Spring 5-15-2016

The Feasibility of Using Metacognitive Strategy Training to Improve Performance, Foster Participation, and Reduce Impairment Following Neurological Injury

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by

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A dissertation presented to the
Graduate School of Arts & Sciences
of Washington University in
partial fulfillment of the
requirements for the degree
of Doctor of Philosophy

May 2016
St. Louis, Missouri

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List of Abbreviations

ADL = activities of daily living

ARAT = Action Research Arm Test

BOLD = blood oxygen level dependent

CFQ = Cognitive Failures Questionnaire

CICI = chemotherapy induced cognitive impairment

CONSORT = Consolidated Standards for Reporting Trials

CO-OP = Cognitive Orientation to daily Occupational Performance

COPM = Canadian Occupational Performance Measure

CPI = Community Participation Indicators

DEX = Dysexecutive Syndrome Questionnaire

DKEFS = Delis-Kaplan Executive Function System

EF = executive function

fMRI = functional magnetic resonance imaging

IADL = instrumental activities of daily living

ICF = International Classification of Functioning, Disability, and Health

MAAT = Memory and Attention Adaptation Training

MCST = metacognitive strategy training

MET = Multiple Errands Test

MoCA = Montreal Cognitive Assessment

MRI = magnetic resonance imaging

NIH = National Institutes of Health

NIHSS = National Institutes of Health Stroke Scale

OODA = object oriented data analysis

OT = occupational therapy

PHQ-9 = Patient Health Questionnaire-9 item

PQRS = Performance Quality Rating Scale

PROMIS (57) = Patient Reported Outcomes Measurement Information System

PS-SES = Participation Strategies Self-Efficacy Scale

rs-fcMRI = resting-state magnetic resonance imaging

SAS = Supervisory Attentional SystemSIS = Stroke Impact Scale

SJR = St. John’s Rehabilitation

TRISL = The Rehabilitation Institute of St. Louis

UC = usual care

Acknowledgments

The studies in this dissertation were supported by the following agencies/awards: (1) Canadian Institutes of Health Research Open Operating Grant, FRN#111200; (2) National Institutes of Health (NIH)-National Center of Medical Rehabilitation Research (NCMRR), award numbers K12HD055931 and K23HD073190; (3) NIH-National Center for Advancing Translational Sciences (NCATS), award number UL1TR000448; (4) NIH-National Institute of Child Health & Human Development, award number U54HD087011; and (5) NIH-National Cancer Institute (NCI), award number P30CA091842. In addition, I would like to acknowledge all of the following people who helped make this dissertation possible: (1) All of the students, faculty, and staff in the Performance, Participation, and Neurorehabilitation Laboratory, especially Meghan Doherty and Alexis Young; (2) All of the people who participated in the studies in this dissertation; (3) All of my collaborators/co-authors on these studies, Sara McEwen, Helene Polatajko, Jorge Rios, Dianne Cirone, Meghan Doherty, Carolyn Baum, Jay Piccirillo, Brad Schlaggar, Dorina Kallogjeri, Becky Coalson, Joyce Nicklaus, and Cynthia Ma; and (4) My dissertation examination committee, Carolyn Baum, Scott Frey, Allison King, Jay Piccirillo, and Desiree White.

This dissertation is dedicated to the following people. First, my mentor Carolyn Baum. Over the years you have had many roles in my life including teacher, Program Chair, pre-doctoral research mentor, career development mentor, employer, and PhD Chair. It has been a privilege to learn from you and your perspective on occupational therapy. I will forever consider it an honor to have you as a life-long colleague and friend. Second, to my extended family. You all have always kept me grounded and are an endless source of perspective, humor, and love. Thank you for always listening to me talk about my research and OT. Finally, to my wife Angie and my children, William, Henry, and baby #3 on the way. No way would this dissertation, my career, or my life be possible without all of you. Unfortunately all of you have had to bear the brunt of the sacrifice necessary for my career and I thank you for doing so willing and selflessly. I love you all.

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May 2016

ABSTRACT OF THE DISSERTATION

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Executive function is central to our ability to learn and participate in everyday life activities and rehabilitation outcomes for individuals with executive dysfunction after neurological injury are poor. The impairments and performance challenges these individuals experience are typically not identified appropriately so they often do not receive adequate rehabilitation and can have significant challenges returning to complex everyday life activities. The vast majority of rehabilitation efforts to support individuals with neurological injuries with executive dysfunction are based on a restoration model that aims to improve cognitive function with the expectation that these gains will translate to everyday life. The available evidence suggests this translation is not happening as improvement in cognitive performance is often not leading to improvement in everyday life activities. Performance-based interventions that target improved engagement in everyday life activity are being developed with the expectation that this approach will remediate/mitigate impairments; however, these performance-based approaches have not been adequately evaluated. The purpose of this dissertation was to evaluate the feasibility and preliminary efficacy of a performance-based intervention approach,

metacognitive-strategy training, on performance and impairment reduction in individuals with central neurological injury.

Preface

This dissertation addresses two fundamental questions: (1) Does engagement in occupation influence health; and (2) Does engagement in occupation remediate impairment? In this context health has a broader meaning beyond absence of disease to also encompass a good quality of life and satisfaction with one's ability to participate in his/her chosen activities (Yerza, 1998). The scientific salience of these questions is apparent in the lack of evidence in rehabilitation that restoration based intervention approaches are leading to improvement in everyday life. These key questions have driven the profession of occupational therapy for 100 years and served as a basis for the distinct value of our profession in the health care system; however, there has been very little work to evaluate their empirical basis. These questions were derived from the work of Adolph Meyer and the philosophical influence he had on the development of occupational therapy.

Adolph Meyer and the Philosophy of Occupational Therapy

Adolph Meyer was a psychiatrist and neurobiologist in the early 1900's. During this time the medical scientific community was deeply entrenched in a period of scientific revolution and a heavy emphasis on discovering disease etiology and developing curative medicines to "fix" disease. Contrary to this focus, Meyer published and practiced his psychobiological approach to working with individuals with mental illness. The basic premise of this approach is that in order to understand and treat mental illness, you have to understand the personal and environmental factors that influence behavior. He said that mental illness was not a specific disease that needed to be excised from the body with medicine but rather an affliction of maladaptation, development of poor habits, and a misuse of time and energy (Meyer, 1922). Meyer was influenced by the historical concepts of moral treatment and the use of occupation in the treatment of individuals with mental illness. He had a strong influence on the formation of the emerging profession of occupational therapy (OT) through his close relationship with OT founders William Rush Dunton and Eleanor Clarke Slagle. It is my assumption that this is also the reason Meyer was invited to present at our national association meeting four years after its founding to present to the group the philosophy of occupation (Meyer, 1922).

One key statement best summarizes Meyer's philosophy of occupation therapy: "**Our role consists of providing opportunities rather than prescriptions. There must be opportunities to work, to do, plan, and create, and to learn to use material.**" As later described in his philosophy, Meyer believed in the curative power of occupation to help individuals recover from mental illness. The Philosophy of Occupation (Meyer, 1922) provided a clear focus and foundation for our profession. Although over time many in our profession have lost sight of this philosophy, leaders in our field such as Mary Reilly, Gail Fidler, Wilma West, Carolyn Baum, and Glen Gillen have helped us refocus on our philosophical foundation provided by Meyer to help us articulate what we now refer to as our distinct value in the health care system in the United States and world. One area in which these questions are particularly salient is in rehabilitation efforts with individuals with executive dysfunction after neurological injury.

Introduction

Executive Dysfunction after Neurological Injury

Although rehabilitation scientists are gaining a firm understanding of how sensory and motor impairment impacts participation, our knowledge of how cognition impacts everyday life is still evolving. It is known that cognition is important to participation in everyday life. This includes an individual's ability to attend to and filter stimuli, encode and recall information, communicate with others, make plans and decisions, self-correct behavior, and use judgment (Goel, Grafman, Tajik, Gana, & Danto, 1997; Katz, 2005; Lezak, 1986). Arguably, one the most critical and often under-recognized cognitive functions that impacts participation is executive function.

To date there is very little consensus on the definition/conceptualization of "executive function" because across health care and scientific disciplines, areas of research, and different clinical settings executive function is typically identified and defined differently. A primary basis for this confusion is the existing models of executive function. Two classic models in the literature are Alan Baddeley's Working Memory Model and the identification of the central executive system (Baddeley, 1996) and Don Norman and Tim Shallice's Supervisory Attentional System (Norman & Shallice, 1986). Baddeley's model conceptualizes executive function as a central executive system that regulates working memory systems (Baddeley, 1996). Norman and Shallice conceptualize executive function as being regulated by attentional processes that select/modify automatic behavioral responses in response to novel tasks and situations (Norman & Shallice, 1986). A more recent model of executive function by Miyake and colleagues (2000) identified latent variables from data collected from healthy controls performing common tasks as well as common executive function based tests; the variables identified were: (1) mental set shifting; (2) information updating/monitoring; and (3) inhibition of prepontent responses (Miyake et al., 2000). Even in light of the data from this study, Miyake and colleagues acknowledged that there is no consensus on what cognitive functions should be considered executive (Miyake et al., 2000). Braver and Ruge (2006) classified existing knowledge from the cognitive neuroscience literature related to executive function and identified seven processes that were considered "executive" based on the available studies: (1) strategic control of memory; (2) stimulus-response interference; (3) response inhibition; (4) underdetermined responding; (5) performance monitoring; (6) task management; and (7) higher cognition (Braver & Ruge, 2006). While there are commonalities between all of these models from the multidisciplinary literature, it is also clear that there is a lack of consensus of what is executive function. This lack of consensus on executive function is likely the primary contributing factor that leads to miscommunication and misunderstanding on the role executive functioning plays in participation. For the purposes of my work, I will start with the International Classification of Functioning, Disability and Health (ICF) definition of executive function. The ICF defines executive functions as "higher-level cognitive functions" and it is described as follows:

> "Specific mental functions especially dependent on the frontal lobes of the brain, including complex goal-directed behaviors such as decision-making, abstract thinking, planning and carrying out plans, mental flexibility, and deciding which behaviors are appropriate under what circumstances; often called executive functions (p. 57) (World Health Organization, 2001)."

Inherent in this definition is the complexity of what executive function is, how it is defined for classification purposes, and what specific actions/behaviors it encompasses. Even in light of this lack of consensus related to what is executive function, it is clear within all of the descriptions that executive function makes it possible for humans to fully participate in everyday life. Executive function allow us to integrate information from the environment with our memory stores in the brain to generate, implement, and correct strategies necessary to accomplish tasks (Goldberg, 2001; Manchester, Priestley, & Jackson, 2004). Executive functioning is the most complex function of the human brain and is central to being able to perform activities in a real-world environment such as home, work, and the community. Unfortunately, this complexity often means that executive functioning can be disrupted in even the mildest neurological injuries that affect the brain. The constantly evolving understanding of what executive function is and its neurological substrates make it challenging for the health care community to appreciate the role executive function has in everyday life and to identify when someone has an impairment.

By definition the frontal lobes of the brain are known to be an integration center of executive function. At one time, executive function was thought to be entirely housed within the frontal lobes and the healthcare community attributed executive dysfunction only to frontal lobe injury. Clinically, we are now aware that individuals can experience executive dysfunction even in absence of frontal lobe injury (Manchester et al., 2004; Tranel, Anderson, & Benton, 1994). These impairments were attributed to neural network models of brain function and how executive function is dependent on neural connections throughout the brain. Empirically, a relatively new neuroimaging technique called resting-state magnetic resonance imaging (rs-fcMRI) has allowed for investigation/identification of these networks. In 2008, a team led by Nico Dosenbach at Washington University that included Brad Schlaggar and Steve Petersen discovered what is referred to as the cognitive control network, specifically the frontal-parietal network (Dosenbach et al., 2006). The function of this network is responsible for the moment-to-moment control of cognitive function. It has been tied to executive function and performance, specifically the ability to transfer knowledge from a learned activity to an unlearned activity (Zanto & Gazzaley, 2013).

Therefore, we now know that almost any diagnosis that affects the brain can potentially affect executive functioning. Executive dysfunction has been documented in many conditions frequently encountered by rehabilitation professionals including but not limited to head injury (Goverover & Hinojosa, 2002), stroke (Baum et al., 2008), Alzheimer disease (Buckner, 2004), spinal cord injury (Hanks, Rapport, Millis, & Deshpande, 1999), Parkinson disease (Cahn et al., 1998; Klepac, Trkulja, Relja, & Babic, 2008), psychiatric disorders (Gildengers et al., 2007; Rempfer, Hamera, Brown, & Cromwell, 2003), autism (Rutherford, Young, Hepburn, & Rogers, 2007), multiple sclerosis (Birnboim & Miller, 2004), and cancer (Nieuwenhuijsen, de Boer, Spelten, Sprangers, & Verbeek, 2008). Most of these conditions have other complex neurological and psychological symptoms that overshadow executive dysfunction; however, it is nevertheless a prominent symptom impacting performance. With that said, there are at least two conditions in which it is known that executive dysfunction has a profound impact on everyday life: mild-moderate stroke (Edwards, Hahn, Baum, Perlmutter, et al., 2006; Wolf, Barbee, & White, 2010) and chemotherapy-induced cognitive impairment (CICI) following treatment for cancer (Collins, MacKenzie, Tasca, Scherling, & Smith, 2012; Falleti, Sanfilippo, Maruff, Weih, & Phillips, 2005). Both of these conditions are considered neurological injuries and typically have executive dysfunction as a prevalent symptom impacting performance and therefore are ideal populations for investigation in this area of study.

Mild-Moderate Stroke

In a study I completed with my colleagues in 2009 with over 7,000 people who had a stroke, it was found that half of all people who have a stroke are classified as having a mild stroke by the National Institute of Health Stroke Scale (NIHSS) (Wolf, Baum, & Connor, 2009). The NIHSS is a 15-item neurologic exam that assesses consciousness, language, neglect, visual-field loss, extra ocular movement, motor strength, ataxia, dysarthria, and sensory loss (Brott et al., 1989). A mild stroke is indicated by a NIHSS score of < 6, whereas 6 to 16 indicates a moderate stroke and 17 to 46 indicates a severe stroke (Khatri, Conaway, & Johnston, 2012). Individuals with milder neurological impairment following stroke exhibit less outward signs of motor impairment, speech difficulty, and are more independent in their activities of daily living (ADL) (Edwards, Hahn, Baum, Perlmutter, et al., 2006; Wolf et al., 2010). The less these outward signs of impairment are apparent the less likely an individual is to receive rehabilitation services (Wolf, Baum, & Connor, 2009). The problem facing both the person with a stroke and the rehabilitation community, however, is that as these individuals are followed over time it is clear that they are experiencing difficulty reintegrating back into everyday life activities (Hildebrand, Brewer, & Wolf, 2012; O'Brien & Wolf, 2010; Rochette, Desrosiers, Bravo, St-Cyr-Tribble, & Bourget, 2007).

There have been several documented studies that have found that even individuals with the mildest neurological impairment post-stroke are experiencing difficulty returning to everyday life activities. Rochette and colleagues (2007) compared levels of participation in participants with mild stroke (n=35) across four times points: (1) pre-morbid; (2) < 3 weeks post-stroke; (3) 3 months post-stroke; and (4) 6 months post-stroke. All of the participants reported significant reductions in their levels of participation across all time points (Rochette et al., 2007). Edwards and colleagues (2006) found that participants with mild stroke were reporting decreased participation in employment, social activities, concentration, and driving post mild stroke that were resulting in a reduced quality of life (Edwards, Hahn, Baum, & Dromerick, 2006). O'Brien and Wolf (2010) surveyed 98 participants with mild stroke who were working at the time of their stroke and found that 37% of the group (n=36) never returned to work following stroke, and of the 63% (n=62) that did return to work another 15% (n = 9) were unemployed 6-months post-stroke; 6-month unemployment total 46% (n = 45). They also found that over half of the individuals who were successful in returning to work reported ongoing symptoms from their stroke that were impacting their work performance, such as difficulty concentrating, difficulty keeping organized, fatigue (O'Brien & Wolf, 2010). It is logical to assume that cognitive function, specifically executive function, is playing a role in these participation changes post-stroke.

In a study by Edwards and colleagues (2006), the authors found that 33% of their participants with mild stroke had four or more sensory or cognitive impairments that were not documented in their medical charts prior to discharge from the acute stroke service (Edwards, Hahn, Baum, Perlmutter, et al., 2006). Consistent with these findings, other studies have also found that cognitive deficits, especially executive function deficits, are often undetected at the time of stroke and these deficits tend to be chronic (Hochstenbach, den Otter, & Mulder, 2003; Nys et al., 2005; Patel, Coshall, Rudd, & Wolfe, 2003; Wolf, Baum, & Conner, 2009; Zinn et al., 2004). To confirm this finding, Wolf and colleagues (2011) using very rigorous criteria to identify specific deficits in executive function, found that 66% of their sample of individuals with mild stroke scored in the deficit range on at least one of four measures of executive function (Wolf et al., 2010). All of these studies highlight an ongoing problem in rehabilitation. Individuals with milder neurological impairment following mild stroke have specific deficits in executive function that are impacting reintegration into complex everyday life activities. These problems experienced by people with mild stroke are consistent with what individuals with chemotherapy-induced cognitive impairment (CICI) following treatment for cancer experience.

Chemotherapy-Induced Cognitive Impairment (CICI)

Although CICI can result from treatment of any cancer that involves the use of chemotherapy, the vast majority of literature in this area is in breast cancer. There were approximately 234,840 cases of breast cancer in the United States in 2015, accounting for 29% of female cancer incidence in the U.S. (American Cancer Society, 2015). Through treatment advances, earlier detection, and an increased awareness throughout the country, death rates from breast cancer have been decreasing for the last 20 years (Breastcancer.org, 2012). This poses a new challenge as a population of breast cancer survivors need ongoing care to address the symptoms and health limitations they experience following treatment for breast cancer. In addition to the potential of needing ongoing healthcare associated with their breast cancer diagnosis, the treatment for breast cancer causes additional chronic symptoms which can impact the survivor's ability to reintegrate into everyday life activities. Over half of newly diagnosed breast cancer cases, more than 143,000, will be women under the age of 65 who will need support returning to family, work and community activities (American Cancer Society, 2015). In spite of the survival benefits of chemotherapy, recent research has found decreased productivity, impaired community involvement, and poor role-functioning resulting from cognitive dysfunctions after chemotherapy (Reid-Arndt, Hsieh, & Perry, 2010; Reid-Arndt, Yee, Perry, & Hsieh, 2009; Ronis, Duffy, Fowler, Khan, & Terrell, 2008; Schou, Ekeberg, Sandvik, Hjermstad, & Ruland, 2005; Tobias et al., 2010). One of the most predominant and well-documented impairments following chemotherapy that is impacting reintegration into everyday life is cognitive dysfunction.

Recent research, including published meta-analyses, has shown that cognitive dysfunction is pervasive following chemotherapy in breast cancer survivors (Collins et al., 2012; Falleti et al., 2005; van Dam et al., 1998), with common symptoms reported by patients including but not limited to memory, thinking clearly and concentrating (Falleti et al., 2005) and complex attention (Vardy, Rourke, & Tannock, 2007). Longitudinal studies have shown that cognitive impairments are identified by both self-report and neuropsychological measures from 4 to 20 years post-chemotherapy (Koppelmans et al., 2012; Kreukels, van Dam, Ridderinkhof, Boogerd, & Schagen, 2008; Yamada, Denburg, Beglinger, & Schultz, 2010). One study examining the long-term effects of chemotherapy reported survivors performed significantly poorer on neuropsychological tests 20 years after chemotherapy than age-matched controls (Koppelmans et al., 2012).

