιθανό να έχει ως συνέπεια την ανάπτυξη μικρής μελανιάς στο χέρι γύρω από το σημείο εισαγωγής της βελόνας. Ένα τέτοιο ενδεχόμενο είναι σπάνιο όταν η διαδικασία εκτελείται από εκπαιδευμένο προσωπικό. Αν όμως μια τέτοια μελανιά αναπτυχθεί, θα πρέπει να γνωρίζετε ότι θα αποχωρήσει χωρίς θεραπεία μέσα σε λίγες εβδομάδες και σπανίως είναι επώδυνη. Υπάρχει επίσης κίνδυνος αιμορραγίας εάν πάσχετε από διαταραχή πήξης του αίματος ή λαμβάνετε φαρμακευτική αγωγή που αναστέλλει την πήξη του αίματος. Εάν οποιαδήποτε από αυτές τις συνθήκες ισχύει στην περίπτωσή σας, θα ήταν καλύτερα να μην δώσετε αίμα για αυτή τη μελέτη.

Για τους λόγους που αναφέρθηκαν πιο πάνω, το πρόσωπο που θα προβεί στη συλλογή αίματος θα σας παρακολουθεί στενά και εάν εμφανιστούν οποιαδήποτε ανησυχητικά συμπτώματα ή συμπτώματα που ο ερευνητής ή οι συνεργάτες του έχουν περιγράψει σε σας, παρακαλούμε όπως ειδοποιήσετε αμέσως τον ερευνητή.

Το αίμα θα φυλαχθεί σε ειδικά διαμορφωμένες εγκαταστάσεις στο Τεχνολογικό Πανεπιστήμιο Κύπρου καθώς και σε εργαστήρια του Πανεπιστημίου Λευκωσίας στα οποία θα γίνουν οι αναλύσεις για εντοπισμό των υπό μελέτη βιολογικών δεικτών. Ο σκοπός για τον οποίο θα γίνει η συλλογή αίματος είναι η ανάλυση του γενετικού σας υλικού καθώς και άλλων βιολογικών δεικτών που μπορεί να σχετίζονται με την θεραπεία. Ως εκ τούτου, τα αποτελέσματα των αναλύσεων δεν μπορούν να χρησιμοποιηθούν για διαγνωστικούς ή άλλους κλινικούς σκοπούς παρά μόνο για σκοπούς ανίχνευσης αλλαγής σε συγκεκριμένους βιολογικούς δείκτες λόγω της συγκεκριμένης θεραπευτικής παρέμβασης.

Επίθετο:		Όνομα:	
Υπογραφή:		Ημερομηνία:	

Μαγνητική Τομογραφία Εγκεφάλου

Θα σας ζητηθεί να επισκεφθείτε ένα διαγνωστικό κέντρο για τη συλλογή μαγνητικής τομογραφίας του εγκεφάλου σας. Το κόστος μεταφοράς στο διαγνωστικό κέντρο θα γίνει με δική σας ευθύνη. Στο διαγνωστικό κέντρο θα σας ζητηθεί να ξαπλώσετε για περίπου 30 λεπτά στο κρεβάτι του μαγνητικού τομογράφου (MRI) για συλλογή εικόνων της δομής και της λειτουργίας του εγκεφάλου σας. Θα σας ζητηθεί να επισκεφθείτε το διαγνωστικό κέντρο μία φορά πριν την έναρξη της θεραπευτικής παρέμβασης, μία φορά αμέσως μετά την ολοκλήρωση της (10 μέρες μετά την πρώτη συλλογή) και ακόμη μία φορά περίπου 6 μηνές μετά.

Οι εικόνες του εγκεφάλου σας θα φυλαχθούν στο Τμήμα Επιστημών Αποκατάστασης του Τεχνολογικού Πανεπιστημίου Κύπρου υπό την καθοδήγηση της Δρ. Μαρίας Καμπανάρου. Ο σκοπός για τον οποίο θα γίνει η συλλογή εικόνων εγκεφάλου είναι η ανίχνευση πιθανών αλλαγών στη δομή και στη λειτουργία του εγκεφάλου σας λόγω της θεραπείας. Ως εκ τούτου, οι εικόνες αυτές δεν μπορούν να χρησιμοποιηθούν για διαγνωστικούς ή άλλους κλινικούς σκοπούς παρά μόνο για σκοπούς ανίχνευσης αλλαγής στη δομή (π.χ. στον όγκο) και τη λειτουργία του εγκεφάλου σας λόγω της συγκεκριμένης θεραπευτικής παρέμβασης.