In the literature reporting cognitive changes following chemotherapy, one specific cognitive function that is consistently reported to be negatively impacted is executive function (Kesler, Kent, & O'Hara, 2011). Deficits in executive processing have been demonstrated mechanistically as there is evidence to support that following chemotherapy individuals with breast cancer have decreased activation in the prefrontal cortex with associated perseverative errors and reduced processing speed (Kesler et al., 2011). Using resting-state functional connectivity MRI (rs-fcMRI), alterations in global and regional functional connectivity have been reported in breast cancer survivors (Bruno, Hosseini, & Kesler, 2012; Kesler et al., 2013). Specific to cognitive impairment in breast cancer survivors, our research team recently found that breast cancer survivors who report CICI compared to those who do not show weaker functional connectivity between regions of the frontal-parietal executive control network measured using rs-fcMRI (Piccirillo et al., 2015). These results underscore the potential of rs-fcMRI as a biomarker to identify and evaluate mechanistic changes associated with CICI. This study assessed the impact of chemotherapy on spontaneous brain activity quantified as temporal correlations in resting state BOLD signal between pairs of regions. The results showed reduction in functional connectivity (i.e., reduced correlation magnitude in the spontaneous BOLD signal) between two regions in the left middle frontal cortex and right parietal cortex in breast cancer survivors with self-reported CICI (n=15) compared to those without CICI (n=13). In addition, weaker functional connectivity on rs-fcMRI was correlated with greater levels of reported cognitive impairment. These two brain regions are components of the frontal-parietal cognitive control network. These results suggest that standard therapeutic levels of chemotherapy for breast cancer patients may result in alterations in a brain network that supports executive function, which in turn may be a contributing factor in cognitive difficulty. These results also demonstrate that changes in executive function are commonly part of CICI in women following treatment for breast cancer.

Schagen and colleagues (2006) showed that over a 6-month period, cognitive function on a composite score of neuropsychological assessments evaluating sustained attention, working memory, processing speed, executive function, and verbal/motor function declined in breast cancer survivors after chemotherapy, but the strongest effects of chemotherapy were on executive function (Schagen, Muller, Boogerd, Mellenbergh, & van Dam, 2006). Wefel and colleagues (2010) found similar results. After controlling for premorbid cognitive dysfunction, 29% of their sample had delayed cognitive decline in learning and memory, executive function, and processing speed as measured by neuropsychological testing following chemotherapy;

executive function was one of the most common domains affected (Wefel, Saleeba, Buzdar, & Meyers, 2010). Studies examining executive function have demonstrated that although not all breast cancer survivors have executive dysfunction following chemotherapy, for those who do the impairment is persistent over time. Similar to what is known in individuals with stroke, these changes in executive function are associated with disruption in participation in everyday life activities.

Difficulty completing complex everyday life activities has been documented in breast cancer survivors (Boykoff, Moieni, & Subramanian, 2009; Munir, Burrows, Yarker, Kalawsky, & Bains, 2010; Munir et al., 2011). Adults at least one year post completion of adjuvant treatment for cancer reported diminished independence, difficulty performing routine complex activities and reduced skill at work leading to financial instability (Boykoff et al., 2009). Poorer executive functioning measured by neuropsychological assessment was associated with decreased social integration, community involvement, and productivity at work (Reid-Arndt et al., 2009). A 2005 study found that a third of cancer survivors had not returned to work six months after diagnosis and that many who had returned to work did so with reduced hours (Bradley, Neumark, Bednarek, & Schenk, 2005). Given what we know about executive dysfunction post-chemotherapy and the effect it has on everyday life activity, there has been relatively little rehabilitation research to address this area.

A recent and prominent example of this issue related to rehabilitation to address CICI in women following treatment for breast cancer is a study conducted by Ferguson and colleagues (2007) and the development of the Memory and Attention Adaptation Training (MAAT) program. The MAAT was used to train participants in compensatory strategies to manage cognitive symptoms for completing daily activities; however, the emphasis was on impairment reduction. Although the RCT study evaluating MAAT found an improvement in verbal memory, there was no statistical difference on self-report of daily cognitive complaints (Ferguson et al., 2007). This study is representative of the current level of knowledge in the field on this topic; there is support for interventions to improve cognitive function, but limited support for the use of these interventions to also improve everyday life performance.

In both individuals with stroke and women with CICI following treatment for breast cancer, the first challenge to address these changes in executive function is related to assessment. There is a well-documented debate related to the best methods to assess executive function changes and the challenges related to assessing executive function clinically. These challenges must be acknowledged and addressed in any research studies that are attempting to intervene with these populations.

Assessment of Executive Function

The three most common ways to assess executive function currently used in practice are neuropsychological assessment, performance-based assessments, and self-report measures (patient-reported outcome measures). In addition, a relatively new method is the use of resting-state functional MRI that can evaluate neural connectivity in cognitive control networks associated with executive function. All of these methods have strengths and limitations and it is important to acknowledge how these measures have evolved to determine the best method to evaluate executive function following neurological injury.

Neuropsychological assessment

Neuropsychological assessments were developed in the mid-twentieth century as tools to help physicians locate brain lesions and identify impairment. They were based on now somewhat outdated theories of brain function that focused on localization of function. The basic focus of the assessments was to capture impairment in a specific brain/cognitive function to determine the area of the brain that was impacted by injury or illness (Marcotte & Grant, 2009; Suchy, 2009). With the advent of neuroimaging, the need for neuropsychological assessments for this purpose was minimized and the use of neuropsychological assessments shifted to capture behavioral changes to predict everyday life function; however, the tools themselves did not change much and were not designed for this purpose (Marcotte & Grant, 2009). Muriel Lezak (2004), a neuropsychologist, in her book on neuropsychological assessment has been saying for years that neuropsychological assessments of executive function are insufficient to assess capacity and predict everyday life performance. Specifically, Lezak and others have said that the neuropsychological tools used to evaluate executive function are highly structured which in essence contradicts our understanding of executive function in that executive function is most salient in unstructured, novel activities (Lezak, Howieson, & Loring, 2004; Suchy, 2009).

Strengths and limitations of neuropsychological assessment of executive function

As previously mentioned, neuropsychological assessments of executive function are typically highly structured. This high-degree of structure allows for rigorous evaluation of the psychometric properties of the assessments. Neuropsychological assessments used in practice typically have a very high degree of reliability, validity and clinical utility. Further, they also typically have age-based criterion scores to allow for comparison to control populations and/or alternate forms that can be used to evaluate outcomes. For these reasons, these instruments are ideal to evaluate the effect of intervention and/or recovery from illness or injury. With that said, the high-degree of structure is also responsible for the primary limitation of neuropsychological assessments. The structure of the assessment requires that the environment is standardized and specific instructions for how to complete the assessment are provided; this negates our understanding of when and how we use executive function in everyday life (Lezak, 2004; Suchy, 2009).

Performance-based assessments

The beginning of performance-based assessments of executive function also occurred in the mid-twentieth century in relation to the development of environmental psychology theories. The leading voice in this field was Kurt Lewin (1943), with his field theory and concept of life space. Lewin's theory said that behavior is a result of myriad internal (person) and external (environmental) factors that are in action at any given time (Lewin, 1943). Building off this work, a contemporary of Lewin's named Egon Brunswik published his concept of representative design for the field of psychology and introduced the term ecological-validity (Brunswik, 1947, 1955). Brunswik was advocating for a paradigm shift away from a traditional scientific method approach that was prevalent in psychology in which all variables but one are held constant. Representative design postulated that if you wish to understand behavior you need to allow individuals to have free behavior in an unrestricted environment. He referred to this as being ecologically-valid. Although both Lewin and Brunswik criticized each other's theories as being limited in their explanation of everyday human behavior, inherently they are addressing the same notion—the interaction with the environment is important to understand behavior. Continuing to build on these concepts, J.J. Gibson introduced the concept of affordances, or what in the environment affords behavior, and the idea that behavior is largely shaped by what is available to us in the environment (Gibson, 1966). Through friendly collegial contact, J.J. Gibson discussed this concept of affordances with cognitive psychologist Donald Norman. Norman, later with Tim Shallice, developed a model of executive function called the Control-to-Action theory which is now known as the Supervisory Attentional System (SAS) (Norman & Shallice, 1986).

SAS postulates that most behavior is automatic (schemas) and can occur without much conscious effort; however, we rely on our supervisory attentional system to identify changes in the task and environment to determine when to suppress or elicit specific schema. Inherent in this model is the concept of affordances and the influence of the environment on behavior. Tim Shallice with Paul Burgess (1991), while working with individuals with neurological injury and strategy application disorder (executive dysfunction), developed the Multiple Errands Test (MET) to evaluate the action of the SAS. The MET is a shopping task that was originally based in a hospital district in London. The MET allowed free behavior in an unrestricted but somewhat standardized environment, and scoring was based on observations (Shallice & Burgess, 1991). The MET is arguably the first performance-based measure of executive function that evolved from the environmental psychology theory of assessing the interaction between the person and the environment. Later descriptions of the MET used Brunswik's term "ecological validity" in its description alluding to this connection (Burgess, Alderman, Evans, Emslie, & Wilson, 1998). In the manuscript describing the MET, Shallice and Burgess acknowledged that it had long been known that individuals could experience profound changes in everyday life when impairment as evaluated by executive function neuropsychological measures was at most minor (Shallice & Burgess, 1991). This phenomenon has since been labeled by colleagues of Paul Burgess, Alan Baddeley and Barbara Wilson, as "dysexecutive syndrome" (Baddeley & Wilson, 1988). The term dysexecutive syndrome is used for two reasons: (1) to remove the connection between executive dysfunction and frontal lobe only injuries and (2) to label a syndrome based on presentation of symptoms instead of being tied to a specific neurological condition.

Strengths and limitations of performance-based assessment of executive function

As our knowledge of brain function evolves with recent investigations of the cognitive control networks, specifically the frontal-parietal network, and their role in moment-to-moment control of cognitive function (executive function) (Dosenbach et al., 2006), performance-based measures offer a complimentary yet distinct method to evaluate executive function compared to neuropsychological assessments. Performance-based measures have been referred to as inherently ecologically-valid because they were structured evaluations of real-world activities (Burgess et al., 1998). Therefore, the real strength of performance-based assessment of executive function lies in their ability to evaluate functional cognitive ability in the context of performing an activity.

Performance-based measures are developed differently than neuropsychological measures in a way that appears not as rigorous. Although performance-based assessments assess the interaction of the person in an environment, to do this there is a cost in the amount of structure that would allow for a higher level of standardization. Compared to neuropsychological measures, the reliability and validity of performance-based measures are typically not as rigorously evaluated nor do they tend to have age-based criterion scores to allow comparison to a control population. Further, performance-based measures have a strong learning effect that only allows for one administration unless there is an alternate form. This means they are typically used as a diagnostic to identify performance limitations as opposed to an outcome measure that can be used to track changes in cognitive performance over time. Finally, performance-based assessments do not provide information related to the specific cognitive impairments that could be impacting performance. If someone does not perform an aspect of the assessment well, it is not always clear whether this degradation in performance was related to an executive function deficit, poor motivation, memory recall, problems with attention, anxiety, etc.

This is the point at which the use of neuropsychological assessments can be of use to help interpret behavior on a performance-based measure. Their simultaneous use provides clinicians with the best possible data to assess capacity/performance.

Self-report measures (patient-reported outcome measures)

Patient reported outcome measures, or self-report measures, are often used in conjunction with both neuropsychological and performance-based assessment to evaluate executive function and performance. Although self-report measures of functioning have been arguably the most widely used and most scrutinized method of assessment over the last century, their popularity has been on the rise over the last 15 years with the NIH Roadmap initiative and the development of the Patient Reported Outcomes Measurement Information System (PROMIS) (Cella et al., 2010; Cella et al., 2007). There was a general recognition within NIH that clinical measures, i.e., laboratory testing, have very little meaning or relevance to everyday life performance; however, the self-report tools in existence were not precise and lacked standardization (Cella et al., 2010; Cella et al., 2007). The PROMIS tools have sought to rectify this problem in several different domains of everyday life function; however, the limitation of self-report measures still remains in assessment of executive function performance. The complexity of executive function and the individualization of everyday life experiences often lead to discrepancies between self-reported problems in everyday life activities and measureable changes or impairments in executive function performance (Chaytor, Schmitter-Edgecombe, & Burr, 2006; Hutchinson, Hosking, Kichenadasse, Mattiske, & Wilson, 2012). For this reason, self-report measures are often used to capture how the individual has or is experiencing changes in everyday life that may not be apparent in objective assessment.

Strengths and limitations of self-report measures of executive function

There are several strengths to using self-report measures of executive function. First as previously mentioned, self-report measures are the only method that captures how the individual perceives they are or are not experiencing everyday life problems related to cognitive loss. Second, self-report measures are convenient and often inexpensive or free to administer. Third, self-report measures do not require extensive training to administer (Buchanan et al., 2010). With that said, the primary limitation with self-report measures is the inability to objectively quantify changes in cognitive performance. Further, some individuals are not able to accurately report problems they may be experiencing secondary to an awareness problem (Buchanan et al., 2010). Awareness, or metacognition, is an individual's knowledge about his/her abilities as well as the individual's ability to monitor behavior to recognize when changes are necessary to improve performance (Toglia & Kirk, 2000). The issue created by the use of self-report measures to evaluate executive function performance is that impaired executive function is often associated with a decrease in our metacognitive abilities (Stuss & Alexander, 2000). Therefore, although self-report measures should be used to capture how the individual perceives his/her changes in performance, there is an ever-present need for an objective measure of executive function that can be used as an outcome measure.

Resting-state functional MRI (rs-fcMRI)

Neuroimaging techniques are part of the evolution of neuropsychological assessment and based on the same medical model; however, the use of neuroimaging grew out of the discrepancy between neuropsychological measures of executive function and self-report of persons with neurological injury. Although this is separate from the literature on dysexecutive syndrome, the central issue is consistent—neuropsychological assessments were not capturing the changes in everyday life persons with neurological injury were experiencing. The most common neuroimaging technique that has been used to evaluate changes in neural activity associated with changes in cognitive performance is functional magnetic resonance imaging (fMRI). When using fMRI, changes in neural activity while the individual is performing a task are measured by evaluating changes in cerebral blood flow. Multiple studies using fMRI have shown that CICI is associated with decreased activation in response to tasks of executive function (Conroy et al., 2013; de Ruiter & Schagen, 2013). An alternative approach to the study of brain function using fMRI is examining intrinsic brain activity that can be imaged when subjects are awake but not performing a task to understand the functional organization of the brain (Power et al., 2011; Yeo et al., 2011). This is referred to as resting-state functional connectivity MRI (rs-fcMRI) which evaluates alterations in global and regional functional connectivity. Recent studies have found alterations in both global and regional functional connectivity using rs-fcMRI in breast cancer survivors (Bruno et al., 2012; Kesler et al., 2013).

Our research team recently found that breast cancer survivors who report CICI compared to those who do not show weaker functional connectivity between regions of the frontal-parietal executive control network measured using rs-fcMRI, and weaker functional connectivity was correlated with greater levels of reported cognitive impairment on the Cognitive Failures Questionnaire (Piccirillo et al., 2015). An advantage that the use of non-invasive rs-fcMRI offers over the other forms of assessment is that it may be more sensitive to executive function changes than neuropsychological measures while being more objective than performance-based measures.

Strengths and limitations of rs-fcMRI

While rs-fcMRI provides an objective way to capture changes in neural connectivity, there is limited data to date that links these changes to changes at the performance and participation level. Individuals may have profound changes in their everyday life activities while underlying neural change is minimal and vice versa. The other limitation of rs-fcMRI is that there is limited data related to which networks are impacted following in CICI and other health conditions. Finally, rs-fcMRI only evaluates neural connectivity at rest. Based on what is known about executive function and the role executive function plays in complex everyday life activity it is not unreasonable to assume that some of other connections may only be active while the person is engaged in activity. Overall, the use of rs-fcMRI to assess cognitive function is still considered experimental.

Assessment: Summary

Overall, the literature related to assessment of executive function is leading to the following conclusions: (1) neuropsychological assessments can be used to evaluate change in specific cognitive constructs but cannot be solely relied on to determine level of impairment; (2) performance-based measures of executive function are more closely related to everyday life activity and are "ecologically-valid," because they measure the integration of cognitive function through the use of a real-world task but should be used in conjunction with neuropsychological measures; (3) self-report measures of cognitive performance are important to determine the individual's perception of his/her capacity but cannot be solely relied on to evaluate changes in executive function performance due to problems with self-report and patient awareness; and (4) early evidence suggests that rs-fcMRI offers an alternative way to evaluate changes in neural connectivity that are associated with self-reported changes in cognitive function but, like neuropsychological assessment, is removed from the actual assessment of daily function. All of these considerations have been built into this dissertation. The primary research questions, however, are focused on which intervention methods can best address executive dysfunction in individuals with mild-moderate neurological impairment.

Intervention Strategies for Executive Dysfunction

There has been an acknowledgement in the cognitive rehabilitation literature of two generally acceptable intervention approaches to address executive function impairment: the compensation model and the restoration model (Schagen & Wefel, 2013). The premise of restoration based methods is that through repetitive practice of cognitive function based training overall cognitive performance will improve (Schagen & Wefel, 2013). Unfortunately, several studies suggest that this approach has little impact on everyday life performance (Ferguson et al., 2007; Poppelreuter, Weis, & Bartsch, 2009; Von Ah et al., 2012). The goal of this type of intervention that targets impairment reduction is that the reduction in impairment will translate to improvement in everyday life activities (Figure 1). The limited effect of restoration-based approaches (smaller arrows in Figure 1) has been recognized and addressed in the neurological injury literature (Cicerone et al., 2000; Cicerone et al., 2011; Haskins, 2012; McEwen et al., 2015).

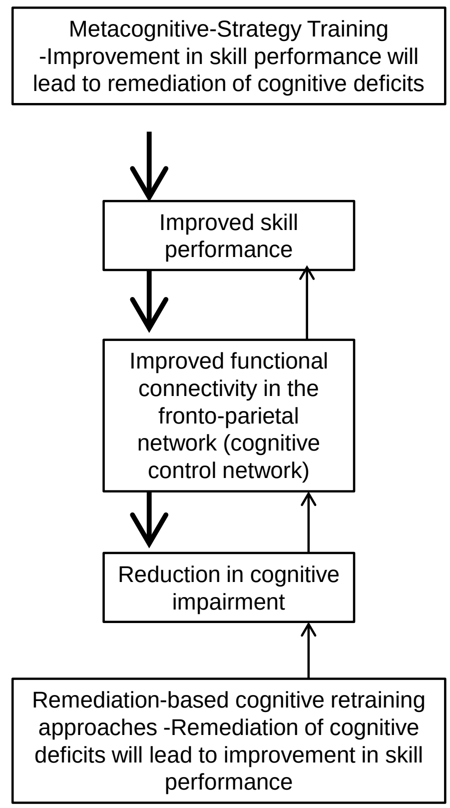


Figure 1: Conceptual Model of the Identification and Treatment of Executive Dysfunction

Currently, the only practice standard to address executive dysfunction is metacognitive strategy training (MCST) (Hoskins, 2012). The goal of MCST is to help patients develop and enhance control over cognitive functions and develop strategies to address cognitive, emotional, and behavioral obstacles. These interventions tend to be targeted at the performance and participation level to help participants improve/learn new skills and strategies to complete everyday life activities, and are usually delivered by occupational therapists. Existing evidence suggests that MCST has a greater positive effect on executive function impairments and performance than restoration-based approaches (McEwen et al., 2015). The larger MCST anticipated effect is reflected in the hypotheses of this proposed area of study and is depicted by the larger arrows in Figure 1. One of the concepts and theories driving MCST is experience-dependent neuroplasticity which postulates that learning new skills leads to structural and functional changes in the brain (May, 2011). The primary hypothesis of experience-dependent neuroplasticity is that the brain can and will change in response to changes in activity (Carey & Seitz, 2007). Some examples of this concept involve studies that have demonstrated hippocampal growth in individuals learning music (Herdener et al., 2010) and changes in the sensorimotor network in dancers (Hänggi, Koeneke, Bezzola, & Jäncke, 2010). From a rehabilitation perspective, the concept of experience-dependent neuroplasticity would involve helping the participant re-engage in occupation as a way to drive neuroplastic change in the brain. Therefore, this type of intervention targets performance and activity participation that will translate to impairment reduction within specific cognitive domains (Figure 1).

One example of this type of MCST intervention is the Cognitive Orientation to daily Occupational Performance (CO-OP) approach. In CO-OP, participants are trained to use the global strategy, GOAL-PLAN-DO-CHECK, to develop a specific plan to improve performance of a self-selected goal, to review performance, and to modify the plan accordingly if performance is not satisfactory. This process is consistent with psychology theories of cognitive flexibility that describe cognitive flexibility as necessary to assess a situation when a non-routine response is required, plan a new response/action to be taken, and use strategies to deal with the demands of the novel environment (Canas, Quesada, Antolí, & Fajardo, 2003; Norman & Shallice, 1986). So although there is some evidence to support the use of MCST with individuals with executive dysfunction, the question remains as to what effect these interventions can have on performance and impairment following mild-moderate neurological injury.

Using an MCST approach, the neuroplastic change that would be directly targeted is the action of the frontal-parietal network, a cognitive control network involved in flexible moment-to-moment task control, which also reflects compositional coding to enable transfer of knowledge to novel tasks (Cole et al., 2013; Dosenbach et al., 2006; Zanto & Gazzaley, 2013). This action can also be defined as cognitive flexibility. This frontal-parietal network has been shown to be effected in women with CICI who have self-reported changes in executive function and everyday life activity (Piccirillo et al., 2015). It can be postulated that using an MCST approach that includes global cognitive strategy use in combination with guided discovery is linked to the changes in cognitive flexibility.

Conclusion

Almost 100 years ago, Adolph Meyer challenged our profession to be different. He asked us to view disease in a different way and to use occupation rather than a sole reliance on medicine a means to address disease. Today we have an opportunity to explore this notion empirically in individuals with executive dysfunction after mild-moderate neurological injury. Impairment-based/restoration methods have an effect on impairment but do not transfer to everyday life. Performance-based approaches (MCST) can improve performance but their effect on impairment is unknown. The purpose of this dissertation was to evaluate these unknown effects of MCST to improve performance and participation as well as reduce impairment in individuals with neurological injuries.

Aims of the Dissertation

1. **Study I**: What is the differential effect of metacognitive strategy training (MCST) compared to usual occupational therapy service on activity performance and transfer to novel activities in individuals with mild to moderate stroke?
    a. Hypothesis: MCST will have a greater effect on activity performance and transfer compared to usual care occupational therapy.
    b. Manuscript (see Appendix): McEwen, S., Polatajko, H., Baum, C., Rios, J., Cirone, D., Doherty, M., & Wolf, T. (2015). Combined Cognitive-Strategy and Task-Specific Training Improve Transfer to Untrained Activities in Subacute Stroke An Exploratory Randomized Controlled Trial. *Neurorehabilitation and neural repair, 29*(6), 526-536.
2. **Study II**: What is the differential effect of MCST compared to usual occupational therapy service on motor and cognitive impairment reduction in individuals with mild to moderate stroke?
    a. Hypothesis: MCST will have a greater effect on motor and cognitive impairment reduction than usual care occupational therapy.
    b. Manuscript (see Appendix): Wolf, T., Polatajko, H., Baum, C., Rios, J., Cirone, D., Doherty, M., & McEwen, S. (2016). Combined cognitive-strategy and task-specific training impacts cognition and upper extremity function in sub-acute

stroke: An exploratory randomized controlled trial. *American Journal of Occupational Therapy, 70*, 7002290010.

3. **Study III**: What is the effect of MCST on: (1) subjective and objective cognitive performance; (2) neural connectivity in the frontal-parietal networks; and (3) the relationship between cognitive performance and neural connectivity in women with chemotherapy-induced cognitive impairment following treatment for breast cancer?
    a. MCST will have a positive impact on subjective and objective cognitive performance that will be correlated to improved connectivity in the frontal-parietal network in women with chemotherapy-induced cognitive impairment following treatment for breast cancer.
    b. Manuscript (see Appendix): Wolf, T., Doherty, M., Kallogjeri, D., Coalson, R. S., Nicklaus, J., Ma, C. X., Schlaggar, B.L., & Piccirillo, J. F. (in review). Cognitive-strategy training improves cognitive performance and neural connectivity in women with chemotherapy-induced cognitive impairment. *Breast Cancer Research and Treatment*.

Methods

Design

The overall research question in this dissertation was to evaluate the feasibility and preliminary efficacy of using MCST to improve performance and reduce impairment in individuals with neurological injury. Two separate projects were conducted to complete the three studies outlined in the study aims (see 1.2.2 Aims of the Dissertation). Study I and Study II were completed with one project using the same methods and sample; a single-blind, randomized controlled trial that evaluated the use of the Cognitive-Orientation to daily Occupational

Performance (CO-OP) intervention (an MCST approach) compared to usual occupational therapy care in persons with sub-acute stroke. This project was conducted at two different sites: (1) Sunnybrook-St. Johns Rehabilitation (SJR) in Toronto, ON; and (2) The Rehabilitation Institute of St. Louis (TRISL) in St. Louis, MO. Study III was a single pilot group pre/post study to evaluate whether MCST has an effect on improving performance and reducing impairment in breast cancer survivors with chemotherapy-induced cognitive impairment (CICI). The table below provides an overview of the methods for both projects (see Table 1). These two projects not only allowed for evaluation of MCST in two separate neurologically impaired populations with executive dysfunction but the second project with breast cancer survivors allowed for an opportunity to evaluate the effect of the intervention using neuroimaging as well as behavioral measures.

Table 1: Overview of the two projects (Study I, II, and III) in this dissertation

	Study I and II	Study III
Design and research approach	Exploratory, single-blind randomized controlled trial (Phase I) with a control arm	Single group, pre-post study
Data collection points	Pre-intervention (Time 1), post-intervention (Time 2), and 3-months after completing the intervention (Time 3)	Pre-intervention (Time 1) and post-intervention (Time 2)
Data collection instruments (see Abbreviations)	PQRS*, COPM*, CPI, SIS, PS-SES, DKEFS*, ARAT*	CFQ*, DEX*, DKEFS*, PROMIS-57, COPM, PHQ-9, MOCA, PS-SES, rs-fcMRI (neuroimaging)
Intervention	Intervention Arm: CO-OP (up to 10 sessions or when goals were met) Control Arm: Usual Care OT (up to 10 sessions)	CO-OP (up to 12 sessions or until goals were met)
Data analysis	Descriptive statistics, change scores (Time 1 to Time 2 and Time 1 to Time 3), Cohen's *d* effect sizes and confidence intervals (parametric data),	Behavioral Data: Descriptive, change scores, median of the difference and 95% CI interval, Wilcoxon signed

	nonparametric effect size *r* was calculated using the formula $r^2=z^2/N$ (non-parametric data)	rank test, non-parametric effect size (r) Neuroimaging Data: Fisher z-transformed Pearson correlation coefficients (between two regions' timecourses as a measure of functional connectivity), Object Oriented Data Analysis (OODA) to evaluate differences pre/post, Pearson correlations between changes in connectivity and behavioral measures

*A primary outcome measure

Participants

The participants in Study I and II were individuals with mild-moderate stroke (n = 35) who were referred for outpatient occupational therapy services at either SJR or TRISL. The participants in Study III were women with chemotherapy-induced cognitive impairment following treatment for breast cancer who were seen at the Siteman Cancer Center at Washington University in St. Louis (n = 14). The tables below provides an over of these two samples (see Table 2 and 3). In addition, the CONSORT diagram depicting participant flow through the RCT associated with Study I and II is provided in the figure below (see Figure #)

Table 2: Overview of the participants in Study I and II in this dissertation

		St. Louis	Toronto	Total
Variable	Group	Mean (SD)	Mean (SD)	Mean (SD)
Days since stroke	UC	41.6 (17.1)	52.0 (25.4)	46.5 (21.3)
	CO-OP	30.5 (10.7)	53.1 (23.9)	40.1 (20.4)
Hours of therapy attended	UC	10.2 (2.8)	17.0 (13.0)	13.3 (9.2)
	CO-OP	7.9 (2.3)	14.4 (8.7)	10.9 (6.8)
Age	UC	50.7 (14.5)	59.3 (12.7)	54.4 (14.0)
	CO-OP	57.4 (15.5)	57.6 (12.7)	57.5 (14.0)
Years of Education	UC	12.2 (1.5)	14.4 (1.9)	13.2 (2.0)
	CO-OP	14.3 (3.0)	15.3 (5.6)	14.7 (4.2)

		n (%)	n (%)	n (%)
Sex (female)	UC	5 (44.4)	2 (28.6)	7 (43.8)

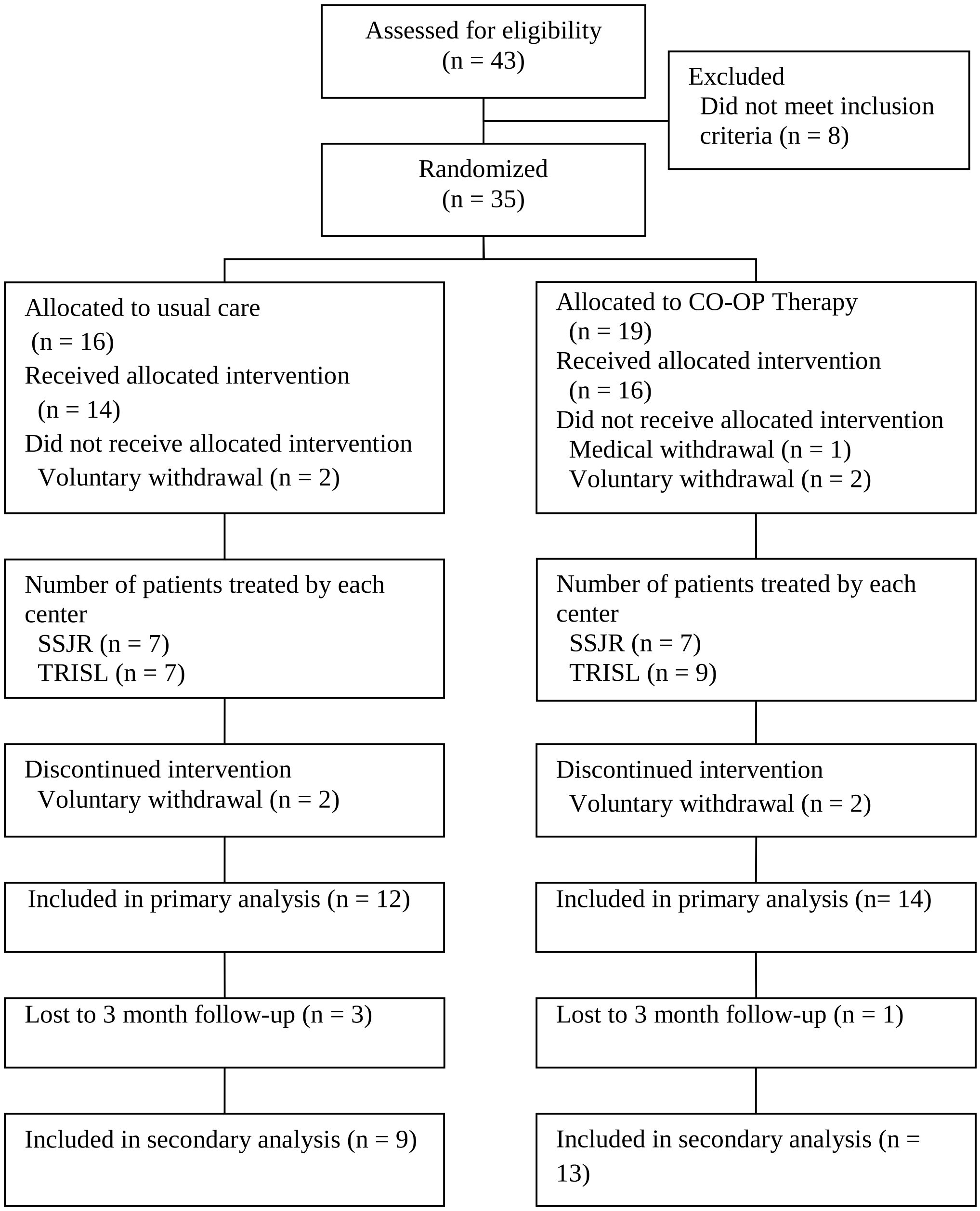
	CO-OP	4 (36.4)	2 (25.0)	6 (31.6)
Stroke side (right)	UC	7 (77.8)	6 (85.7)	13 (81.3)
	CO-OP	6 (54.5)	5 (62.5)	11 (57.9)
Handedness (right)	UC	8 (88.9)	6 (85.7)	14 (87.5)
	CO-OP	9 (81.8)	8 (100)	17 (89.5)
Living Arrangement (with others)	UC	8 (88.9)	7 (100)	15 (93.8)
	CO-OP	7 (63.6)	7 (87.5)	14 (73.7)
Ethnicity				
Caucasian	UC	2 (25.0)	5 (71.4)	7 (46.7)
	CO-OP	5 (45.5)	4 (50.0)	9 (47.4)
African American	UC	6 (75.0)	0	6 (40.0)
	CO-OP	6 (54.4)	4 (50.0)	10 (52.6)
Asian	UC	0	1 (14.3)	1 (6.7)
	CO-OP	0	0	0
Other	UC	0	1 (14.3)	1 (6.7)
	CO-OP	0	0	0

UC=usual care; CO-OP=Cognitive Orientation to daily Occupational Performance. From "Combined Cognitive-Strategy and Task-Specific Training Improve Transfer to Untrained Activities in Subacute Stroke: An Exploratory Randomized Controlled Trial," by S. McEwen, H. Polatajko, C. Baum, J. Rios, D. Cirone, M. Doherty, & T.Wolf, 2015, Neurorehabilitation and Neural Repair, 29, 532. http://dx.doi.org/10.1177/1545968314558602. Copyright © 2015 by the American Society of Neurorehabilitation. Used with permission.

Table 3: Overview of the participants in Study III in this dissertation

Variable	Median (Min-Max) or Percentage
Age (Years)	50.50 (36-65)
Time since completion of chemotherapy (months)	9.5 (7-34)
	n (%)
Race	
• Caucasian	12 (86%)
• African American	1 (7%)
• Asian	1 (7%)
Highest level of education	
• High School or Associate Degree	2 (14%)
• Bachelor's Degree	3 (21%)
• Master's or Doctoral Degree	9 (65%)
Work Status	
• Full-time	12 (86%)
• Part-time	1 (7%)
• Retired	1 (7%)

Figure 2: CONSORT Diagram from Study I and II



From “Combined Cognitive-Strategy and Task-Specific Training Improve Transfer to Untrained Activities in Subacute Stroke: An Exploratory Randomized Controlled Trial,” by S. McEwen, H. Polatajko, C. Baum, J. Rios, D. Cirone, M. Doherty, & T.Wolf, 2015, Neurorehabilitation and Neural Repair, 29, 532. http://dx.doi.org/10.1177/1545968314558602. Copyright © 2015 by the American Society of Neurorehabilitation. Used with permission.

Procedure Overview

Study I and II

Following informed consent, a blinded rater screened the participants to determine final eligibility and those who passed the screening measures immediately completed a portion of the baseline assessment (Time 1). As part of the baseline assessment, participants were scheduled to return for a second testing session to complete an occupational interview led by a licensed occupational therapist. The interview was conducted using the Canadian Occupational Performance Measure (COPM), during which participant selected at least five activity performance goals. Three of these goals were used as part of the CO-OP intervention and the remaining two goals not discussed during the intervention were used to evaluate transfer. All five goals from the COPM were used to complete the assessment of objective activity performance (the Performance Quality Rating Scale (PQRS)). A third baseline testing session was scheduled to complete the PQRS. To complete the PQRS, structured observations of the participants performing each of their COPM goals were recorded. These videos were later randomized by participant, by goal, and by time (baseline, post-intervention, and follow-up) and scored by a blind rater. Upon PQRS completion, participants were randomly assigned to the treatment group (CO-OP) or the control group (usual care occupational therapy). Each group completed a maximum of 10 intervention sessions prior to completing the post-intervention assessment (Time 2). Some participants in CO-OP did not receive the maximum of 10 sessions if his/her goals were met prior to this number being reached. All participants regardless of group allocation continued with usual care occupational therapy as needed following the completion of the post-intervention assessment (Time 2). A follow-up assessment (Time 3) was completed three months after the post-intervention assessment.

Study III

Breast cancer patients were referred to the study from Siteman Cancer Center. Patients who were interested completed a survey over the phone or online to determine the presence of self-reported chemotherapy-induced cognitive impairment (CICI). Those patients with self-reported CICI were then scheduled for a face-to-face baseline assessment and at the completion of the assessment were scheduled for the neuroimaging assessment. After completing all the baseline testing and neuroimaging, participants participated in a 12-session (or until their goals were met) metacognitive strategy training intervention (CO-OP) with a trained occupational therapist. Following the completion of the intervention, participants completed the same assessment battery and neuroimaging that was completed at baseline.

Analysis

Study I and II

All data were clean and checked for accuracy. The distribution of the data was evaluated using histograms and Shapiro-Wilk tests. Descriptive statistics for the primary outcomes for both Study I and II were calculated and comparisons were made between performance sites and between the two treatment groups (usual care and CO-OP). For parametric data, Time 1 to Time 2 and Time 1 to Time 3 mean change scores and standard deviations were calculated and Cohen's *d* effect sizes with confidence intervals were calculated. For non-parametric data, medians and ranges were reported and a nonparametric effect size *r* was calculated using the formula $r^2=z^2/N$ (Fritz, Morris, & Richler, 2012).

Study III

Behavioral data: all data were cleaned and checked for accuracy. The data were not normally-distributed so non-parametric methods were employed. All demographic and outcome variables were described using median and range. A change score was calculated for each outcome variable (pre/post) and the median of the difference and 95% CI interval was calculated and reported. Differences in pre-post test scores were evaluated with Wilcoxon signed rank tests and non-parametric effect size (r) calculations were also performed.

Neuroimaging data: timecourses were calculated for each subject and each scan for the two frontal-parietal control regions under investigation (Piccirillo et al., 2015) and Fisher z-transformed Pearson correlation coefficients were calculated between the two region's timecourses in a single scan. This correlation is the measure of functional connectivity between the two regions. Functional connectivity across the brain was compared between days using Object Oriented Data Analysis (OODA). (La Rosa et al., in press). Pearson correlations were calculated to evaluate the relationship between the changes in functional connectivity and changes in the behavioral outcome measures.

Results

This dissertation presents new knowledge related to the use of MCST to not only improve performance and participation following neurological injury but also remediate impairment. Across all three studies, the use of CO-OP was associated with improved subjective and objective performance and also a decrease in cognitive and physical impairment. Below is an overview of the results of each of the three studies in this dissertation. The summaries provided in the overview of the results represent the primary findings from each study. The full results and graphics can be found in the manuscripts for each study in the appendix (see Appendix).

Study I

Given the preliminary nature of this study, the primary goal was to estimate the potential effects of CO-OP compared to usual care occupational therapy on trained and untrained activities rather than complete hypothesis testing. For normally distributed data, the effect size estimations were calculated using Cohen's *d* which can be interpreted as follows: 0.2 - small effect; 0.5 - medium effect; and 0.8 - large effect (Cohen, 1988). At Time 2 assessment (immediately post-intervention), CO-OP had a medium effect over usual care on objective assessment of trained activities (d = 0.5) and a large effect on objective assessment of untrained activities (d = 1.2) measured by the PQRS. At Time 3 (3-month follow-up after Time 2 assessment), CO-OP had a large effect over usual care on both objective trained (d = 1.6) and objective untrained activities (d = 1.1) measured by the PQRS.

There was no effect of CO-OP over usual care on subjective changes in performance and satisfaction with performance of trained or untrained activities measured by the COPM at Time 2; however, there was a small effect at Time 3 in subjective changes in performance and satisfaction with performance of trained and untrained activities favoring CO-OP (d = 0.1 to 0.2). Also at Time 3, CO-OP had a medium effect over usual care for changes in the secondary outcomes of perceived change in community participation measured by the CPI (d = 0.7) and self-efficacy measured by the PS-SES (d = 0.7).