Η τεχνική της μαγνητικής τομογραφίας (MRI) είναι μια από τις πιο προηγμένες και κατατοπιστικές διαγνωστικές διαδικασίες που είναι διαθέσιμες σήμερα. Το MRI είναι μια μέθοδος απόκτησης εικόνων των δομών στο εσωτερικό του σώματός σας, χρησιμοποιώντας ένα μεγάλο μαγνήτη και ραδιοκύματα (αντί ακτίνες Χ ή ακτινοβολία) για τη λήψη εικόνων. Είναι εντελώς ανώδυνη και δεν υπάρχουν γνωστές βλαβερές παρενέργειες της μαγνητικής τομογραφίας. Αυτό που απατείται είναι να παραμείνετε ακίνητη/ος πάνω στο κρεβάτι ενώ είστε μέσα στον μαγνητικό τομογράφο. Ενώ ο τομογράφος θα κατασκευάζει τις εικόνες του εγκεφάλου σας, θα ακούσετε κάποια βουητά και δυνατούς ήχους. Αυτό είναι μέρος της κανονικής λειτουργίας του τομογράφου και δεν πρέπει να σας ανησυχεί.

Λόγω της χρήσης ραδιοκυμάτων από τον μαγνητικό τομογράφο, τα άτομα με καρδιακό βηματοδότη, κλιπ ανευρύσματος εγκεφάλου, καθώς και μεταλλικά εμφυτεύματα ή άλλες ηλεκτρικές συσκευές στο σώμα τους δεν θα πρέπει να εισέρχονται στο δωμάτιο του μαγνητικού τομογράφου. Είναι σημαντικό να ενημερώσετε τους ερευνητές στο Έντυπο Ελέγχου Ασφαλείας Μαγνητικού Τομογράφου που θα σας ζητηθεί να συμπληρώσετε πριν την εξέταση, αν έχετε οποιαδήποτε από αυτές τις μεταλλικές συσκευές στο σώμα σας. Επίσης, δεδομένου ότι οι επιπτώσεις της μαγνητικής τομογραφίας στο έμβρυο είναι άγνωστες, παρακαλείστε να ενημερώσετε τους ερευνητές στο πιο πάνω έντυπο εάν είστε έγκυος ή νομίζετε ότι μπορεί να είστε έγκυος.

Παρέμβαση με Διακρανιακή Μαγνητική Διέγερση

Θα σας ζητηθεί να συμμετάσχετε σε 10 συνεχόμενες ημερίσιες συνεδρίες στο εργαστήριο Διακρανιακής Μαγνητικής Διέγερσης στο Τεχνολογικό Πανεπιστήμιο Κύπρου. Οι συνεδρίες θα περιλαμβάνουν ενεργοποίηση του φλοιού του εγκεφάλου σας με τη χρήση Διακρανιακής Μαγνητικής Διέγερσης (ΔΜΔ). Κάθε συνεδρία ΔΜΔ θα έχει διάρκεια περίπου 30 λεπτά. Κατά τη διάρκεια της ΔΜΔ, θα ενεργοποιήσουμε τα κύτταρα του εγκεφάλου σας με μια σειρά από μαγνητικούς παλμούς που παράγονται από ένα μονωμένο πηνίο το οποίο θα τοποθετήσουμε στο τριχωτό της κεφαλής σας. Αυτοί οι μαγνητικοί παλμοί ταξιδεύουν μέσω του τριχωτού της κεφαλής και του κρανίου σας προκαλώντας μικρής έντασης ηλεκτρικό ρεύμα στο φλοιό (το εξωτερικό τμήμα του εγκεφάλου).

Επίθετο:		Όνομα:	
Υπογραφή:		Ημερομηνία:	

Είναι σημαντικό να γνωρίζετε ότι οι μαγνητικοί παλμοί μπορεί να προκαλέσουν μια μικρή αίσθηση ελαφρού χτυπήματος πάνω στο τριχωτό της κεφαλής σας. Αυτή η αίσθηση συνήθως δεν είναι δυσάρεστη αλλά μερικές φορές μπορεί όντως να προκαλέσει μια ενοχλητική αίσθηση. Είναι σημαντικό να γνωρίζετε πως μπορείτε ανά πάσα στιγμή να ζητήσετε να σταματήσει η διαδικασία και να αποχωρήσετε χωρίς δικαιολογία και με καμία συνέπεια από την αποχώρηση σας.

Όπως υποδηλώνει το όνομα, η ΔΜΔ χρησιμοποιεί μαγνητικά πεδία. Ως εκ τούτου, μπορεί να προβεί επιβλαβής σε άτομα που έχουν μεταλλικά ή ηλεκτρονικά εμφυτεύματα στο σώμα τους. Παρακαλείστε να ενημερώσετε τους ερευνητές σημειώνοντας τις απαντήσεις σας στο Έντυπο Ελέγχου Ασφαλείας που θα σας ζητηθεί να συμπληρώσετε πριν την έναρξη της συνεδρίας ΔΜΔ, σε περίπτωση που έχετε κάποιο από αυτά. Επίσης, δεδομένου ότι οι επιπτώσεις της ΔΜΔ στο έμβρυο είναι άγνωστες, σας συμβουλεύουμε να μην λάβετε μέρος στο πείραμα εάν είστε έγκυος ή νομίζετε πως υπάρχει περίπτωση να είστε έγκυος. Επίσης, σας συμβουλεύουμε να μην λάβετε μέρος, αν έχετε πιει αλκοόλ τις τελευταίες 24 ώρες, αν έχετε χρησιμοποιήσει ναρκωτικές ουσίες κατά τον τελευταίο μήνα ή εάν δεν είχατε έναν καλό ύπνο το βράδυ πριν από το πείραμα.