Study II

The analysis for Study II used the same methods as Study I; however, the outcome measures were different. Rather than evaluating the impact of CO-OP on performance outcomes, the goal of Study II was to evaluate the effect of CO-OP over usual care on measures of impairment and recovery. The SIS (ADL, mobility, hand, and recovery domains) and DKEFS

Trailmaking Test data were normally distributed so Cohen's *d* effect size calculations were used. The results showed that following the intervention (Time 2), CO-OP had a large effect over usual care on perceived stroke recovery measured by the SIS overall recovery score (*d*=0.8), and a medium effect over usual care for self-perceived changes physical function as measured by the SIS-16 physical summary score (*d*=0.5), self-perceived changes in hand function measured by the SIS (*d*=0.5), and executive function measured by the DKEFS Trailmaking Test (*d*=0.5). At follow-up (Time 3), there was a medium effect of CO-OP over usual care on hand function as measured by the SIS (d=0.6), and executive function as measured by the DKEFS Trailmaking Test (*d*=0.5).

The remaining data in this study, the ARAT and the remaining SIS domains (communication, physical, emotion, and memory domains), were all found to be non-normally distributed, therefore a non-parametric effect size *r* ($r^2=z^2/N$) was calculated. The effect size *r* can be interpreted that 0.1 represents a small effect, 0.3 a medium effect, and 0.5 a large effect (Fritz et al., 2012). Following the intervention, a small to medium effect of CO-OP over usual care was found on the objective arm function measured by the ARAT and self-perceived recovery in all of the SIS domains listed above (*r* = .2 to .4). At follow-up, CO-OP had a medium effect over usual care in self-perceived changes in communication on the SIS (*r* = .4) and a medium effect over usual care on objective measurement of arm function measured by the ARAT (*r* = .3).

Study III

The goal of Study III was to estimate the effect of CO-OP on subjective and objective measures of cognitive function and neural connectivity in women with chemotherapy-induced cognitive impairment (CICI) following treatment for breast cancer. The primary outcome measures were the CFQ, the DEX, and the DKEFS Trailmaking subtest. A secondary goal was to evaluate the effect of the intervention on changes in perceived performance and recovery of function. The secondary outcome measures where the PROMIS-57, the COPM, the PHQ-9, and the PS-SES. The data were not normally distributed so a non-parametric effect size r ($r^2=z^2/N$) was calculated (0.1 represents a small effect, 0.3 a medium effect, and 0.5 a large effect) (Fritz et al., 2012). The results show that CO-OP had a very large effect on all the primary behavioral outcome measures in our sample (n = 14): (1) subjective cognitive function (CFQ) effect size r = -.85; (2) objective cognitive function (DKEFS Trailmaking) r = -.50; and (3) subjective executive function (DEX) r = -.75. CO-OP also had a small to very large effect on all secondary outcomes: (1) subjective changes in performance/satisfaction with performance (COPM) effect size r = -.88; (2) subjective depressive symptoms (PHQ-9) effect size r = -.53; and (3) subjective patient-reported outcomes/recovery (PROMIS-57) effect size r = -.12 to -.88.

Only 10 of the 14 participants had enough clean frames of MRI data to be included in analysis. The amount of data kept did not differ between the two scans (p=.59). A one-tailed, paired t-test on the connection between the two frontal-parietal control regions under investigation in this study (Piccirillo et al., 2015) showed trend level significance (p=.054), demonstrating an increase in functional connectivity strength after treatment in 6 of the 10 subjects. The change in functional connectivity explains 35% of the change in subjective depressive symptoms measured by the PHQ-9 and 26% of the change in objective cognitive function measured by the DKEFS Trailmaking Test. In this limited sample, these correlations of functional connectivity change with change in behavioral scores had trend-level significance (p=.057 to .108).

General Discussion

Overall, the findings of this dissertation support promising new knowledge to move forward with investigating the use of MCST intervention with individuals with neurological injury. There are three primary findings across the three studies that will be discussed further in this section: (1) the use of MCST to improve occupational performance and the transfer of these gains to untrained tasks; (2) the use of MCST to support executive function changes following neurological injury and the link to performance of activities in everyday life; and (3) the use of MCST to support engagement in activity as a method to remediate cognitive and physical impairment. Following this discussion, the limitations of the findings from these studies will be discussed as well as future work that is necessary to address these limitations and confirm the findings of the studies in this dissertation

MCST and Teaching for Transfer

The underlying intention and theory behind MCST and the concepts of teaching for transfer are inextricably intertwined. Our early understanding about metacognitive strategies came from working with children in school settings and how children learn new information (Flavell, 1979). Similarly and around the same time, the concept of teaching for transfer was also developed in educational settings through observations of students failing to apply knowledge/skills learned in one setting/context to another (Perkins & Salomon, 1988). The underlying goal behind the development of both concepts was the same: to understand how children learn best in a controlled setting in a way that will help them in everyday life. While these concepts/theories came out of educational psychology, their application in healthcare and other populations has lagged behind; however, the applicability of the concepts related to learning and skill acquisition is central to rehabilitation as the goal of rehabilitation is essentially the same: how do we best help our patients learn new skills in a controlled environment that will help them improve their health and participation in everyday life? Most predominate interventions used with individuals with neurological injuries are not built on these concepts and therefore transfer of skills learned in rehabilitation is typically limited or absent (McEwen et al., 2015; Veerbeek et al., 2014).

The intervention used in this dissertation, the Cognitive-Orientation to daily Occupational Performance (CO-OP), is a MCST intervention built on concepts of teaching for transfer (Polatajko & Mandich, 2004; Polatajko, Mandich, & McEwen, 2012). The concepts of teaching for transfer as they apply to rehabilitation were best highlighted by Chantal Geusgens and colleagues (2007) who outlined six principles of transfer that need to be incorporated into rehabilitation in order to promote transfer: (1) must teach what transfer is; (2) the connection between what is learned and where it is learned must be broken; (3) transfer does not occur automatically-you must teach it; (4) must know/teach when transfer can be applied; (5) general knowledge transfers-specific knowledge does not; and (6) must know how transfer works. This article was addressing limitations to promote transfer in current cognitive rehabilitation approaches that did not incorporate these principles for individuals with neurological injury (Geusgens, Winkens, van Heugten, Jolles, & van den Heuvel, 2007). These principles of teaching for transfer make it clear that transfer cannot be expected to occur spontaneously even though this is a common expectation of impairment-based intervention approaches. Prior to this dissertation, however, the differences in how the two different interventions, MCST/CO-OP and usual care/impairment-based intervention, differed in terms of their ability to support the transfer of skills gain in rehabilitation to untrained skills/activities in everyday life was relatively unknown.

The results of Studies I and II both showed the use of a MCST intervention, based on concepts of teaching for transfer, not only improved skill performance but also had more of an effect on transfer to skills that were untrained in treatment. In Study I and II, the effect of CO-OP over usual care in objective change in skill performance of trained and untrained activities was extremely large and the effect was maintained or increased at follow-up (d = .5 to 1.6). These findings are consistent with other studies using CO-OP in inpatient settings with individuals with neurological injury which found a positive effect of CO-OP over attention control to improve even basic self-care activities (Skidmore et al., 2014). Collectively, the results from this dissertation and existing literature provide initial support for the notion that concepts of teaching for transfer must be embedded into rehabilitation and that the expectation of transfer using more conventional usual-care methods may be misguided. Future studies are needed to confirm the findings from these studies to produce this effect on transfer and to investigate the active ingredients/mechanisms responsible for these results. This dissertation attempted to begin to address these questions by investigating the role of executive function in MCST. As discussed in the introduction of this dissertation, executive function is intertwined with our metacognitive abilities and the specific action of our cognitive control brain networks is inextricably tied to ability to transfer knowledge from one skill to another.

Executive Function and Occupational Performance

As discussed in detail in the introduction of this dissertation, executive function allows us to integrate information from the environment with our memory stores in the brain to generate, implement, and correct strategies necessary to accomplish tasks (Goldberg, 2001; Manchester et al., 2004). The frontal lobes of the brain are considered a hub for executive function; however, executive function relies on diffuse neural networks throughout the brain (Alvarez & Emory, 2006). Of particular importance is the role of the cognitive control networks, specifically the frontal-parietal network (Dosenbach et al., 2006). This network is responsible for moment-to-moment control of cognitive function and has been tied to executive function and performance, specifically the ability to transfer knowledge from a learned activity to an unlearned activity (Zanto & Gazzaley, 2013). Imaging studies have confirmed the link between these frontal brain regions and the role executive function plays in early-mid skill acquisition. During early skill acquisition, the prefrontal brain areas associated with executive function have increased activation which is reduced as a new skill is mastered; this activation then increases if the task demands/context is changed (Jueptner et al., 1997; Meister et al., 2005; Puttemans, Wenderoth, & Swinnen, 2005). This is particularly important in rehabilitation as individuals with neurological injuries are learning new skills to manage their ability to participate in everyday life activities. For this reason, executive function is central to our ability to investigate the underlying mechanisms associated with the effect of MCST and our ability to transfer knowledge to different skills and/or contexts. The need to acknowledge and manage executive function is just beginning to be recognized as an important issue to be addressed in rehabilitation.

In rehabilitation, it is common that even if the patients choose the therapy goal, the treatment activity and environment is structured for them and they are instructed on how, when, and why to complete the activity; thereby negating the executive function components of the activity (Lezak, Howieson, Loring, 2004). MCST, specifically CO-OP, challenges the individual to not only participate in the activity but also to come up with his/her own plan for how, when, why, and where to participate in the activity. In doing so, there is a challenge to their executive function in a way that will be available for later introspection and application in novel contexts (McEwen, Polatajko, Huijbregts, & Ryan, 2010; Skidmore et al., 2014; Skidmore et al., 2014).

Studies I and II in this dissertation support this notion. Not only did participants improve in their occupational performance, the improvement transferred to novel activities and there was a measureable positive effect on cognitive flexibility (executive function) in those who received CO-OP compared to those who received usual care. These findings give rise to a new potential hypothesis—that executive function may best be studied and understood as a central driver in occupational performance.

Occupational performance is the interaction of the person, the environment, and the occupation/activity he/she is doing (Christiansen, Baum, & Bass-Haugen, 2015). If we understand executive function as how we recall, manipulate, and hold online our previous knowledge (person factor), while we analyze and adapt to our surrounding environment (environmental factor), in order to accomplish an activity (occupation) than the notion that executive function can be analyzed in its entirety by examining its component functions is erroneous. If our understanding lies in the interaction of these components then we have to evaluate the interaction in order to gain a global understanding of executive function. An approach that can evaluate this notion is to evaluate the impact of engagement in activity that is challenging executive function abilities on measureable executive function abilities. This dissertation was built on the foundational theory for occupational therapy from Adolph Meyer that engagement in activity can have a positive impact on remediating impairments

Engagement in Activity Leads to Remediation of Deficits

In the preface for this dissertation, the philosophy of Adolph Meyer was presented as a guiding philosophy for this dissertation. One of the key statements from his philosophy for our profession of occupational therapy was presented: "**Our role consists of providing opportunities rather than prescriptions. There must be opportunities to work, to do, plan,**

and create, and to learn to use material" (Meyer, 1922). Meyer believed in the curative power of occupation to help individuals recover from mental illness. This dissertation sought to apply this philosophy to addressing the impairments experienced by individuals with neurological injury, specifically individuals with mild-moderate stroke and individuals who have completed treatment for cancer with cognitive impairments. Our current literature has shown that impairment based approaches do reduce impairment (Connell, McMahon, Eng, & Watkins, 2014; Teasell, Foley, Salter, & Jutai, 2008; Veerbeek et al., 2014); however, as previously discussed these improvements are not translating into improved participation in everyday life activities. The question remained, does providing opportunities to engage in activity also lead to a reduction in impairment and a subsequent improvement in health?

The results from all three studies in this dissertation provide preliminary and promising support that engagement in activity can lead to a reduction in impairment. In Study II, CO-OP had a positive effect over usual care on all subjective and objective assessments of cognitive and physical function. In Study III, CO-OP was associated with a large effect on changes to subjective and objective cognitive function as well has subjective positive changes in global daily functioning. Further, Study III found a positive change in neural connectivity in the frontal-parietal cognitive control network which was associated with positive changes in objective executive function assessment. While all of these studies were preliminary in nature, they lend support for Meyer's original notion that engagement in activity can help remediate impairment. While these results are definitely promising, there are some limitations to the studies that limit the generalizability at this time.

Limitations of Study Findings

All three studies were preliminary and were intended to evaluate the feasibility of delivering the CO-OP intervention to the population of interest and also to estimate the potential effect of the interventions. Inherently, given the well-defined process for intervention development, these findings all need to be confirmed in larger scale studies that are intended to evaluate the primary hypotheses that have been established by these early phase studies. These future studies are addressed below.

Specific to Study I and II, these studies were completed using a pragmatic trial which is not typical for an early-phase trial. This was done intentionally as one of the goals of the study was to evaluate the feasibility of administering CO-OP in a subacute setting. Therefore, inherent in using this approach in an early phase study are some limitations that must be addressed in future studies. First, we were not able to control or track the receipt of other rehabilitation services. All participants in this study received at least some additional rehabilitation services other that occupational therapy. While ideally the randomized design helped minimize this effect, we were not able to statistically ensure this happened. Second, what constituted usual care for these participants had to be discerned from the use of therapy notes which could have confounded the results. Finally, for Study II, the impact of the intervention on impairment was a secondary outcome; the primary outcome was the effect on occupational performance and transfer to other activities (Study I). While a measureable positive effect on upper extremity function and executive function was detected, these outcomes were not accounted for in the design of the study and several of the individuals were already at ceiling on their performance on these outcome measures at baseline. These findings have to be confirmed in a study that is powered to these specific impairment outcomes and take into account baseline level of function in these domains in the inclusion/exclusion criteria.

In regards to Study III, this study was the very first to evaluate the use of CO-OP using both behavioral measures and neuroimaging. Given that it was the first feasibility study, a single group, pre/post design was used. There are several inherent limitations in this design which most notably may be that changes in outcome measures cannot be compared to an active or inactive control group to determine if the changes are attributable to the intervention or simply the passage of time. The effect size estimations from this study will need to be used to power a two-group randomized study to address this limitation. Also, there are many complex and intertwined brain networks that would be associated with participation in everyday life activities. This study targeted the action of one specific network, the frontal-parietal cognitive control network, as was found to experience degradation as a result of chemotherapy (Piccirillo et al., 2015). There are very likely several networks that may be impacted by chemotherapy treatment and that may be responsible for global changes in function following MCST intervention. This will also need to be explored in future studies.

Overall, there is one primary limitation of all three studies in this dissertation. Neurological injuries are known to impact executive function; however, currently one of the prerequisites to using CO-OP is the ability to have metacognitive awareness and monitoring which is an executive ability. At this time, it is unknown if MCST approaches like CO-OP can or should be used with individuals with more profound cognitive loss following neurological injury and who is the “best” population for MCST. This needs to be further explored in future studies as well.

Future Research Questions

As alluded to throughout this dissertation and discussion, this dissertation has added new knowledge to the field about the potential impact and use of MCST to improve outcomes for individuals with neurological injury. The results from this dissertation have spawned the need to address additional research questions that must be answered to continue the investigation of the use of MCST to impact these outcomes.

From Study I and II, another study powered to the primary outcome of changes in performance and transfer needs to be conducted to confirm the findings of this dissertation. In this study, additional therapies received needs to be controlled and/or tracked and the active control group intervention needs to be well-defined. In addition, another study that is powered to the secondary outcomes of improved cognitive and physical impairment needs to be conducted to confirm these findings. In this study, parameters related to a level of cognitive and/or physical impairment must be defined as an inclusion criteria for the study in addition to the other considerations discussed above related to defining the control intervention and tracking other therapies.

From Study III, a two-group randomized study needs to be designed and powered based on the results of this study to confirm the effects observed compared to an active control group. The active control condition should ideally also target the defined impairments and neural networks under investigation. In addition, further exploration into the impact on chemotherapy on neural networks needs to continue to help better define the mechanistic changes associated with changes in occupational performance following chemotherapy.

Conclusion

While there are several considerations that must be taken into account when interpreting the findings of the studies in this dissertation overall the results are very promising. The results all support the feasibility of administering MCST in a variety of settings with different populations of people with neurological injury which provide the foundation for future work.

Most notably, all three studies provide preliminary support to continue the investigation of the use of MCST to not only improve performance but also to remediate impairment post-neurological injury which will directly improve health.

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Appendices

Manuscripts

The manuscripts associated with the studies in this dissertation which have either been accepted for publication or submitted for publication are provided below. The paper number corresponds with the study number used throughout the dissertation to describe the studies. For papers 1 and 2 which have been published, the typeset version has been provided.

Paper I: Combined Cognitive-Strategy and Task-Specific Training Improve Transfer to Untrained Activities in Subacute Stroke: An Exploratory Randomized Controlled Trial, by S. McEwen, H. Polatajko, C. Baum, J. Rios, D. Cirone, M. Doherty, & T. Wolf, 2015, Neurorehabilitation and Neural Repair, 29, 532. http://dx.doi.org/10.1177/1545968314558602. Copyright © 2015 by the American Society of Neurorehabilitation. Used with permission.

Neurorehabilitation and
Neural Repair
2015, Vol. 29(6) 526–536

DOI: 10.1177/1545968314558602
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Combined Cognitive-Strategy and Task-Specific Training Improve Transfer to Untrained Activities in Subacute Stroke: An Exploratory Randomized Controlled Trial

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Abstract

Purpose. The purpose of this study was to estimate the effect of the Cognitive Orientation to daily Occupational Performance (CO-OP) approach compared with usual outpatient rehabilitation on activity and participation in people <3 months poststroke. *Methods.* An exploratory, single-blind, randomized controlled trial, with a usual-care control arm, was conducted. Participants referred to 2 stroke rehabilitation outpatient programs were randomized to receive either usual care or CO-OP. The primary outcome was actual performance of trained and untrained self-selected activities, measured using the Performance Quality Rating Scale (PQRS). Additional outcomes included the Canadian Occupational Performance Measure (COPM), the Stroke Impact Scale Participation Domain, the Community Participation Index, and the Self-Efficacy Gauge. *Results.* A total of 35 eligible participants were randomized; 26 completed the intervention. Post intervention, PQRS change scores demonstrated that CO-OP had a medium effect over usual care on trained self-selected activities (d = 0.5) and a large effect on untrained activities (d = 1.2). At a 3-month follow-up, PQRS change scores indicated a large effect of CO-OP on both trained (d = 1.6) and untrained activities (d = 1.1). CO-OP had a small effect on COPM and a medium effect on the Community Participation Index perceived control and on the Self-Efficacy Gauge. *Conclusion.* CO-OP was associated with a large treatment effect on follow-up performances of self-selected activities and demonstrated transfer to untrained activities. A larger trial is warranted.

Keywords
stroke, rehabilitation, Cognitive Orientation to daily Occupational Performance, cognition, participation, self-efficacy

Introduction

Individuals living with the effects of a stroke continue to experience significant challenges with their functional health, despite advances in rehabilitation. Approximately half of those living in the community after their stroke are dependent in terms of activities of daily living,[1] and the majority have not achieved their individual functional goals.[2] They experience participation restrictions,[3-5] have limitations in performing meaningful activities,[6] and are significantly less active than age-matched controls.[7] Evidence suggests that treatments that incorporate repetitive task-specific training are the most effective of contemporary rehabilitation approaches to improve gait speed and upper-extremity activities and are recommended over traditional neurodevelopmental approaches.[8,9] However, the effect seems to be limited to the specific tasks trained,[9] and retention of learning has not been consistently demonstrated.[10] In contrast, the Cognitive Orientation to daily Occupational Performance (CO-OP) approach, which superimposes cognitive and metacognitive elements on task-specific training, is associated with improvements in both trained and untrained activities, and the newly acquired skills are retained.[11,12]

CO-OP is a complex treatment approach that differs from other contemporary stroke rehabilitation approaches in that it combines theory and evidence from both motor and cognitive sciences and situates them in an educational, client-centered framework. It is defined as "a client-centred, performance-based, problem solving approach that enables skill acquisition through a process of strategy use and guided discovery."[13, p2] The clinical objectives are skill acquisition, cognitive strategy use, and generalization and transfer of learning. Elements from the motor domain are

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used primarily to meet the clinical objective of skill acquisition; these include practicing specific functional tasks (ie, task-specific training), usually as a whole task, such as dressing, cutting food, or walking outdoors, rather than task components such as reaching, grasping, or balance training in isolation from the task.