Παρέχοντας μια συνεχή σειρά μαγνητικών ερεθισμάτων με τη χρήση ΔΜΔ σε σύντομο χρονικό διάστημα υπάρχει μικρός κίνδυνος για παρενέργειες. Με ισχυρούς παλμούς, σε υψηλές συχνότητες, είναι δυνατόν να προκληθούν επιληπτικές κρίσεις σε ευαίσθητα άτομα με οικογενειακό ιστορικό επιληψίας. Παρακαλείστε να ενημερώσετε τους ερευνητές μέσω του Εντύπου Ελέγχου Ασφαλείας, αν έχετε ιστορικό επιληψίας εσείς ή κάποιος στην οικογένειά σας.

Είναι σημαντικό να γνωρίζετε ότι η ΔΜΔ έχει χρησιμοποιηθεί με ασφάλεια τα τελευταία περίπου 30 χρόνια σε χιλιάδες άτομα σε όλο τον κόσμο. Ένας έμπειρος ερευνητής θα χειρίζεται το μηχάνημα ΔΜΔ και θα είναι παρόν καθ'όλη τη διάρκεια του πειράματος.

Με τη χρήση χαμηλότερης έντασης παλμών όπως αυτούς που χρησιμοποιούμε στη συγκεκριμένη περίπτωση, σύμφωνα με τις κατευθυντήριες γραμμές ασφαλείας που ισχύουν διεθνώς, δεν γνωρίζουμε να έχουν αναφερθεί περιπτώσεις πρόκλησης επιληπτικών κρίσεων λόγω ΔΜΔ και η τεχνική φαίνεται να είναι απολύτως ασφαλής. Στην απίθανη περίπτωση επιληπτικής κρίσης, θα σας δοθούν οι κατάλληλες πρώτες βοήθειες αφού όλοι οι ερευνητές μας είναι εκπαιδευμένοι στην παροχή Πρώτων Βοηθειών. Η μόνη άλλη γνωστή παρενέργεια της ΔΜΔ, σε ένα μικρό ποσοστό των ατόμων, είναι η πρόκληση ασθενούς πονοκεφάλου σε κάποιες περιπτώσεις, ο οποίος υποχωρεί σε διάστημα λίγων ωρών. Σύμφωνα με την επιστημονική βιβλιογραφία δεν υπάρχει καμία μακροπρόθεσμη παρενέργεια της ΔΜΔ.

Παρέμβαση με Πρόγραμμα Εκπαίδευσης Μνήμης

Θα σας ζητηθεί να συμμετάσχετε σε 10 συνεχόμενες ημερήσιες συνεδρίες εκπαίδευσης της βραχύχρονης μνήμης σας. Η κάθε συνεδρία λογοθεραπείας θα έχει διάρκεια περίπου 60 λεπτά. Συγκεκριμένα, θα σας ζητηθεί να εκτελέσετε κάποιες ασκήσεις στον ηλεκτρονικό υπολογιστή. Για τις ασκήσεις αυτές θα σας ζητηθεί να απομνημονεύστε κάποιες κάρτες με αντικείμενα, στη συνέχεια να απομνημονεύστε ορισμένες κάρτες επιλεκτικά, και να ταξινομήστε τις κάρτες. Το πρόγραμμα εκπαίδευσης της μνήμης θα εφαρμόζεται αμέσως μετά τη θεραπεία της Διακρανιακής Μαγνητικής Διέγερσης σε κάποιο κατάλληλο χώρο των εργαστηρίων του Τεχνολογικού Πανεπιστημίου Κύπρου.

Επίθετο:		Όνομα:	
Υπογραφή:		Ημερομηνία:	

Στόχος μας είναι να δούμε αν το συγκεκριμένο πρόγραμμα εκπαίδευσης μνήμης μπορεί μόνο του ή σε συνδυασμό με Διακρανιακή Μαγνητική Διέγερση μπορεί να βελτιώσει τα προβλήματα επικοινωνίας που αντιμετωπίζετε.

Όλα τα δεδομένα που θα συλλεχθούν θα φυλαχθούν σε ειδικό χώρο του Τμήματος Επιστημών Αποκατάστασης του Τεχνολογικού Πανεπιστημίου Κύπρου υπό την καθοδήγηση της Δρ. Μαρίας Καμπανάρου. Δεν είστε υποχρεωμένοι να συμμετάσχετε στην έρευνα και η συμμετοχή σας σε αυτή τη μελέτη δεν σας εγγυάται άμεσα ιατρικά οφέλη αλλά ούτε και τα αποκλείει.