A limitation of task-specific training, when used alone, is that generalization to other situations and transfer to other tasks, are generally not demonstrated,[9] and improvements gained in therapy are not consistently maintained once therapy stops.[10,14] In CO-OP, retention, generalization and transfer have consistently been reported.[11,12,15,16] This may, in part, be because of the cognitive and metacognitive elements that are superimposed on the task-based training. In CO-OP, a global cognitive strategy, adapted from Meichenbaum's goal-plan-do-check,[17] teaches participants to problem solve and self-monitor their own task performance. Additionally, within each task performance, therapists use a conversation-based teaching and feedback technique known as *guided discovery*,[18] in which participants are guided through questions, cues, and coaching to solve task performance problems on their own, rather than being given explicit instructions. Through this process, they learn to analyze their own performance and to subsequently develop performance strategies to overcome issues. This differs markedly from traditional approaches, in which it is the therapist who does the analysis of performance breakdowns, develops performance strategies, and explicitly teaches the patient how to use those performance strategies.

Preliminary evidence to support CO-OP's benefits for individuals poststroke was first demonstrated in people more than six months poststroke.[11,12,19] Two single-case experimental series showed not only improved activity performance and retention of learning following CO-OP intervention[11] but also improvement in untrained activities, suggesting the occurrence of transfer to new skills.[12] Because it is relatively well established that stroke outcomes are improved if rehabilitation occurs in the first few months following the event[8,20,21] and because past CO-OP participants recommended that the strategies be taught much earlier in the rehabilitation process,[22] we sought to investigate the efficacy of the approach in subacute stroke. Therefore, the primary objective of this exploratory trial was to estimate, in people <3 months poststroke, the effect of CO-OP compared with usual occupational therapy on immediate and longer-term activity performance and participation.

Methods

A single-blind, exploratory, randomized controlled trial, with a usual care control arm, was conducted. Participants referred to outpatient stroke rehabilitation programs at 2 university-affiliated, freestanding rehabilitation centers were randomized to receive either the usual outpatient program, which included occupational therapy (usual care) or the usual outpatient program with CO-OP replacing usual occupational therapy (CO-OP).

Sampling and Randomization Procedures

Patients who had sustained an ischemic stroke (ICD-10 codes I63 and I64) referred to outpatient rehabilitation at Sunnybrook–St John's Rehab in Toronto, ON, Canada, or The Rehabilitation Institute of St Louis, MO, between March 2011 and March 2013 were included. Exclusion criteria were the following: >3 months poststroke when starting outpatient rehabilitation, hemorrhagic stroke, other neurological diagnoses, major psychiatric illness, moderate or severe aphasia (combined scores of 6 or less on Canadian Institute of Health Information[23] items 64 and 66), or cognitive impairment (Montreal Cognitive Assessment[24] scores of 21 or less). It was estimated a priori that a sample size of 14 per group would provide 82% power to detect a between-group difference of 1.3 units on the Canadian Occupational Performance Measure (COPM).[25] To ensure balanced group sizes, a consulting statistician prepared a blocked randomization procedure stratified by site. A block size of 6 and an allocation ratio of 1:1 were used to ensure equal assignment to the treatment and control groups for every 6 patients entered in the study at each center. The random number function in Excel (Microsoft Corporation, Microsoft Excel 2010, Version 14.0.) was used to create a random sort order within each block. To ensure allocation concealment, an administrative assistant at each site, not associated with the study, created sequentially numbered sealed opaque envelopes for the study coordinator at each site. The study coordinator was not involved in the assessment or treatment of any of the participants. Treatment allocation was not completed until after consent was obtained and all inclusion/exclusion criteria had been reviewed. Because knowledge of blocking reduces the unpredictability of the next assignment, the study investigators, project coordinators, and treating therapists were all blinded to the randomization procedure and block size.

Assessment and Intervention Procedures

At time 1, participants underwent a baseline assessment battery conducted by a research assistant who was blinded to group allocation. Following that, a research occupational therapist, not involved with delivering either intervention and also blinded, conducted a goal-setting interview using the COPM. During this interview, participants selected the 4 to 6 personally meaningful functional activity goals that were the most important to them. The participants then had a third baseline assessment session in which they were videorecorded performing those self-selected activity goals.

Following the time 1 assessments, both the CO-OP and Usual Care groups received usual outpatient stroke rehabilitation with specific services based on their individual needs, such as physical therapy, speech-language pathology, or nursing. The Usual Care group received usual outpatient occupational therapy from therapists employed by the participating sites, whereas the CO-OP group received occupational therapy from CO-OP-trained occupational therapists who were part of the research team. Treatments were generally twice per week; sessions were 45 minutes long for the CO-OP group and ranged from 45 to 60 minutes long for the Usual Care group. Because the participants had a range of stroke severities and rehabilitation needs and, as is typical in usual outpatient rehabilitation, the number of sessions varied. The number of treatment sessions attended by an individual participant depended on his or her needs, the clinical judgment of the treating occupational therapist, and the institutional policies. The CO-OP group received a maximum of 10 CO-OP intervention sessions, and any additional sessions that more complex patients needed were conducted as usual care. These additional usual care sessions were tracked and counted as part of the total number of CO-OP treatments. A limitation on the number of sessions received by the usual care group was institutional policy. In Toronto, clients were limited to a maximum of 32 treatment sessions, and in St Louis, clients were limited by the number of sessions covered by their insurance provider or other means of payment.

CO-OP Intervention Description

Complete details about the theoretical underpinnings and the implementation of the CO-OP approach have been published in a textbook.[13] In this study, CO-OP treatment occurred separately from the rest of the outpatient team to avoid contamination. During the first session, the CO-OP therapist reviewed the goals previously established in the COPM interview and worked with the participant to decide on which 3 of those would become the focus of intervention sessions. Also in the first session, the CO-OP therapist used a visual presentation to teach the participant the global cognitive strategy, goal-plan-do-check.[17] In subsequent sessions, the goal-plan-do-check strategy was used iteratively as the main problem-solving framework to facilitate activity acquisition. The participant would work on one or more of the 3 goals set, guided by the therapist, to discover a plan to achieve the goal. The participant would then do the plan and subsequently check to see if the plan was implemented and if it worked—that is, whether the goal was achieved. If the goal was not achieved, the participant was guided to analyze the performance breakdown and modify or create a new plan. Within the plan phase, the therapist used guided discovery to help the participant analyze the performance breakdown and discover domain-specific strategies to overcome the particular performance problems of that client with that activity. Thus, the plan-do-check process was repeated until the performance breakdown was successfully overcome, repeatedly; then, going to the next performance breakdown until all were overcome and the goal was achieved, repeatedly. It is important to note that although in CO-OP the focus is on performing the task to be learned, there is no particular emphasis on the number of repetitions. Repetitions are never stipulated; rather, the number of times a particular task is practiced depends on the quality and consistency of the performance. Once the participant is satisfied with the performance on the particular part of the task being worked on, as determined by the check in the global cognitive strategy, the next breakdown is identified, and a new learning cycle begins. This is repeated until the goal is achieved.

Usual Care Description

Participants randomized to the usual care group received usual outpatient occupational therapy with one modification. As described above, a nontreating research occupational therapist blinded to group allocation administered the COPM to assist participants in self-selecting personally meaningful goals, prior to beginning therapy. This was a departure from usual administration of the COPM because it tends to be conducted by the treating occupational therapist if done at all. The COPM results were made available to the treating occupational therapist, but no instructions were given regarding what to do with the information.

A survey given during the preparation for this study indicated that usual care consisted of a combination of functional, task-based training and component-based training, as deemed necessary by the treating therapists.

CO-OP Intervention Fidelity

Two therapists, one in Toronto and one in St Louis, were trained in CO-OP with a standard 2-day CO-OP workshop. For ongoing training, consolidation, and fidelity purposes, the 2 CO-OP therapists were then videorecorded treating a series of pilot participants and received feedback until they were consistently scoring full marks on an intervention fidelity checklist. Once the intervention began, videos from sessions 3, 6, and 10 were reviewed and scored using the same intervention fidelity checklist to ensure ongoing fidelity.

Outcomes Measures

Table 1 provides an overview of instrument characteristics and timing of their administration. Research staff blinded to group allocation conducted assessments prior to the intervention starting (time 1), after discharge from occupational

Table 1. Outcome Measures and Timing.

Outcome	Description and Properties	Timing
Performance Quality Rating Scale (PQRS)	The PQRS rates videorecorded performance of participant-selected activities on a 10-point scale, with a score of 1 indicating "can't do the skill at all" and 10 indicating "does the skill very well."[15] The activities performed and videorecorded are determined using the COPM, and most, but not all, goals selected by participants are amenable to videorecording. The PQRS has substantial test-retest reliability and good internal responsiveness.[26]	Times 1, 2, and 3
Canadian Occupational Performance Measure (COPM)	The COPM is a standardized instrument for eliciting performance issues from the client perspective and for capturing perceived changes in performance over time.[25] The COPM was used to elicit 4-6 participant-selected goals as well as for rating self-perceived performance and performance satisfaction for each goal on a 10-point scale, for each participant. The COPM has demonstrated a test-retest reliability of 0.89 in people with stroke.[27] A change of 2 points or more on the COPM is considered clinically significant.[25]	Times 1, 2, and 3
Community Performance Indicators (CPI)	The CPI is a complex self-report measure of community participation. In this study, we analyzed 2 enfranchisement factors: importance of participation (14 items) and control over participation (13 items). Participants rate items on a 5-point scale; these are converted using a Rasch-based key form to a score of 0-100.[28,29] There is good evidence of validity and reliability for these factors	Times 2 and 3
Stroke Impact Scale (SIS)	The SIS[30] is a 59-item questionnaire based measure of the perceived impact of stroke on function and everyday life. The SIS evaluates 8 domains, including participation. Each item is scored on a 5-point Likert scale related to the degree of difficulty the person with stroke is experiencing. The SIS is widely used in stroke intervention studies as an outcome measure and the psychometric properties of the instrument are well defined.[30-32]	SIS Participation Domain, times 2 and 3.
Self-Efficacy Gauge (SEG)	The SEG was designed to measure an individual's confidence in his or her ability to perform daily occupations that span a range of self-care, productivity, and leisure activities. Participants are asked to rate their confidence in their ability to perform 28 items, each on a 10-point scale, with 1 representing *not confident at all* and 10 representing *completely confident*. The SEG has very high internal consistency (0.94) and test-retest reliability (0.90).[33]	Times 1,2, and 3

therapy or after 10 sessions (time 2), and 3 months after time 2 (time 3). Because the number of intervention sessions varied among participants based on the severity of their stroke and their individual rehabilitation needs, representatives from usual care, either therapists or administrative staff, were asked to inform the study coordinator when the participant was discharged from occupational therapy or when 10 sessions were completed, whichever came first. Time 2 assessments were performed at this point as an attempt to assess initial outcomes after a similar treatment dosage. Because many of the participants had been discharged home from acute care hospital only a few days before the time 1 assessment and because the questions posed in the participation measures are designed for people who have been in the community for at least a few weeks, these were administered only at time 2 and time 3 to ensure their validity.

The primary study outcome was change in actual performance quality of self-selected activities, measured with the Performance Quality Rating Scale (PQRS).[15] The PQRS is a 10-point scale used to rate videorecorded performances of participant-selected activities. The participants perform the activities selected in the COPM interview in a safe environment but unaided by physical support or verbal cueing. The video recordings are rated on a scale of 1 to 10 in which 1 indicates *can't do the activity at all* and 10 indicates *does the activity very well*. In this study, an independent, blinded observer viewed the videos in randomized, nonchronological order. The PQRS has substantial test-retest reliability and good internal responsiveness.[26]

The COPM was included as an indicator of perceived performance quality and satisfaction with performance quality. The secondary study outcome was participation, assessed with the Stroke Impact Scale participation domain and the Community Participation Index. Additionally, self-efficacy was measured using the Self-Efficacy Gauge.

Data Analysis

Data analysis was conducted using SPSS version 21 (IBM Corp. Released 2012; IBM SPSS Statistics for Windows, Version 21.0) and Microsoft Excel (Microsoft Corporation, Microsoft Excel 2010, Version 14.0). The data were cleaned, checked for accuracy and missing values, and checked for normal distribution using the Shapiro-Wilk test. Descriptive statistics were compiled for all variables, and baseline comparisons between sites and between the groups were made.

Time 1 to time 2 and time 1 to time 3 mean change scores and standard deviations were calculated for normally distributed data, and Cohen's *d* effect sizes and confidence intervals were calculated. For nonnormally distributed data, medians were determined, and a nonparametric effect size *r* was calculated using the formula $r^2 = z^2/N$.[34]

CO-OP therapist logs and institutional patient records were reviewed to establish which self-selected activities were trained during the outpatient rehabilitation program. Records from occupational therapy sessions were reviewed by occupational therapists from the research team (DC and MD) for evidence of training. A self-selected activity was considered trained if there was any indication of practicing all or part of it or any indication of discussions or education concerning the activity. If no evidence of training was found it was considered untrained. In 4 cases, only partial records were available, in which case trained and untrained goals were confirmed by examining typical therapy activities by the same therapist with other participants. For COPM and PQRS scoring and analysis, trained and untrained activity scores were grouped, summed, and averaged separately to give a single trained and a single untrained score for each participant.

The ethics review boards at the relevant institutions approved this study.

Results

Figure 1 is the CONSORT diagram depicting participant flow through the study. A total of 35 eligible participants were randomized: 20 from St Louis and 15 from Toronto. Of those, 26 completed the intervention. Table 2 provides summary scores for participant demographics by site and by group. Participants in Toronto had more years of education ($P = .03$), and participants in St Louis began outpatient rehabilitation approximately 17 days sooner following their stroke than did participants in Toronto ($P = .04$). Otherwise, there were no significant between-site differences at baseline. The 2 treatment groups were equivalent at baseline on all variables examined. After excluding 2 extreme outliers, who had more than 100 treatment sessions—one in each treatment group and both from St Louis—those in the usual care group who completed the study had an average of 13.3 occupational therapy sessions (range = 3-30); those in the CO-OP group had an average of 12.2 occupational therapy sessions (range = 5-33). CO-OP therapists scored an average of 80% accuracy on CO-OP fidelity checklists.

Table 3 provides an overview of the 178 goals selected during the COPM interviews. A total of 23 of the 178 goals, such as "weight management" or "traveling to see family" could not be videorecorded and thus did not have PQRS scores associated with them. As an individual's PQRS score was based on an average of scores from all his or her self-selected activities, the loss of some activities that could not be videorecorded did not cause missing PQRS data; all participants who completed the intervention had at least 1 trained and 1 untrained activity that could be included in the analysis.

Table 4 displays summary statistics, change scores, and effect sizes. The effect size of Cohen's *d* can be interpreted as follows: 0.2 represents a small effect; 0.5 represents a medium effect; and 0.8 represents a large effect.[35] CO-OP's effect over usual care at time 2 was medium for PQRS-trained activities ($d = 0.5$) and large for PQRS untrained activities ($d = 1.2$). Large effects for time 3 change scores were found for both PQRS trained ($d = 1.6$) and untrained activities ($d = 1.1$). There was no effect of CO-OP over usual care on time 2 COPM change scores, a small effect at time 3 for changes in COPM performance and satisfaction of untrained goals, and a small effect for changes in performance of untrained goals. At time 3, CO-OP had a medium effect over usual care for change in CPI perceived control ($d = 0.7$) and the SEG ($d = 0.7$).

Discussion

Incorporating the CO-OP approach as part of an outpatient rehabilitation program is associated with a large effect at follow-up on actual performance of trained and untrained self-selected functional activities compared with programs incorporating usual occupational therapy. This suggests not only improved performance on skills trained in rehabilitation but also transfer of cognitive strategy training to permit those living with the effects of stroke to learn new skills outside of the rehabilitation setting as the need arises. This discussion elaborates on the features of the CO-OP approach that may contribute to transfer of learning to untrained activities, on the small effect of perceived performance, and on study limitations.

Transfer of skills learned in rehabilitation to novel skills is necessary to achieve optimal long-term functional health

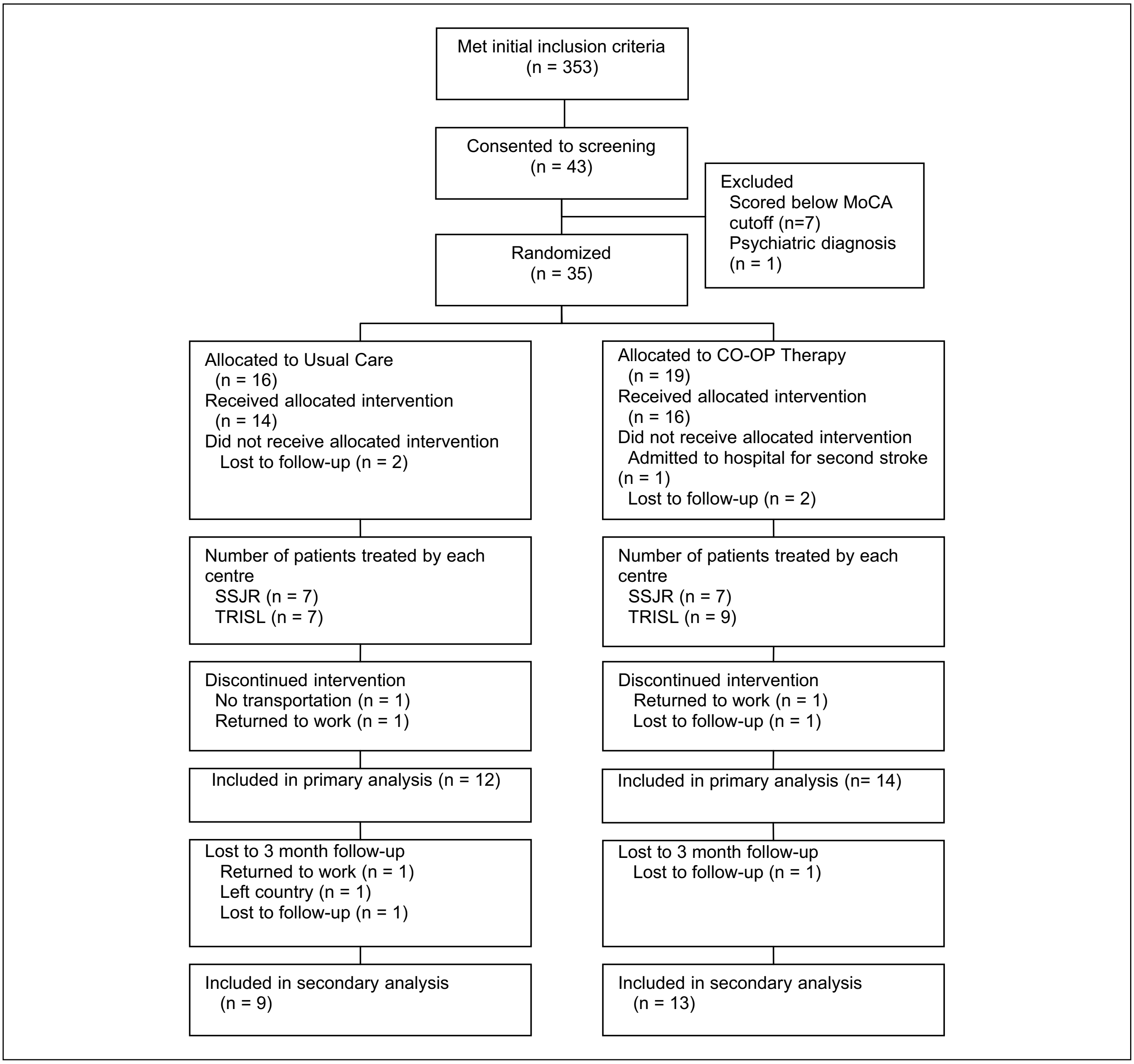

Figure 1. CONSORT diagram.
Abbreviations: CO-OP, Cognitive Orientation to daily Occupational Performance; MoCA, Montreal Cognitive Assessment; SSJR, Sunnybrook–St John's Rehab; TRISL, The Rehabilitation Institute of St Louis.

because rehabilitation programs are unable to teach clients all the activities they may need at home and in the community or even all variations of a single activity. Measurement of transfer of cognitive strategy training to real-world situations has been accomplished by the assessment of untrained tasks, by standardized assessment of daily tasks, or by participant or proxy self-report of daily-life situations.[36] In this study, the primary indicator of transfer was change in performance on self-selected tasks or activities not addressed during the intervention sessions with the therapist (untrained tasks). This type of far transfer (transfer to a completely unrelated task) is expected with cognitive strategy training because the therapist's primary emphasis is on teaching problem solving skills rather than on teaching the particular functional skill itself.[36]

Therapists trained to use the CO-OP approach are explicitly taught to work toward generalization and transfer.[13] Other CO-OP features may also contribute to transfer, including guided discovery, performance analysis, and self-discovery of performance strategies. Transfer is reported to be more closely linked to variable practice than blocked practice.[37] One theory for explaining this phenomenon is

Table 2. Demographics.