Τα αποτελέσματα αναμένεται να συμβάλουν στην επιστημονική γνώση σχετικά με την νευρολογική αποκατάσταση και να ωφελέσουν ασθενείς με νευρολογικά προβλήματα λόγω εγκεφαλικού επεισοδίου. Εάν επιθυμείτε να συμμετάσχετε, μπορείτε να αποχωρήσετε ανά πάσα στιγμή χωρίς καμία επίπτωση. Το συγκεκριμένο Έντυπο Συγκατάθεσης, το Ενημερωτικό Έντυπο ΔΜΔ, το Έντυπο Ελέγχου Ασφαλείας ΔΜΔ, και το Έντυπο Ελέγχου Ασφαλείας Μαγνητικού Τομογράφου που θα πρέπει να συμπληρώσετε, έχουν ελεγχθεί και εγκριθεί από την Κυπριακή Εθνική Επιτροπή Βιοηθικής.

Μέρος των δειγμάτων σας **μπορεί να** φυλαχθεί **για περίοδο μέχρι 10 χρόνια** για πιθανή μελλοντική χρήση που θα σχετίζεται με τους σκοπούς της έρευνας. Με την παρούσα συγκατάθεση, μπορείτε να δώσετε εάν το επιθυμείτε συγκατάθεσή όπως το δείγμα σας ή οποιοδήποτε υλικό που προκύπτει από το δείγμα σας, καθώς επίσης και οι πληροφορίες που συλλέγονται να αποθηκευθούν για πιθανή μελλοντική έρευνα. Παρακαλούμε σημειώσετε και υπογράψτε αριστερά εάν αποδέχεστε ή δεξιά εάν δεν αποδέχεστε.

Εκτός από τους σκοπούς του παρόντος προγράμματος που θα διαρκέσει 5 χρόνια **Αποδέχομαι όπως:**	Εκτός από τους σκοπούς του παρόντος προγράμματος που θα διαρκέσει 5 χρόνια **Δεν αποδέχομαι όπως:**
Υπογραφή:	**Υπογραφή:**
Τα βιολογικά μου δείγματα και όλες οι λοιπές πληροφορίες που θα συλλεγούν για τους σκοπούς του παρόντος ερευνητικού προγράμματος <u>μπορούν να κρατηθούν **για μέχρι 10 χρόνια** και να χρησιμοποιηθούν σε μελλοντικές μελέτες</u> αφού πρώτα εγκριθεί κάτι τέτοιο από την Εθνική Επιτροπή Βιοηθικής Κύπρου μέσω νέας αίτησης ή μετά από σχετικό αίτημα ανανέωσης σε περίπτωση επέκτασης της παρούσας μελέτης από τον υπεύθυνο ερευνητή του προγράμματος. Κατανοώ ότι θέματα εμπιστευτικότητας ισχύουν πάντοτε. Ως δότης βιολογικών δειγμάτων και δεδομένων θα γνωρίζετε επακριβώς τον υπεύθυνο ερευνητή που θα έχει ευθύνη για την φύλαξη των δειγμάτων/δεδομένων σας όπως επίσης και τον ακριβή γεωγραφικό χώρο όπου θα διαφυλαχθεί το αρχείο σε περίπτωση αλλαγής.	

Επιθυμείτε να λάβετε έκθεση από τον υπεύθυνο Λογοθεραπτή που θα περιγράφει τα αποτελέσματα της έρευνας που σας αφορούν; ΝΑΙ / ΟΧΙ

Εάν επιθυμείτε να εκφράσετε με οποιονδήποτε τρόπο ανώνυμα ή επώνυμα σχόλια ή παράπονά για αυτή την έρευνα μπορείτε να επικοινωνήσετε με την εξής ανεξάρτητη αρχή:
Δρ. Χαράλαμπος Χρυσοστόμου, Προϊστάμενος Υπηρεσίας Έρευνας και Διεθνούς Συνεργασίας, Τεχνολογικό Πανεπιστήμιο Κύπρου
Τηλέφωνο: +357 25 002562, Ηλεκτρονικό ταχυδρομείο (email): c.chrisostomou@cut.ac.cy

Επίθετο:	....	Όνομα:	....
Υπογραφή:		Ημερομηνία:	

Appendix III: Safety Screening for TMS eligibility

ΕΝΤΥΠΟ ΑΝΙΧΝΕΥΤΙΚΟΥ ΕΛΕΓΧΟΥ ΓΙΑ ΔΙΑΚΡΑΝΙΑΚΗ ΜΑΓΝΗΤΙΚΗ ΔΙΕΓΕΡΣΗ (ΔΜΔ)

Παρακάτω είναι ένα ερωτηματολόγιο που χρησιμοποιείται για να καθορίσει αν οι πιθανοί συμμετέχοντες είναι κατάλληλοι για ΔΜΔ.

ΠΑΡΑΚΑΛΩ ΣΥΜΠΛΗΡΩΣΤΕ ΤΟ ΠΑΡΑΚΑΤΩ ΕΝΤΥΠΟ:

Δημογραφικά Στοιχεία

Ημερ. γέννησης: ....

Τόπος γέννησης: ....

Μητρική/ές γλώσσα/ες: Κυπριακή   Άλλη

(ονομάστε την άλλη γλώσσα) ....

Μόρφωση: Δημοτικό / Γυμνάσιο / Λύκειο / Κολλέγιο /

Πανεπιστήμιο / Μεταπτυχιακό / Διδακτορικό

Άλλο: ....

Επάγγελμα: ....

Διεύθυνση: ....

....

Τηλ. επικοινωνίας: ....

_____   _____

Υπογραφή Συμμετέχοντα   Ημερομηνία

_____   _____

Υπογραφή Μάρτυρα   Ημερομηνία

ΟΝΟΜΑ ΑΣΘΕΝΟΥΣ ή/και ΕΘΕΛΟΝΤΗ:

Παρακαλώ σημειώστε ό,τι ισχύει:

Νευρολογική ή Ψυχιατρική διαταραχή	ΝΑΙ	ΟΧΙ
Τραύμα στο κεφάλι	ΝΑΙ	ΟΧΙ
Εγκεφαλικό επεισόδιο	ΝΑΙ	ΟΧΙ
Χειρουργική επέμβαση στον εγκέφαλο	ΝΑΙ	ΟΧΙ
Μέταλλο ή μεταλλικά ρινίσματα στο κρανίο ή στα μάτια	ΝΑΙ	ΟΧΙ
Εγκεφαλική βλάβη	ΝΑΙ	ΟΧΙ
Βηματοδότη	ΝΑΙ	ΟΧΙ
Ιστορικό με σπασμούς ή/και επιληπτικές κρίσεις	ΝΑΙ	ΟΧΙ
Οικογενειακό ιστορικό επεισοδίων επιληψίας	ΝΑΙ	ΟΧΙ
Εμφυτευμένες ηλεκτρονικές συσκευές (π.χ. κοχλιακό εμφύτευμα)	ΝΑΙ	ΟΧΙ
Ενδοκρανιακές γραμμές	ΝΑΙ	ΟΧΙ
Σκλήρυνση κατά Πλάκας	ΝΑΙ	ΟΧΙ
Κατάθλιψη	ΝΑΙ	ΟΧΙ
Θεραπεία με Αντικαταθλιπτικά (π.χ. Αμιτρυπτιλήνη, Αλοπεριδόλη)	ΝΑΙ	ΟΧΙ
Εμφυτευμένη αντλία παροχής φαρμακευτικής αγωγής	ΝΑΙ	ΟΧΙ
Ενδοκρανιακή πάθηση	ΝΑΙ	ΟΧΙ
Αλφισμός (λευκοπάθεια)	ΝΑΙ	ΟΧΙ
Έντονο άγχος/ανησυχία	ΝΑΙ	ΟΧΙ
Κυοφορούσα αυτή την περίοδο	ΝΑΙ	ΟΧΙ
Χρόνιοι πονοκέφαλοι	ΝΑΙ	ΟΧΙ
Συχνές τάσεις λιποθυμίας	ΝΑΙ	ΟΧΙ
Έχετε πιει αλκοόλ τις τελευταίες 24 ώρες;	ΝΑΙ	ΟΧΙ
Έχετε κάνει χρήση ναρκωτικών ουσιών τον τελευταίο μήνα;	ΝΑΙ	ΟΧΙ
Είχατε ικανοποιητικό βραδινό ύπνο το βράδυ πριν το πείραμα;	ΝΑΙ	ΟΧΙ

Δηλώνω υπεύθυνα ότι όλες οι πληροφορίες που παρέχονται στο παρόν έντυπο ελέγχου ΔΜΔ είναι αληθείς και πλήρεις από κάθε άποψη.

_____   _____
   Υπογραφή Συμμετέχοντα   Ημερομηνία

_____   _____
      Υπογραφή Μάρτυρα   Ημερομηνία

Appendix IV: Handedness Screening

Ερωτηματολόγιο Εκτίμησης Προτίμησης Χεριού του Εδιμβούργου*
(Edinburgh Handedness Inventory)**

Ονοματεπώνυμο Ασθενή: _____

Παρακαλείστε να σημειώσετε με ένα (1) την προτίμησή σας για χρήση του αριστερού ή του δεξιού χεριού σας στις ακόλουθες δραστηριότητες/αντικείμενα.

Σε περίπτωση που η προτίμηση είναι τόσο ισχυρή που ποτέ δεν θα χρησιμοποιούσατε την άλλη πλευρά, εκτός αν είναι απολύτως αναγκαίο, βάλτε δύο (2).

Εάν είστε αδιάφοροι, βάλτε ένα σε κάθε στήλη (1 | 1).

Ορισμένες από τις δραστηριότητες απαιτούν και τα δύο χέρια. Σε αυτές τις περιπτώσεις, το μέρος της εργασίας ή του αντικειμένου για το οποίο είναι επιθυμητή η προτίμηση χεριού υποδεικνύεται σε παρένθεση.