Variable	Group	n	St Louis Mean (SD)	Toronto Mean (SD)	t	Total Mean (SD)
Days since stroke	UC	15	41.6 (17.1)	52.0 (25.4)	−2.50	46.5 (21.3)
	CO-OP	19	30.5 (10.7)	53.1 (23.9)		40.1 (20.4)
Therapy sessions (number)	UC	11	10.2 (2.8)	17.0 (13.0)	−0.96	13.3 (9.2)
	CO-OP	14	10.0 (5.4)	14.4 (8.7)		12.2 (7.3)
Age	UC	16	50.7 (14.5)	59.3 (12.7)	−0.85	54.4 (14.0)
	CO-OP	19	57.4 (15.5)	57.6 (12.7)		57.5 (14.0)
Years of education	UC	16	12.2 (1.5)	14.4 (1.9)	−1.33	13.2 (2.0)
	CO-OP	19	14.3 (3.0)	15.3 (5.6)		14.7 (4.2)
			n (%)	n (%)	χ^2	n (%)
Sex (female)	UC	16	5 (44.4)	2 (28.6)	1.23	7 (43.8)
	CO-OP	19	4 (36.4)	2 (25.0)		6 (31.6)
Stroke side (right)	UC	16	7 (77.8)	6 (85.7)	0.10	13 (81.3)
	CO-OP	18	6 (54.5)	5 (62.5)		11 (57.9)
Handedness (right)	UC	16	8 (88.9)	6 (85.7)	0.59	14 (87.5)
	CO-OP	19	9 (81.8)	8 (100)		17 (89.5)
Living arrangement (with others)	UC	16	8 (88.9)	7 (100)	2.03	15 (93.8)
	CO-OP	19	7 (63.6)	7 (87.5)		14 (73.7)
Ethnicity						
Caucasian	UC		2 (25.0)	5 (71.4)		7 (46.7)
	CO-OP		5 (45.5)	4 (50.0)		9 (47.4)
African American	UC		6 (75.0)	0		6 (40.0)
	CO-OP		6 (54.4)	4 (50.0)		10 (52.6)
Asian	UC		0	1 (14.3)		1 (6.7)
	CO-OP		0	0		0
Other	UC		0	1 (14.3)		1 (6.7)
	CO-OP		0	0		0

the learned-variability model of skill transfer, in which learning a skill involves learning how to do the skill in different ways and learning when to alter it.[38] In CO-OP, learned variability occurs through the use of guided discovery combined with performance analysis within the plan and check phases of the goal-plan-do-check framework. The client is taught to check or self-analyze his or her performance breakdowns and is guided to identify different plans or strategies until settling on one that works best to perform the task at hand, learning different ways to do the skill as part of the process. Additionally, clients are guided to identify their own strategies rather than being assigned strategies by the therapist. There is experimental evidence to suggest that providing time to attend to performance issues and subsequently self-select a strategy is more strongly associated with transfer than being given a strategy.[39]

Evidence from a neuroimaging study suggests that the combined training of motor and cognitive systems has a positive impact on transfer. Olsson et al[40] conducted an experiment comparing motor practice, mental practice, and combined motor and mental practice to learn a finger tapping task and unexpectedly discovered improvements on a novel transfer task only in the combined training group. Functional magnetic imaging data indicated overall broader cortical activity in the combined training group and showed that the posterior cerebellar hemisphere was involved in transfer.

Transfer is also linked to high self-efficacy,[41] and high self-efficacy is linked to better functional outcomes in stroke.[42] Stevens et al[41] demonstrated that practice of an easier task rather than a more difficult task was associated with higher self-efficacy, and subsequently, that higher self-efficacy predicted better ability on a transfer task. These authors speculated that self-efficacy, rather than implicit learning, is a mediator of transfer to a similar but more difficult task, although they are cautious to emphasize that further research is required to confirm this finding. Interestingly, in this CO-OP study, an unexpected medium effect of CO-OP on self-efficacy was shown. We speculate that following CO-OP, self-efficacy in a broad range of daily activities likely comes from having experienced success with the self-selected activities practiced in therapy, the attribution of that success to the newly learned ability to problem solve

Table 3. Summary of Participant-Selected Goals.

Goal Category	Number	Examples
Activity and participation goals		
Handyman work	5	Repairing car; using hedge clippers
Cleaning	14	Housework; helping with dishes: making bed
Laundry	6	Laundry; folding laundry
Cooking	19	Cooking; getting items from kitchen
Eating	10	Cutting food; using a knife and fork to eat
Dressing	15	Dressing; putting on socks; using a zipper
Personal hygiene	5	Hygiene after toileting; hair care
Opening medicine bottles	2	
Using a door knob	1	
Walking	16	Walking outdoors; walking without device
Climbing stairs	1	
Transfers	8	Bathtub; toilet; car
Caregiving roles	3	Caregiving for husband; playing with kids
Work	7	Return to work; apply for job; school; volunteering
Manage finances	2	
Communicating over the phone	1	
Keyboarding/Computer use	8	Keyboarding; typing e-mail; use computer mouse
Handwriting	3	Write legibly
Office activities	6	Folding paper and putting it in envelopes
Drive	5	
Use public transportation	2	
Attending outings with friends/family	2	Traveling to see family
Grocery shopping	7	Groceries; shop without getting lost
Recreation	16	Go to casino; floor hockey; play drums; fishing; dancing
Sitting and standing more independently for synagogue	1	
Total activity and participation	164	
Impairment goals		
Concentration/memory/multitasking	3	Improve memory for day-to-day activities
Balance	4	Balance for walking and gardening
Endurance	2	Increase endurance for traveling
Weight management	1	
Strengthening	3	Strength for manual labor at work
Total impairment	14	

performance issues, and the subsequent willingness to try new activities at home independently. Thus, it is plausible that improved self-efficacy is an outcome of CO-OP, and self-efficacy then mediates transfer.

Self-efficacy and the ability to transfer new learning from rehabilitation to the real world may both be mediators of participation. It may be that improvements in self-efficacy need to be in place before measurable improvements in participation are seen. For example, the changes in the Community Participation Index for the CO-OP group were higher for the perceived control over participation domain than for involvement in living situations domain, suggesting a degree of confidence in the ability to participate but less actual involvement. This may be because the transition from confidence and ability to actual doing takes more time.

Limitations

This was an exploratory study with the objective of estimating CO-OP's effect relative to a control treatment in preparation for a larger, more definitive trial. As such, the sample size was too small to find statistically significant differences for most outcomes or to stratify groups on potential key confounders, such as stroke severity. The sample size also limited the statistical analysis to univariate procedures without the capacity to control for the effect of potential confounders, such as site and dosage.

The decision to have a usual care control meant that the comparison treatment was unstandardized. Both control programs were in university-affiliated hospitals linked to well-regarded academic programs, and the control treatment is believed to have been close to current best practice—that is,

Table 4. Means, Standard Deviations, Change Scores, and Cohen's *d* Effect Size.[a]

Outcome	Group	Time 1, Mean (SD)	Time 2, Mean (SD)	Time 1 − Time 2, Change Score, Mean (SD)	Effect Size *d* (95% CI)	Time 3, Mean (SD)	Time 1 − Time 3, Change Score, Mean (SD)	Effect Size *d* (95% CI)
PQRS trained	UC	5.7 (1.9)	7.5 (2.0)	1.8 (2.9)		6.9 (1.4)	1.5 (2.2)	
	CO-OP	4.3 (2.0)	7.1 (1.7)	2.9 (1.4)	0.5 (−0.4 to 1.4)	8.3 (1.2)	4.5 (1.7)	1.6 (0.5-2.7)
PQRS untrained	UC	5.1 (1.7)	5.6 (2.0)	0.5 (2.5)		7.1 (0.7)	1.5 (2.0)	
	CO-OP	4.8 (1.8)	7.7 (2.0)	2.9 (1.4)	1.2 (0.1-2.2)	8.3 (1.7)	3.6 (2.3)	1.1 (−0.1 to 2.3)
COPM-performance	UC	4.2 (1.9)	6.8 (2.4)	2.3 (2.1)	−0.1 (−0.8 to 0.7)	6.6 (3.0)	2.3 (2.5)	
trained	CO-OP	4.6 (1.8)	6.2 (2.5)	1.5 (3.0)		7.7 (2.2)	2.9 (1.8)	0.4 (−0.5 to 1.2)
COPM-performance	UC	3.8 (1.5)	5.9 (2.5)	1.9 (2.3)	−0.1 (−0.9 to 0.7)	6.7 (2.7)	2.4 (2.5)	
untrained	CO-OP	4.7 (2.0)	6.1 (2.9)	1.3 (3.1)		7.8 (2.2)	3.1 (2.7)	0.2 (−0.7 to 1.0)
COPM-satisfaction	UC	3.9 (2.5)	6.0 (2.2)	1.8 (2.3)		7.3 (2.5)	3.7 (3.3)	
trained	CO-OP	3.8 (2.1)	5.8 (3.0)	1.9 (2.8)	0.1 (−0.7 to 0.9)	7.2 (2.9)	3.2 (1.8)	0.1 (−1.0 to 0.8)
COPM-satisfaction	UC	3.5 (1.7)	5.6 (2.7)	1.7 (2.1)		6.8 (2.7)	2.8 (2.3)	
untrained	CO-OP	4.0 (1.9)	5.7 (3.0)	1.5 (3.3)	0.0 (−0.8 to 0.7)	7.5 (2.6)	3.2 (3.0)	0.2 (−0.7 to 1.1)
CPI-importance of	UC	—	53.3 (12.5)	—	—	50.7 (8.1)	−0.5 (5.2)	
participation	CO-OP	—	52.1 (8.1)	—		52.4 (10.5)	1.2 (5.9)	0.3 (−0.6 to 1.2)
CPI-control over	UC	—	64.1 (16.5)	—	—	61.9 (13.2)	−3.0 (11.4)	
participation	CO-OP	—	58.4 (9.3)	—		63.8 (12.6)	3.4 (7.2)	0.7 (−0.2 to 1.6)
CPI-satisfaction with	UC		69.0			140.0	20.7	
participation[b]	CO-OP		70.3			85.0	13.5	0.2
SIS-participation	UC	—	54.6 (13.7)	—	—	56.9 (13.3)	1.9 (12.5)	
	CO-OP	—	47.9 (16.8)	—		56.6 (16.7)	8.0 (9.9)	0.5 (−0.4 to 1.4)
SEG	UC	211.7 (51.7)	227.5 (42.0)	3.8 (48.9)		228.3 (28.1)	9.4 (41.8)	
	CO-OP	198.4 (45.3)	224.6 (45.2)	23.2 (38.9)	0.4 (−0.3 to 1.2)	239.2 (36.3)	38.8 (38.1)	0.7 (−0.2 to 1.6)

Abbreviations: SD, standard deviation; CI, confidence interval; PQRS, Performance Quality Rating Scale; UC, usual care; CO-OP, cognitive orientation to daily occupational performance; COPM, Canadian Occupational Performance Measure; CPI, Community Performance Indicators; SIS, Stroke Impact Scale; SEG, Self-Efficacy Gauge.
[a]Effect sizes: 0.2, small effect; 0.5 medium effect; 0.8 large effect.
[b]Data were not normally distributed; therefore, median and nonparametric effect size *r* are reported.

interdisciplinary treatment, largely based on repetitive functional task training, with treatment of impairments and components when deemed appropriate by the therapist.

For the purposes of blinding and consistency between the 2 treatment groups, the COPM was administered by a research therapist with no clinical relationship with the patient, rather than by the treating therapist as is usually done. This may have resulted in a disconnect between the participant and the treating therapist regarding the self-selected goals, may have had implications for the relatively smaller effect of CO-OP on COPM, and may be something to reconsider in future studies.

A final important limitation of this study was the relatively short follow-up period, which was just 3 months after the postintervention assessment and an average of 7 months following the stroke. To get a better estimate of the stability of the treatment effects and the impact on participation, future studies should follow participants for at least 1 year after discharge.

Conclusion

CO-OP, incorporated as part of a usual outpatient stroke rehabilitation program, was associated with a large treatment effect compared with usual outpatient rehabilitation alone on follow-up performances of both trained and untrained self-selected activities. Results also suggest a medium effect on changes in participation from postintervention to follow-up and on self-efficacy. A larger-scale trial is warranted.

Acknowledgments

The authors acknowledge the assistance of Alisa Grigorovich, Tanya Ramsey, Carin Roth, Tammy Craig, Kimberly Walker, and Duana Russell-Thomas as well as the staff in the Performance, Participation, and Neurorehabilitation Laboratory in the Program in Occupational Therapy at Washington University in St Louis for their assistance with assessment, evaluation, and treatment.

Authors' Note

ClinicalTrials.gov Identifier: NCT01309165.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was funded by a Canadian Institutes of Health Research Open Operating Grant (FRN#111200) and was supported by the St John's Rehab Hospital and The Rehabilitation Institute of St Louis. SM's salary support came from the St John's Rehab Foundation. TW received salary support from the National Center for Medical Rehabilitation Research (NCMRR) in the National Institute of Child Health and Human Development (NICHD) of the National Institutes of Health under award numbers K12HD055931 and K23HD073190. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Paper II: Combined cognitive-strategy and task-specific training impacts cognition and upper extremity function in sub-acute stroke: An exploratory randomized controlled trial, by T. Wolf, H. Polatajko, C. Baum, J. Rios, D. Cirone, M. Doherty, & S. McEwen, 2016, American Journal of Occupational Therapy, 70, 7002290010. http://dx.doi.org/10.5014/ajot.2016.017293. Copyright © 2016 by the American Occupational Therapy Association. Used with permission.

Combined Cognitive-Strategy and Task-Specific Training Affects Cognition and Upper-Extremity Function in Subacute Stroke: An Exploratory Randomized Controlled Trial

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MeSH TERMS
- activities of daily living
- cognition
- movement
- occupational therapy
- recovery of function
- stroke

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The purpose of this study was to estimate the effect of Cognitive Orientation to Daily Occupational Performance (CO–OP) compared with usual occupational therapy on upper-extremity movement, cognitive flexibility, and stroke impact in people less than 3 mo after stroke. An exploratory, single-blind randomized controlled trial was conducted with people referred to outpatient occupational therapy services at two rehabilitation centers. Arm movement was measured with the Action Research Arm Test, cognitive flexibility with the Delis–Kaplan Executive Function System Trail Making subtest, and stroke impact with subscales of the Stroke Impact Scale. A total of 35 participants were randomized, and 26 completed the intervention. CO–OP demonstrated measurable effects over usual care on all measures. These data provide early support for the use of CO–OP to improve performance and remediate cognitive and arm movement impairments after stroke over usual care; however, future study is warranted to confirm the effects observed in this trial.

Wolf, T. J., Polatajko, H., Baum, C., Rios, J., Cirone, D., Doherty, M., & McEwen, S. (2016). Combined cognitive-strategy and task-specific training affects cognition and upper-extremity function in subacute stroke: An exploratory randomized controlled trial. *American Journal of Occupational Therapy, 70,* 7002290010. http://dx.doi.org/10.5014/ajot.2016.017293

Although the death rate from stroke continues to decline in the United States and globally, the number of people living with chronic symptoms is rising. More than 7 million people have experienced stroke, and it is now the leading cause of long-term disability in the United States (National Stroke Association, 2015).

Although current best evidence has shown that repetitive practice of functional tasks is associated with improvements, such as better gait speed and upper-extremity function (French et al., 2008), most occupational therapy practitioners continue to use impairment-based approaches that emphasize remediation of impairments (Connell, McMahon, Eng, & Watkins, 2014; Teasell, Foley, Salter, & Jutai, 2008; Veerbeek et al., 2014). The expectation with these impairment-based rehabilitation approaches, also called *bottom-up approaches,* is that gains in the targeted component (e.g., motor function) will translate into improvement in performance in everyday life activity. Unfortunately, evidence suggests that gains do not occur; almost half of the people living in the community with stroke are still dependent in the activities necessary to support their daily lives (Appelros, Samuelsson, Karlsson-Tivenius, Lokander, & Terént, 2007). Most of them have significant restrictions in their everyday life participation compared with their age-matched peers (Alzahrani, Ada, & Dean, 2011; Hackett, Glozier, Jan, & Lindley, 2012; Mayo, Wood-Dauphinee, Côté, Durcan, & Carlton, 2002).

For occupational therapy practitioners, this lack of association between impairment-based approaches and improvement in everyday activity should not be surprising. During the inception of the profession of occupational therapy in the early 1900s, Adolph Meyer established the philosophical foundation for occupational therapy. He challenged the profession to view disease not merely as a demon that had to be excised from the body, but rather as an affliction of maladaptation that can be addressed with a well-fitted use of time and occupation (Meyer, 1922). Mary Reilly (1962) further supported this foundation of occupational therapy in her 1962 Eleanor Clarke Slagle lecture when she declared the hypothesis of occupational therapy to be that "man, through the use of his hands, as energized through mind and will, can influence the state of his own health" (p. 92). Thus, for more than a century, occupational therapy theorists have espoused top-down approaches with the assumption that engagement in occupation can improve health and remediate impairment. Although increasing evidence has shown that bottom-up approaches do not improve occupation, little information exists on the impact of top-down approaches on impairment.

Cognitive Orientation to Daily Occupational Performance (CO–OP; McEwen, Polatajko, Huijbregts, & Ryan, 2010) is a top-down approach that reduces impairments and improves health. *CO–OP* is defined as "a client-centered, performance-based, problem solving approach that enables skill acquisition through a process of strategy use and guided discovery" (Polatajko et al., 2001, p. 108). The goal of CO–OP is to focus treatments directly on improving performance in everyday life activity rather than treating the underlying impairments and hoping for secondary improvement in meaningful activities. CO–OP was originally developed for use with pediatric populations, but a growing body of literature has supported its use to improve performance in people with stroke. Early evidence from two single-case experimental series in people with chronic stroke showed improvement in trained and untrained activities (McEwen et al., 2010; McEwen, Polatajko, Huijbregts, & Ryan, 2009). This improvement in activity performance was also demonstrated in an early-phase pilot clinical trial that compared people with chronic stroke with an active control group (Polatajko, McEwen, Ryan, & Baum, 2012). Although these early results with people with chronic stroke were promising, the general consensus is that rehabilitation early after stroke can have a greater effect on outcomes (Ploughman, 2002; Salter, Foley, & Teasell, 2010; Teasell et al., 2008).