Δραστηριότητα/ Αντικείμενο	Αριστερό Χέρι	Δεξί Χέρι
1. Γράψιμο		
2. Σχεδιασμός/ ζωγραφική		
3. Ρίξιμο/ Πέταγμα		
4. Ψαλίδι		
5. Οδοντόβουρτσα		
6. Μαχαίρι (χωρίς πιρούνι)		
7. Κουτάλι		
8. Σκούπα (πάνω χέρι)		
9. Άναμα ενός σπίρτου (σπίρτο)		
10. Άνοιγμα κουτιού (καπάκι)		
Σύνολο:	**AX=**	**ΔX=**
Αθροιστικό Σύνολο:	**ΑΣ=AX+ΔX=**	
Διαφορά :	**Δ=ΔX-AX=**	
Αποτέλεσμα:	**A=(Δ/ΑΣ) x 100 =**	
Ερμηνεία: Αριστερόχειρας: ΔX <-40 Αμφιδέξιος: -40 ≤ ΔX ≤ +40 Δεξιόχειρας: ΔX> +40		

*Προσαρμοσμένο στην ελληνική γλώσσα για ερευνητικούς σκοπούς
** Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. Neuropsychologia, 9, 97-113.

Appendix V: I.A.D.L. Instrumental Activities of Daily Living

Τεχνολογικό Πανεπιστήμιο Κύπρου | Σχολή Επιστημών Υγείας
Τμήμα Επιστημών Αποκατάστασης
Λογοθεραπεία

ΟΝΟΜΑΤΕΠΩΝΥΜΟ ΑΣΘΕΝΟΥΣ: ....

ΗΜΕΡΟΜΗΝΙΑ:...

I.A.D.L. Instrumental Activities of Daily Living
Κλίμακα Καθημερινών Δραστηριοτήτων
Κλίμακα Καθημερινών δραστηριοτήτων προσδιοριζόμενη από το νοσηλευτικό περίγυρο

Α. ΙΚΑΝΟΤΗΤΑ ΧΡΗΣΙΜΟΠΟΙΗΣΗΣ ΤΟΥ ΤΗΛΕΦΩΝΟΥ:

1. Χρησιμοποιεί το τηλέφωνο κανονικά. ☐

2. Καλεί ορισμένα πολύ γνωστά του νούμερα. ☐

3. Απαντά στο τηλέφωνο, αλλά δεν το χρησιμοποιεί αυθόρμητα. ☐

4. Δεν χρησιμοποιεί καθόλου το τηλέφωνο αυθορμήτως. ☐

Β. ΤΑ ΨΩΝΙΑ

1. Ψωνίζει κανονικά. ☐

2. Κάνει ορισμένα ψώνια (περιορισμένος αριθμός αγορών, το λιγότερο) ☐

3. Πρέπει να συνοδεύεται για να ψωνίσει. ☐

4. Εντελώς ανίκανος να ψωνίσει ☐

Γ. ΠΡΟΕΤΟΙΜΑΣΙΑ ΓΕΥΜΑΤΩΝ

* Δεν εφαρμόζεται: δεν προετοίμαζε ποτέ του γεύματα ☐

1. Προβλέπει, προετοιμάζει και σερβίρει κανονικά τα γεύματα. ☐

2. Προετοιμάζει κανονικά τα γεύματα, εάν του διαθέτουν τα ανάλογα υλικά. ☐

3. Ξαναζεστάνει και σερβίρει τα προετοιμασμένα γεύματα ή προετοιμάζει γεύματα, αλλά με λίγο έως πολύ ανεπαρκή τρόπο. ☐

4. Είναι απαραίτητο να του ετοιμάζει κάποιος τα γεύματα και να του τα σερβίρει. ☐

1

Δ. ΟΙΚΙΑΚΕΣ ΕΦΑΡΜΟΓΕΣ

*   Δεν εφαρμόζεται: Δεν έκανε ποτέ του οικιακές εργασίες.   ☐

1. Διατηρεί το σπίτι του μόνος του ή με βοήθεια κατά
περίπτωση (για τις βαριές εργασίες).   ☐

2. Φέρει εις πέρας ορισμένες καθημερινές ελαφρές εργασίες,
όπως πλύσιμο πιάτων, στρώσιμο κρεβατιών.   ☐

3. Φέρει εις πέρας ορισμένες καθημερινές εργασίες
αλλά δεν μπορεί να διατηρήσει ένα κανονικό επίπεδο
καθαριότητας.   ☐

4. Έχει ανάγκη βοήθειας για όλες τις οικιακές εργασίες.   ☐

5. Είναι ανίκανος να συμμετάσχει σε οποιαδήποτε εργασία.   ☐

Ε. ΠΛΥΣΙΜΟ ΡΟΥΧΩΝ

*   Δεν εφαρμόζεται: Δεν έχει ποτέ του ασχοληθεί με το πλύσιμο
των ρούχων του.   ☐

1. Πλένει μόνος του όλα του τα ρούχα.   ☐

2. Πλένει τα μικρά ρούχα, τις κάλτσες κ.λ.π.   ☐

3. Όλα τα ρούχα πρέπει να πλυθούν από ένα άλλο άτομο.   ☐

ΣΤ. ΜΕΣΟ ΜΕΤΑΦΟΡΑΣ

1. Χρησιμοποιεί τα δημόσια μέσα μεταφοράς με τρόπο
ανεξάρτητο, ή οδηγεί το αυτοκίνητο του.   ☐

2. Οργανώνει τις μετακινήσεις του με ταξί, αλλιώς δεν
χρησιμοποιεί κανένα δημόσιο μέσο μεταφοράς.   ☐

3. Χρησιμοποιεί τα δημόσια μεταφορικά μέσα με την
βοήθεια ενός συνοδού   ☐

4. Περιορισμένες μετακινήσεις με ταξί η με αυτοκίνητο
και με την βοήθεια κάποιου άλλου.   ☐

5   Δεν μετακινήται/ταξιδεύει καθόλου

2

Η. ΥΠΕΥΘΥΝΟΤΗΤΑ ΩΣ ΠΡΟΣ ΤΗΝ ΘΕΡΑΠΕΥΤΙΚΗ ΑΓΩΓΗ

1. Είναι υπεύθυνος για τη σωστή λήψη των φαρμάκων του,
   εάν του έχουν προετοιμαστεί οι ξεχωριστές δόσεις.

2. Είναι υπεύθυνος για τη λήψη των φαρμάκων του,
   εάν του έχουν προετοιμαστεί οι ξεχωριστές δόσεις.

3. Είναι ανίκανος να πάρει μόνος του τα φάρμακα του, ακόμη και
   εάν του έχουν προετοιμαστεί από πριν σε ξεχωριστές δόσεις.

Θ. ΙΚΑΝΟΤΗΤΑ ΣΤΗΝ ΔΙΑΧΕΙΡΙΣΗ ΧΡΗΜΑΤΟΣ

* Δεν εφαρμόζεται: ποτέ του δεν διαχειρίστηκε χρήματα

1. Διαχειρίζεται τα οικονομικά του με τρόπο αυτόνομο
   (προϋπολογισμός, σύνταξη επιταγών).

2. Διαχειρίζεται τις καθημερινές αγορές αλλά χρειάζεται βοήθεια
   στη διαχείριση των οικονομικών, στις μεγάλες αγορές κτλ.

3. Δεν μπορεί να συμμετάσχει σε καμία οικονομική συναλλαγή.

ΣΥΝΟΛΙΚΟ ΑΘΡΟΙΣΜΑ:

Source: Lawton, M.P., and Brody, E.M. "Assessment of older people: Self-maintaining and instrumer activities of daily living." Gerontologist 9:179-186, (1969).

3

Appendix VI

Beck's Depression Inventory

Το ερωτηματολόγιο του Beck (B.D.I.). ερωτηματολόγιο τύπου Α, ανδρική μορφή.

A. Συναίσθημα
0. δεν αισθάνομαι λυπημένος
1. αισθάνομαι λυπημένος ή μελαγχολικός
2. είμαι λυπημένος ή μελαγχολικός συνεχώς και δεν μπορώ να απαλλαγώ από αυτό
3. ειμαι τόσο μελαγχολικός ή δυστυχισμένος ώστε αυτο μου προξενεί πόνο
4. ειμαι τόσο μελαγχολικός ή δυστυχισμένος ώστε δεν μπορώ να το αντέξω

B. Απαισιοδοξία
0. Δεν είμαι ιδιαίτερα απιασιόδοξος ή αποθαρρυμένος για το μέλλον
1. Αισθάνομαι χωρίς θάρρος για το μέλλον
2. Μου φαίνεται οτι δεν έχω τίποτα καλό να περιμένω απο το μέλλον
3. Μου φαίνεται οτι δεν θα ξεπεράσω τις δυσκολίες μου
4. Μου φαίνεται οτι το μέλλον είναι χωρίς ελπίδα και οτι τα πράγματα δεν μπορεί να φτιάξουν

Γ. Αίσθημα αποτυχίας
0. Δεν αισθάνομαι αποτυχημένος
1. Μου φαίνεται οτι ειμαι αποτυχημένος περισσότερο απο τους άλλους ανθρώπους
2. Αισθάνομαι οτι έχω πετύχει στη ζωή μου πολύ λίγα πράγματα άξια λόγου
3. Καθώς σκέπτομαι τη ζωή μου μέχρι τώρα το μόνο που βλέπω είναι πολλές αποτυχίες
4. Αισθάνομαι οτι είμαι τελείως αποτυχημένος σαν άτομο (σύζυγος – πατέρας)