With this in mind, our research group undertook an early-phase clinical trial using CO–OP with people less than 3 mo after stroke compared with usual and customary care delivered in the occupational therapy outpatient setting. On the primary outcome, objective performance of meaningful, functional activities as measured by the Performance Quality Rating Scale (PQRS; Martini, Rios, Polatajko, Wolf, & McEwen, 2015), CO–OP was found to have a medium effect ($d = 0.5$) over usual care on self-selected trained activities and a large effect ($d = 1.2$) on untrained activities. The effect on trained activities increased at 3 mo after intervention ($d = 1.6$), whereas the effect on untrained activities was maintained ($d = 1.1$; McEwen et al., 2015). Because of previous preliminary evidence that CO–OP may affect impairments and components of stroke impact (McEwen et al., 2010), we also sought to explore its effect on a group of secondary outcomes postulated to be affected by this complex, client-centered, performance-based, problem-solving approach. Specifically, our objective was to estimate the effect of CO–OP compared with usual occupational therapy on immediate and longer term secondary outcomes for upper-extremity movement, cognitive flexibility, and stroke impact in people less than 3 mo after stroke.

Method

This study was a single-blind, exploratory, randomized controlled trial with participants referred to outpatient stroke rehabilitation. The study was conducted at two rehabilitation centers collaborating with university investigators. All participants in this study were randomized to receive either usual outpatient occupational therapy provided at the institution (usual care) or CO–OP. All participants received other health care services as was typical at the centers, including, but not limited to, physical therapy, speech–language pathology, counseling, and nursing. Eligibility for participation in this study, however, was related only to occupational therapy services. The study was reviewed and approved by the Washington University in St. Louis School of Medicine Human Research Protection Office and the research ethics board of Sunnybrook Health Sciences Centre. A complete description of this study's methods can be found in the previously published primary results article (McEwen et al., 2015).

Participants

Patients with ischemic stroke who were referred for outpatient therapy services at either Sunnybrook–St. John's Rehab (Toronto) or The Rehabilitation Institute of St. Louis were recruited for participation in this study.

Anyone who met these criteria was considered eligible. Patients were excluded on the basis of the following criteria: (1) more than 3 mo after stroke at the time of enrollment, (2) not referred to receive occupational therapy, (3) any prior neurological diagnoses other than stroke, (4) any major psychiatric illness, (5) moderate or greater aphasia as determined by combined scores of 6 or less on the Canadian Institute for Health Information (CIHI) National Rehabilitation Reporting System (NRS) Listing of Data Elements (CIHI, 2009) Items 64 and 66, and (6) significant cognitive impairment as determined by a score of 21 or less on the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005).

A blocked randomization procedure stratified by site was used to determine group allocation. A statistician external to the study team developed the randomization sequence. A block size of 6 and an allocation ratio of 1:1 were used to ensure equal distribution in groups of 6 at each site. Group allocation was completed after consent and final determination of eligibility. The entire study team was blinded to the randomization procedure and block size.

Procedures

Participants with consent completed a baseline assessment (Time 1) with a rater blinded to allocation before starting the intervention. The baseline assessment also included the MoCA and the CIHI to determine final eligibility. After the baseline assessment, eligible participants completed an occupational interview using the Canadian Occupational Performance Measure (COPM; Law et al., 1998) with an occupational therapist, who was also blinded to group allocation, to establish goals for participation in this study.

During the COPM interview, participants selected functional activity goals that would become the focus of CO–OP treatment. After completion of the COPM, participants completed a third assessment to obtain PQRS scores. To complete the PQRS, participants were videotaped performing the self-selected goals from the COPM; the videos were later scored by a rater who was blinded to group allocation.

Next, participants were randomized to either CO–OP or usual care by the study coordinator at each site, and the results of the COPM were distributed to each participant's treating occupational therapist. Participants had a range of stroke impairments and rehabilitation needs; therefore, the number of treatment sessions varied. However, the CO–OP group received a maximum of 10 CO–OP intervention sessions, and any additional sessions received were through usual care. After completion of the intervention, participants completed a postintervention assessment (Time 2) and a 3-mo follow-up assessment (Time 3) that included all the outcome measures described subsequently.

Intervention

Cognitive Orientation to Daily Occupational Performance. Complete details about the theoretical underpinnings and implementation of the CO–OP approach have been previously published (Polatajko et al., 2001). In this study, CO–OP treatment was delivered in a separate location and with separate occupational therapists from those who administered the usual-care intervention. The first therapy session included a review of the CO–OP treatment model and the global strategy of Goal–Plan–Do–Check, adapted from Meichenbaum and Goodman (1971). In the first session, the participant and therapist also collaborated using results from the COPM to select three goals to address in treatment.

Throughout the subsequent therapy sessions, the participant used the problem-solving strategy Goal–Plan–Do–Check to address and master each goal activity. After the participant identified a goal for each session, the therapist used the process of guided discovery to help the participant establish a plan to accomplish the goal. The plan could have many parts and address aspects of the environment, the person, and how the activity was done. Performance problems related to the activity were assessed collaboratively by the participant and the therapist, and the therapist encouraged problem solving to allow the participant to self-discover domain-specific strategies specific to the activity such as modifying the task or changing body position to resolve the performance problem. Next, the participant executed the selected strategy (do the plan) and then checked to evaluate the success of the plan. The check presents an opportunity to refine or modify the plan or to decide that the goal was met. To achieve the goal, the Plan–Do–Check portion was often repeated more than once. The participant decided when the goal was achieved and the preferred plan to achieve the goal, not the therapist.

Usual Care. Usual-care therapy took place at one of two freestanding rehabilitation centers and was done by the usual staff, who were unaffiliated with the research group. The clinicians received no direction from the research study staff. They were provided with the COPM results and personalized activity goals for each participant; however, no information was given to the usual-care therapist about how to use the COPM results. During study preparation, a survey conducted at both sites with a sample of experienced therapists indicated that usual-care stroke rehabilitation consisted of a combination of functional, task-based training, such as practicing dressing, and component-based training, such as grasping objects, chosen by each individual therapist to meet individual patient needs.

Outcome Measures

Table 1 provides an overview of the study outcome measures. All measures were administered at baseline (Time 1), postintervention (Time 2), and at 3 mo after completion of the postintervention assessment (Time 3). Although the total number of intervention sessions varied, therapists in both arms of this study were instructed to inform the study coordinator when the participant was being discharged from occupational therapy or when the maximum of 10 intervention sessions was reached, whichever came first, to complete the posttreatment assessment. This instruction was given to ensure dose equivalence at Time 2, considering the necessary variability that was expected in the number of treatment sessions in this population.

The video of the PQRS was rated on a scale ranging from 1 (*can't do the activity at all*) to 10 (*does the activity very well*) by an independent blinded rater who viewed and scored the PQRS videos in randomized order (by participant, goal, and time). All raters were trained by the study investigators and had to demonstrate competency in administration of all the assessments with people with stroke before they were qualified to administer the assessments to study participants.

Analysis

After data cleaning and accuracy checks, analyses were conducted using IBM SPSS Statistics (Version 21; IBM Corporation, Armonk, NY) and Excel (Microsoft, Redmond, WA). Normal distribution was verified using the Shapiro–Wilk test. Descriptive statistics for the primary outcomes, PQRS, COPM, and participation were previously reported (McEwen et al., 2015). Descriptive statistics for Action Research Arm Test (ARAT; Lyle, 1981), Delis–Kaplan Executive Function System (D–KEFS; Delis, Kaplan, & Kramer, 2001), and Stroke Impact Scale (SIS; Duncan, Bode, Min Lai, & Perera, 2003) domains related to function were calculated, and baseline comparisons were made between sites and between groups. Time 1 to Time 2 and Time 1 to Time 3 mean change scores and standard deviations were calculated for normally distributed data, and Cohen's d effect sizes and confidence intervals were calculated. For non-normally distributed data, medians and ranges were determined, and a nonparametric effect size r was calculated using the formula $r^2 = z^2/N$ (Fritz, Morris, & Richler, 2012).

Table 1. Description of Outcome Measures

Instrument	Construct	Description
Delis–Kaplan Executive Function System (D–KEFS) Trail Making subtest (Condition 4)	Cognitive function (executive function)	The D–KEFS is a standardized executive function battery with subtests to assess 9 components of executive function, all of which have adequate test–retest reliability and internal consistency. For the purposes of this study, Condition 4 of the Trail Making subtest was used as a gross measure of executive function. It assesses visual–motor skills, visual scanning abilities, number and letter sequencing, and cognitive flexibility.
Action Research Arm Test (ARAT)	Upper-extremity function	The ARAT measures upper-extremity impairment and activity limitation by assessing upper-extremity capacity. It has 19 items with four subscales: Grasp, Grip, Pinch, and Gross Movement.
Stroke Impact Scale (SIS)	Health status	The SIS is a self-report measure to evaluate the impact that stroke has had on a participant's function. The following domains were evaluated in this study: Strength, Hand Function, Mobility, Activities of Daily Living, Memory, Emotion, Recovery, and Communication. The Participation domain was not evaluated because it was previously reported on.
Canadian Occupational Performance Measure (COPM)	Self-reported occupational performance: trained and untrained goals	The COPM is a standardized instrument for eliciting performance issues from the client's perspective and for capturing perceived changes in performance over time. The COPM was used to elicit 4–6 participant-selected goals and to rate self-perceived performance and performance satisfaction for each goal on a 10-point scale for each participant.
Performance Quality Rating Scale (PQRS)	Objective rating of performance of COPM goals	The PQRS rates the video-recorded performance of participant-selected activities on a 10-point scale (ranging from 1 = *can't do the skill at all* to 10 = *does the skill very well*). The activities performed and video recorded are determined using the COPM, and most, but not all, goals selected by participants are amenable to video recording.

Note. From "Combined Cognitive-Strategy and Task-Specific Training Improve Transfer to Untrained Activities in Subacute Stroke: An Exploratory Randomized Controlled Trial," by S. McEwen, H. Polatajko, C. Baum, J. Rios, D. Cirone, M. Doherty, & T. Wolf, 2015, in *Neurorehabilitation and Neural Repair, 29,* 529. http://dx.doi.org/10.1177/1545968314558602. Copyright © 2015 by the American Society of Neurorehabilitation. Adapted with permission.

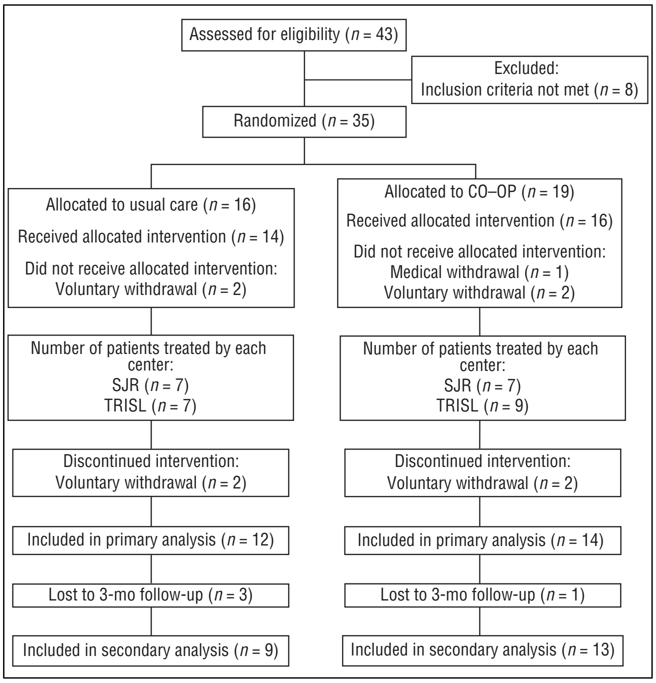

Figure 1. CONSORT (CONsolidated Standards Of Reporting Trials) diagram of participant flow through the study.

Note. CO–OP = Cognitive Orientation to Daily Occupational Performance; SJR = St. John's Rehab; TRISL = The Rehabilitation Institute of St. Louis. From "Combined Cognitive-Strategy and Task-Specific Training Improve Transfer to Untrained Activities in Subacute Stroke: An Exploratory Randomized Controlled Trial," by S. McEwen, H. Polatajko, C. Baum, J. Rios, D. Cirone, M. Doherty, & T. Wolf, 2015, *Neurorehabilitation and Neural Repair, 29,* 531. http://dx.doi.org/10.1177/1545968314558602. Copyright © 2015 by the American Society of Neurorehabilitation. Used with permission.

Results

A CONSORT (CONsolidated Standards Of Reporting Trials) diagram depicts participant flow through the study (Figure 1). A total of 35 participants were randomized between The Rehabilitation Institute of St. Louis (n = 20) and St. John's Rehab in Toronto (n = 15). Of these 35 participants, 26 completed the intervention and the postintervention assessment (Time 2). Table 2 provides demographic data for participants by group and site. Overall, participants in St. Louis started outpatient occupational therapy services sooner than participants in Toronto (p = .04); however, participants had no other significant differences between sites at baseline. Table 2 shows that participants in both groups received almost an equal number of occupational therapy sessions; however, for this analysis, two outliers were removed, one from each treatment group, who had received more than 100 sessions of occupational therapy, perhaps related to their ability to pay privately for services.

Table 3 displays score and change score means and standard deviations and effect sizes for all normally distributed data for stroke impact and cognitive flexibility between the CO–OP and the usual-care groups. Cohen's d effect size interpretation is as follows: 0.2 = small effect, 0.5 = medium effect, and 0.8 = large effect. At Time 2, CO–OP had a large effect over usual care for SIS Recovery (d = 0.8) and a medium effect over usual care for changes in the SIS Physical summary score (strength, hand function, mobility, and ADL/IADL scores), SIS Hand Function, and the D–KEFS Trail Making subtest (d = 0.5). At Time 3, there was a medium effect for SIS

Table 2. Participant Demographics (*N* = 35)

	M (*SD*) or *n* (%)		
Characteristic and Group	St. Louis	Toronto	Total
Days since stroke			
UC	41.6 (17.1)	52.0 (25.4)	46.5 (21.3)
CO–OP	30.5 (10.7)	53.1 (23.9)	40.1 (20.4)
Therapy, hr			
UC	10.2 (2.8)	17.0 (13.0)	13.3 (9.2)
CO–OP	7.9 (2.3)	14.4 (8.7)	10.9 (6.8)
Age, yr			
UC	50.7 (14.5)	59.3 (12.7)	54.4 (14.0)
CO–OP	57.4 (15.5)	57.6 (12.7)	57.5 (14.0)
Education, yr			
UC	12.2 (1.5)	14.4 (1.9)	13.2 (2.0)
CO–OP	14.3 (3.0)	15.3 (5.6)	14.7 (4.2)
Female			
UC	5 (44.4)	2 (28.6)	7 (43.8)
CO–OP	4 (36.4)	2 (25.0)	6 (31.6)
Right-side stroke			
UC	7 (77.8)	6 (85.7)	13 (81.3)
CO–OP	6 (54.5)	5 (62.5)	11 (57.9)
Right-handedness			
UC	8 (88.9)	6 (85.7)	14 (87.5)
CO–OP	9 (81.8)	8 (100)	17 (89.5)
Living with others			
UC	8 (88.9)	7 (100)	15 (93.8)
CO–OP	7 (63.6)	7 (87.5)	14 (73.7)
Ethnicity			
White			
UC	2 (25.0)	5 (71.4)	7 (46.7)
CO–OP	5 (45.5)	4 (50.0)	9 (47.4)
African-American			
UC	6 (75.0)	0	6 (40.0)
CO–OP	6 (54.4)	4 (50.0)	10 (52.6)
Asian			
UC	0	1 (14.3)	1 (6.7)
CO–OP	0	0	0
Other			
UC	0	1 (14.3)	1 (6.7)
CO–OP	0	0	0

Note. CO–OP = Cognitive Orientation to Daily Occupational Performance; *M* = mean; *SD* = standard deviation; UC = usual care. From "Combined Cognitive-Strategy and Task-Specific Training Improve Transfer to Untrained Activities in Subacute Stroke: An Exploratory Randomized Controlled Trial," by S. McEwen, H. Polatajko, C. Baum, J. Rios, D. Cirone, M. Doherty, & T. Wolf, 2015, *Neurorehabilitation and Neural Repair, 29,* 532. http://dx.doi.org/10.1177/1545968314558602. Copyright © 2015 by the American Society of Neurorehabilitation. Used with permission.

Table 3. Comparisons Between Groups for Stroke Impact and Cognitive Flexibility

Outcome Measure and Group	M (SD)				M (SD)		
	Time 1	Time 2	Time 1–2 Change Score	d[a] [95% CI]	Time 3	Time 1–3 Change Score	d[a] [95% CI]
SIS ADLs							
UC	59.6 (13.8)	58.2 (15.6)	−0.5 (18.6)	0.6 [−0.2, 1.4]	64.7 (10.8)	7.3 (14.1)	0.1 [−0.8, 1.0]
CO–OP	54.8 (14.6)	64.4 (15.0)	8.4 (10.9)		64.9 (11.7)	8.5 (10.1)	
SIS Mobility							
UC	57.6 (14.7)	64.4 (15.2)	4.6 (19.7)	0.2 [−0.6, 0.9]	64.9 (11.2)	9.6 (16.3)	0.1 [−0.8, 1.0]
CO–OP	54.4 (46.9)	62.4 (17.1)	7.0 (7.9)		69.3 (11.8)	10.7 (10.8)	
SIS Hand Function							
UC	38.3 (26.7)	39.0 (30.2)	3.7 (16.4)	0.5 [−0.3, 1.3]	44.4 (30.2)	9.8 (17.1)	0.6 [−0.3, 1.5]
CO–OP	32.8 (27.0)	46.0 (27.6)	11.7 (15.9)		51.6 (24.8)	20.7 (16.9)	
SIS							
UC	60.0 (11.4)	62.4 (12.7)	1.6 (15.3)	0.5 [−0.3, 1.3]	65.8 (8.1)	7.4 (12.1)	0.2 [−0.7, 1.1]
CO–OP	55.9 (14.8)	64.2 (14.0)	7.8 (7.7)		67.7 (10.7)	9.9 (11.4)	
SIS Recovery							
UC	58.1 (22.2)	50.0 (18.3)	−5.5 (16.3)	0.8 [0.0, 1.6]	66.7 (11.7)	11.1 (18.3)	0.0 [−0.9, 0.9]
CO–OP	58.9 (19.1)	67.5 (15.2)	7.1 (14.8)		72.3 (17.7)	11.4 (13.4)	
D–KEFS Condition 4							
UC	5.4 (4.2)	6.4 (4.9)	0.9 (2.0)	0.5 [−0.3, 1.3]	6.9 (4.5)	1.3 (3.8)	0.5 (−0.4, 1.4)
CO–OP	5.3 (3.8)	8.1 (3.3)	2.6 (4.3)		9.0 (3.3)	3.4 (4.6)	

Note. ADLs = activities of daily living; CI = confidence interval; CO–OP = Cognitive Orientation to Daily Occupational Performance; D–KEFS = Delis–Kaplan Executive Function System; *M* = mean; *SD* = standard deviation; SIS = Stroke Impact Scale; UC = usual care.
[a]Effect size: 0.2 = small effect, 0.5 = medium effect, and 0.8 = large effect.

Hand Function ($d = 0.6$) and the D–KEFS Trail Making subtest ($d = 0.5$). ARAT and SIS Communication, Physical summary score, Emotion, and Memory domains were all found to be non-normally distributed, thus nonparametric analyses were conducted.

Table 4 displays score and change score medians and ranges and the nonparametric effect size r ($r^2 = z^2/N$) for stroke impact and arm movement between the CO–OP and the usual-care groups. Effect size r interpretation is as follows: 0.1 = small effect, 0.3 = medium effect, and 0.5 = large effect (Fritz et al., 2012). At Time 2, changes in the ARAT and SIS domains all showed a small to medium effect of CO–OP over usual care. At Time 3, changes in SIS Communication showed a medium effect of CO–OP over usual care, and changes in the ARAT showed a small effect of CO–OP.