Δ. Απώλεια ικανοποίησης
0. Δεν αισθάνομαι ιδιαίτερα δυσαρεστημένος
1. Αισθάνομαι βαρυεστημένος σχεδόν όλη την ώρα
2. Δεν απολαμβάνω τα πράγματα όπως πρώτα
3. Δεν με ευχαριστεί πια τίποτα
4. Αισθάνομαι δυασαρεστημένος με το κάθε τι

Ε. Αίσθημα ενοχής
0. Δεν αισθάνομαι ιδιαίτερα ένοχο τον εαυτο μου
1. Πολλές φορές αισθάνομαι κακός ή χωρίς αξία
2. Αισθάνομαι πολύ ένοχος
3. Τον τελευταίο καιρό αισθάνομαι κακός ή χωρίς αξία σχεδόν όλη την ώρα
4. Αισθάνομαι οτι ειμαι πολύ κακός ή ανάξιος

Ζ. Αίσθημα τιμωρίας
0. Δεν αισθάνομαι οτι τιμωρούμαι
1. Αισθάνομαι οτι κάτι κακό μπορεί να μου συμβεί
2. Αισθάνομαι οτι τιμωρούμαι ή οτι θα τιμωρηθώ
3. Αισθάνομαι οτι μου αξίζει να τιμωρηθώ
4. Θέλω να τιμωρηθώ

Η. Μίσος για τον εαυτό
0. Δεν αισθάνομαι απογοητευμένος απο τον εαυτό μου
1. Αισθάνομαι απογοητευμένος απο τον εαυτό μου
2. Δεν μου αρέσει ο εαυτός μου
3. Σιχαίνομαι τον εαυτό μου
4. Μισώ τον εαυτό μου

Θ. Αυτομομφή
0. Δεν αισθάνομαι οτι είμαι χειρότερος από τους άλλους
1. Είμαι αυστηρός με τον εαυτό μου για τις αδυναμίες μου
2. Κατηγορώ τον εαυτό μου για τα λάθη μου
3. Κατηγορώ τον εαυτό μου για κάθε κακό που μου συμβαίνει

Ι. Ευχές αυτοτιμωρίας
0. Δεν μου έρχονται σκέψεις να κάνω κακό στον εαυτό μου
1. Μου έρχονται σκέψεις να κάνω κακό στον εαυτό μου αλλά ποτέ δεν θα έκανα κάτι τέτοιο
2. Μου φαίνεται οτι θα ήταν καλύτερα να πέθαινα
3. Μου φαίνεται οτι η οικογενια μου θα ήταν καλύτερα αν πέθαινα
4. Έχω συγκεκριμένα σχέδια αυτοκτονίας
5. Θα αυτοκτονούσα αν μπορούσα

Κ. Κλάμα
0. Δεν κλαίω περισσότερο απο το συνηθισμένο
1. Κλαίω τώρα περισσότερο απ' οτι συνήθως
2. Κλαίω συνεχώς, δεν μπορώ να το σταματήσω
3. Άλλοτε μπορούσα να κλάψω αλλά τώρα μου είναι αδύνατο να κλάψω αν και το θέλω

Λ. Ευερεθιστότητα
0. Δεν είμαι περισσότερο εκνευρισμένος τώρα απ' οτι συνήθως
1. Ενοχλούμαι ή εκνευρίζομαι περισσότερο απ' οτι συνήθως
2. Αισθάνομαι διαρκώς εκνευρισμένος
3. Δεν εκνευρίζομαι τώρα για πράγματα που με νευρίαζαν συνήθως

Μ. Κοινωνική απόσυρση
0. Δεν έχω χάσει το ενδιαφέρον μου για τους άλλους ανθρώπους
1. Ενδιαφέρομαι τώρα λιγότερο για τους άλλους ανθρώπους απ' ότι παλαιότερα
2. Έχω χάσει το περισσότερο ενδιαφέρον μου για τους άλλους ανθρώπους και τα αισθήματα μου για αυτούς έχουν λιγοστέψει
3. Έχω χάσει όλο το ενδιαφέρον μου για τους άλλους ανθρώπους και δεν νοιάζομαι καθόλου για αυτούς

Ν. Αναποφασιστικότητα
0. Είμαι το ίδιο αποφασιστικός όπως πάντα
1. Τελευταία αναβάλω το να παίρνω αποφάσεις
2. Έχω μεγάλη δυσκολία στο να παίρνω αποφάσεις
3. Δεν μπορώ να πάρω πια καμία απόφαση

Ξ. Σωματικό εγώ
0. Δεν μου φαίνεται οτι η εμφάνιση μου ειναι χειρότερη απο ποτέ
1. Ανησυχώ μήπως μοιάζω γερασμένος και αντιπαθητικός
2. Αισθάνομαι οτι έγινε τέτοια αλλαγή επάνω μου, ώστε να φαίνομαι αντιπαθητικός
3. Μου φαίνεται οτι είμαι άσχημος και αποκρουστικός

Ο. Μείωση της παραγωγικότητας
0. Τα καταφέρνω στην δουλειά μου όπως και πρώτα