Table 4. Comparison Between Groups for Stroke Impact and Arm Movement

Outcome Measure and Group	Median (Range)				Median (Range)		
	Time 1	Time 2	Time 1–2 Change Score	r[a]	Time 3	Time 1–3 Change Score	r[a]
SIS Physical							
UC	42.5 (10–80)	37.5 (10–80)	−2.5 (−70 to 20)	.3	45 (25–80)	5.0 (−20 to 20)	.2
CO–OP	45 (15–80)	50 (20–80)	2.5 (−5 to 20)		55 (20–80)	10.0 (−5.0 to 25.0)	
SIS Memory							
UC	67.1 (34.3–80)	71.4 (48.6–80)	0 (−25.7 to 40)	.3	62.9 (51.4–74.3)	−2.9 (−17.1 to 40)	.2
CO–OP	62.9 (11.4–80)	67.1 (2.9–80)	4.3 (−8.6 to 40)		77.1 (0–80)	5.7 (−14.3 to 37.1)	
SIS Emotion							
UC	61.1 (28.9–77.8)	66.7 (17.8–80)	−1.1 (−22.2 to 11.1)	.3	66.7 (57.8–77.8)	2.2 (−13.3 to 13.3)	.2
CO–OP	60 (24.4–80)	66.7 (26.7–80)	7.8 (−35.6 to 13.3)		71.1 (20–77.8)	6.7 (−42.2 to 17.8)	
SIS Communication							
UC	77.1 (40–80)	78.6 (54.3–80)	0 (−20 to 2.9)	.4	74.3 (54.3–80)	0 (−11.4 to 8.6)	.4
CO–OP	65.1 (22.9–80)	72.9 (28.6–80)	1.43 (−11.4 to 20)		71.4 (42.9–80)	2.9 (−5.7 to 34.3)	
ARAT							
UC	55 (0–57)	50 (0–57)	0 (−24 to 5)	.2	55 (4–57)	1 (−5 to 10)	.1
CO–OP	50 (0–57)	55 (0–57)	0 (−5 to 11)		55 (2–57)	2.5 (−1 to 18)	
ARAT (Impairment)[b]							
UC	22 (0–47)	5 (0–47)	−1.5 (−24 to 5)	.3	30 (4–55)	8 (1 to 10)	.3
CO–OP	4 (0–45)	10 (0–49)	0 (−5 to 11)		22 (2–56)	12 (−1 to 18)	

Note. ARAT = Action Research Arm Test; CO–OP = Cognitive Orientation to Daily Occupational Performance; SIS = Stroke Impact Scale; UC = usual care.
[a]Effect size: 0.1 = small effect, 0.3 = medium effect, 0.5 = large effect. [b]UC group, $n = 7$; CO-OP group, $n = 8$.

Given that the primary outcome of this study was to evaluate the effect of CO–OP on performance, no inclusion or exclusion criteria were related to upper-extremity function. Therefore, as the data show, the sample in both intervention groups included a wide range of upper-extremity function. Therefore, we also evaluated the effect of the interventions only in participants who had an impairment as defined by the ARAT (i.e., score <49). This criterion for impairment was established in an ongoing clinical trial, conducted by Catherine Lang and colleagues (NCT01146379), to evaluate the necessary dose of task-specific training to improve upper-extremity function. In participants with upper-extremity impairment (CO–OP group, $n = 8$; usual-care group, $n = 7$), a medium effect of CO–OP over usual care was still maintained at follow-up (see Table 4).

Discussion

The results of this study suggest that CO–OP, a top-down intervention focused primarily on skill performance, may have a broader positive effect on stroke recovery than usual care and a broader effect than might be expected of a top-down approach. In addition to positive gains in the targeted areas, subjective and objective occupational performance (McEwen et al., 2015), these data support a positive effect of CO–OP over usual occupational therapy on upper-extremity function, cognitive flexibility, and perceived body functions, areas not directly targeted during treatment. Note that the effect size estimates reported are the effect of CO–OP compared with usual occupational therapy services, rather than the absolute effect of CO–OP.

Although overall the differential effect on some secondary measures lessened between Time 2 and follow-up, there was still a measureable positive effect of CO–OP over usual care on all of the outcomes except the single SIS question related to self-report global recovery. This question asks participants to rate overall recovery from stroke on a scale ranging from 0 to 100. The CO–OP participants reported consistently better overall recovery over time, whereas the usual-care group decreased from baseline to postintervention assessment before improving at follow-up. Overall, the mean change scores for overall recovery for the CO–OP group were consistently higher than those for the usual-care group. The differential and positive effect of CO–OP on the objective measure of cognitive flexibility (D–KEFS Trail Making subtest) was maintained at a moderate level through the 3-mo follow-up. The differential and positive effect of CO–OP was moderate ($r = .3$) on the objective measure of arm movement (ARAT) postintervention and lessened minimally to $r = .2$ at 3-mo follow-up.

The explanation for the differential and positive effect of CO–OP over usual care remains unknown; however, some potential hypotheses could explain the results. First, CO–OP's focus on skill performance, cognitive strategy use, and guided discovery could serve as a catalyst that provides an initial increase in both effect and efficiency (rate of effect) over usual care, as seen at Time 2. This hypothesis could be tested in a future study and would provide support for the use of CO–OP to expedite recovery poststroke. Second, almost all of the CO–OP participants received some usual-care occupational therapy after their 10 CO–OP sessions, which may have influenced the results at follow-up. We postulate that this situation may have caused confusion and mixed messages because participants went from a largely self-directed approach to a more traditional therapist-led approach. Future studies could evaluate whether additional CO–OP sessions instead of usual care would lead to maintenance of the larger differential effect observed postintervention.

CO–OP's stated clinical objectives also include cognitive strategy use and transfer and generalization beyond the specific activities trained. Therefore, some of the moderate effects on secondary outcomes are perhaps expected. It can be postulated that using the CO–OP approach that implements global cognitive strategy in combination with guided discovery is linked to changes in cognitive flexibility. In CO–OP, participants are trained to use the global strategy Goal–Plan–Do–Check to develop a specific plan to improve performance of a self-selected goal, review performance, and modify the plan accordingly if performance is not satisfactory. This process is consistent with psychology theories of cognitive flexibility that describe cognitive flexibility as necessary to assess a situation when a nonroutine response is required, plan a new response or action to be taken, and use strategies to deal with the demands of the novel environment (Cañas, Quesada, Antolí, & Fajardo, 2003; Norman & Shallice, 1986). Therefore, the CO–OP process, in essence, helps to retrain cognitive flexibility in a way that usual care, which most likely focuses on remediation of habitual activities and function, does not. This effect could explain the gains in cognitive flexibility in the CO–OP group and the relative stability in such flexibility in the usual-care group. It is also consistent with at least one other study that has evaluated the use of key CO–OP components with people with stroke (Skidmore et al., 2014).

CO–OP has been found to have a medium effect over usual care on self-efficacy in ability to perform daily activities (McEwen et al., 2015). It can be postulated that this increase in self-efficacy leads to increased motivation to participate in everyday life activities and thereby increased use of the impaired upper extremity. This improvement in self-efficacy could also explain the differential effect on self-perception of function observed between the two groups. Regardless, the measurable effect of CO–OP over usual care provides preliminary evidence to support the use of CO–OP to improve occupational performance and remediate impairments in arm movement and cognitive flexibility. These results bring into question the continued clinical practice of focusing treatment on impairments with the hopes that reducing impairments will lead to meaningful occupational changes. The causal relationship between the effects observed remains unknown and is an area for future investigation.

This study has several limitations on the generalizability of the findings. First, all CO–OP participants were eligible to receive additional occupational therapy services after their completion of 10 CO–OP sessions. The majority of participants did receive additional usual-care occupational therapy services between the post-intervention and the follow-up assessment that could not be controlled for in the data analysis because of the relatively small sample. Although dosage data were collected and were comparable between groups, there were unequal numbers of sessions between sites. In addition, the content of these additional sessions is largely unknown and may have biased the results. These additional sessions may potentially be responsible for the decrease in the differential effect between CO–OP and usual care at follow-up.

Second, for unknown reasons, there were more dropouts between Time 2 and 3 in the usual-care group (i.e., 3 participants) than in the CO–OP group (i.e., 1 participant); therefore, effect sizes between Time 2 and Time 3 could not be directly compared. Third, this early-phase feasibility study had a small sample with the aim to identify within-group and between-groups effects on a wide range of outcomes. The study was not powered for hypothesis testing, and further research is required to confirm the effects found. Fourth, little information was available to evaluate what specifically constituted usual-care occupational therapy at each site. The study team was limited to self-report from the therapists and daily notes; however, these items were not sufficiently descriptive. Future studies will have to document and classify usual-care occupational therapy more thoroughly. Fifth, upper-extremity dysfunction was not a specified inclusion criterion for this study. Therefore, the final sample had unequal upper-extremity function between groups. A future study that targets upper-extremity function as a primary outcome will need to take this function into account in the design of the study.

Finally, the effect of the interventions on impairment remediation was considered a secondary outcome in this study. Therefore, data were limited to evaluate the effect of the interventions on impairment and function. Future studies should more thoroughly evaluate potential outcome measures to try to capture this effect with more sensitive and comprehensive tools.

Implications for Occupational Therapy Practice

This study's findings have the following implications for occupational therapy practice:

- CO–OP, a top-down performance-based approach, has a positive effect on performance and impairment reduction in this early-phase study.
- The generalizability of these findings is currently limited, and future research is necessary to confirm them.
- These findings call into question the continued use of impairment-based rehabilitation methods to improve occupational performance and reduce impairment after stroke.

Conclusion

CO–OP, a top-down intervention targeting performance, cognitive strategy use, and transfer and generalization has a measureable effect not only on performance but also on impairment reduction and stroke impact. Specifically, measurable effects of CO–OP were seen in cognitive flexibility, arm function, and most self-reported stroke impact domains compared with usual-care occupational therapy. This early-phase feasibility study provides support for the use of CO–OP over usual care; however, it has several limitations on generalizability of the results. Future investigation is warranted to confirm and expand these findings. ▲

Acknowledgments

This study was funded by a Canadian Institutes of Health Research Open Operating Grant (Funding Reference No. 111200) and was supported by the St. John's Rehab Hospital and The Rehabilitation Institute of St. Louis. The authors acknowledge the assistance of Alisa Grigorovich, Tanya Ramsey, Carin Roth, Tammy Craig, Kimberly Walker, and Duana Russell-Thomas and of the staff in the Performance, Participation, and Neurorehabilitation Laboratory in the Program in Occupational Therapy at Washington University in St. Louis in assessment, evaluation, and treatment. Sara

McEwen's salary support came from the St. John's Rehab Foundation. Timothy J. Wolf received salary support from the National Center for Medical Rehabilitation Research, National Institute of Child Health and Human Development, National Institutes of Health under award numbers K12HD055931 and K23HD073190. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Paper III: Cognitive-strategy training improves cognitive performance and neural connectivity in women with chemotherapy-induced cognitive impairment.

Cognitive-strategy training improves cognitive performance and neural connectivity in women with chemotherapy-induced cognitive impairment

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Abstract

Importance: One of the prevalent symptoms following treatment for breast cancer is chemotherapy-induced cognitive impairment (CICI), reported by 16-75% of breast cancer survivors. To date there is limited research to support best practice for how to assess and treat CICI.

Objective: To evaluate the effect of metacognitive strategy training (MCST) on cognitive performance and on neural connectivity in the frontal-parietal network in women with CICI following treatment for breast cancer.

Design: Single group, pre/post study was conducted. After completing the baseline assessment battery and neuroimaging, participants completed a 12-session MCST intervention. Following the completion of the intervention, subjects completed the same assessment battery and neuroimaging that was completed at baseline within four weeks post-intervention.

Setting: Academic medical center research facility.

Participants: Consecutive sampling of women seen at Siteman Cancer Center at Washington University School of Medicine in St. Louis, MO who met the initial key inclusion/exclusion criteria: completed chemotherapy for treatment for breast cancer, no other neurological or psychiatric diagnoses, self-reported CICI, and no contraindications for the use of MRI.

Intervention: The Cognitive-Orientation to daily Occupational Performance approach (CO-OP) is a MCST intervention that trains participants in the use of both global and domain specific strategies through the use of guided discovery. This process allows participants to develop their individualized plans for how to address their chosen activity-based goals. Sessions are 45-minutes in duration with a trained occupational therapist.

Main Outcomes and Measures: Subjective cognitive impairment: (1) the Cognitive Failures Questionnaire (CFQ); and (2) the Dysexecutive Syndrome Questionnaire (DEX). Objective cognitive impairment: the Delis-Kaplan Executive Function System (DKEFS) Trailmaking subtest.

Results: CO-OP had a small to large positive effect on all primary (cognitive) and secondary (quality of life and psychosocial) behavioral outcome measures (r = -.12 to -.88). There was also a positive change in functional connectivity in a frontal-parietal cognitive control network connection in 6 of the 10 subjects, which was correlated to changes on the behavioral measures.

Conclusions and Relevance: This study found that CO-OP was associated with a positive effect on cognitive performance and neural connectivity in women with CICI following treatment for breast cancer.

Introduction

Breast cancer is the most common malignancy in women with an estimated incidence of 234,840 in 2015, accounting for 29% of female cancer incidence in the United States.[1] The use of chemotherapy has led to significant improvements in survival in breast cancer patients[2,3] and is administered to the majority of patients with early stage disease to reduce the risk of recurrence.[4] In spite of the survival benefits, chemotherapy has been associated with decreased productivity, impaired community involvement, and poor role-functioning resulting from cognitive dysfunctions following treatment.[5-9] Cancer survivors have cognitive deficits in several domains after chemotherapy but most often in executive function (planning, problem solving, multitasking). Women with such executive function (EF) deficits following breast cancer treatment report changes in everyday life activities, such as work/productivity, community involvement, driving, and financial management.[5-9] These cognitive changes are referred to as chemotherapy-induced cognitive impairments (CICI) or “chemobrain.” The rate of CICI in the published literature ranges 16-75%.[10,11]

Clinically, executive function impairment related to CICI is most often identified using self-report measures and neuropsychological assessments; however, self-report measures do not provide an objective method to compare cognitive abilities between participants, and neuropsychological assessments have limited ability to capture real-world cognitive performance.[12-15] Non-invasive neuroimaging is a promising complementary assessment to identify deficits in EF associated with CICI and a relatively new neuroimaging method being used for this purpose is resting-state functional connectivity MRI (rs-fcMRI). During rs-fcMRI, intrinsic brain activity is imaged when subjects are at wakeful rest and not performing a task, to understand the functional organization of the brain.[16,17] Using rs-fcMRI, alterations in global and regional functional connectivity have been reported in breast cancer survivors.[18,19] Using rs-fcMRI, our research team recently found that breast cancer survivors who report CICI, compared to those who do not, show weaker functional connectivity between two regions of the frontal-parietal executive control network.[20] In addition, weaker functional connectivity correlated with greater levels of reported cognitive impairment.[20]

There are two common intervention approaches to address cognitive impairment: the compensation model and the restoration model.[21] The premise of restoration-based methods is that through repetitive practice of cognitive retraining activities, overall cognitive performance will improve.[21] Unfortunately, several studies suggest that this approach has little impact on everyday life performance.[22-24] In contrast to the restoration model, the compensation model includes interventions like metacognitive-strategy training (MCST). MCST interventions tend to be targeted at the performance and participation level to help participants improve/learn new skills to complete everyday life activities, and are usually delivered by occupational therapists. There is some existing evidence that suggests that MCST has more of a positive effect on EF impairments and performance than remediation/retraining-based approaches.[25] One of the concepts and theories driving MCST is experience-dependent neuroplasticity, which postulates that learning new skills leads to functional changes in the brain.[26] The MCST approach directly targets the action of the frontal-parietal network, a cognitive control network involved in flexible moment-to-moment task control that also reflects compositional coding to enable transfer of knowledge to novel tasks.[27-29] Given the results of our preliminary study that showed the negative impact of CICI on this frontal-parietal network and what is known about metacognitive-strategy training, the purpose of this study was to evaluate the effect of MCST on cognitive performance and on neural connectivity in the frontal-parietal network in women with CICI following treatment for breast cancer.

Methods

A single group, pre/post study was conducted. Participants were recruited from breast cancer patients in the clinical database at Washington University Faculty Practice Plan Division of Breast Oncology at Washington University in St. Louis. This study was reviewed and approved by the Washington University Human Research Protection Office (HRPO) and the Protocol Review Monitoring Committee (PRMC) at Siteman Cancer Center.

Participants

Participants were recruited from the Siteman Cancer Center at Washington University School of Medicine. **Inclusion criteria**: (1) females 35-70 years old; (2) self-reported CICI (Global Rating of Cognition dysfunction as “Moderately” “Strongly “or “Extremely” and a Cognitive Failures Questionnaire (CFQ) score >30); (3) completed adjuvant (or neoadjuvant) chemotherapy at least 6 months prior to participation; (4) able to read, write, and speak English fluently; (5) able to provide valid informed consent; (6) have a life expectancy of greater than 6 months at time of enrollment; (7) females diagnosed with breast cancer (invasive ductal or lobular BrCA Stages I, II, or III) and completed chemotherapy within the preceding two years; (8) on stable doses (i.e., no changes in past 90 days) of medications that are known to impact cognitive function (i.e., anti-depressants). **Exclusion criteria**: (1) prior cancer diagnoses of other sites with evidence of active disease within the past year; (2) active diagnoses of any acute or chronic brain-related neurological conditions that can alter normal brain anatomy or function (e.g., Parkinson’s disease, dementia, cerebral infarcts); (3) severe depressive symptoms (Personal Health Questionnaire (PHQ-9) score of ≥21); (4) history of traumatic brain injury; (5) weigh over 350 pounds (weight limit of MRI machine); (6) received skull-based radiation treatment within the past year for any reason; (7) implanted metal objects not compatible with MRI, electrodes, pacemakers, intracardiac lines, or medication pumps; (8) history of claustrophobia or inability to lie flat that will preclude undergoing MRI; (9) any medical condition which would render the study unsafe or not in the best interest of the participant; and (10) male gender. The clinical coordinators in the breast oncology division identified female breast cancer patients based on criteria related to age, diagnosis, co-morbidities, and language. The remaining inclusion/exclusion criteria were evaluated by the research coordinator.

No study of which we are aware has examined the effect of metacognitive strategy training for CICI at a brain network level of investigation. Therefore, effect sizes of alterations in cortical network correlations, which are required for sample size determination, are unknown. The purpose of this pilot study was to evaluate if MCST could have a measureable effect on subjective and objective cognitive performance and also on neural connectivity, as measured by resting state functional connectivity MRI. A sample of 14 participants was determined based on the experience of the research team as the minimum sample necessary in a repeated measures design to detect a change in signal in the neuroimaging data.

Assessment and Intervention Procedures

Breast cancer patients who received chemotherapy at Siteman Cancer Center at Washington University School of Medicine and met the inclusion/exclusion criteria for the study were identified and contact information was forwarded to our research team. Patients who were interested were asked to complete a screening battery over the phone or via a web-based survey to evaluate eligibility and identify if they have CICI (Global Rating of Cognition dysfunction as "Moderately" "Strongly "or "Extremely" and a Cognitive Failures Questionnaire (CFQ) score

>30). Study data were collected and managed using Research Electronic Data Capture (REDCap) tools hosted at Washington University in St. Louis.[30] REDCap is a mature, secure web-based application designed to support data capture for research studies.

Those patients with self-reported CICI were then scheduled for a face-to-face assessment to determine final eligibility. After providing informed consent, eligible patients were asked to complete the baseline assessment battery and were scheduled for the neuroimaging assessment. After completing the baseline assessment battery and neuroimaging, participants completed a 12-session metacognitive strategy training intervention with a trained occupational therapist. Each session lasted 45 minutes and the intervention was completed over the course of 12 to 14 weeks. Participants may have completed less sessions if they met their baseline goals before the completion of 12 sessions. Following the completion of the intervention, subjects completed the same assessment battery and neuroimaging that was completed at baseline within four weeks post-intervention.

Intervention Description: Cognitive Orientation to daily Occupational Performance (CO-OP)

CO-OP: A Metacognitive- Strategy Training Treatment Approach

Cognitive Orientation to daily Occupational Performance (CO-OP) is a metacognitive-strategy training treatment approach that incorporates both global and domain-specific cognitive strategies.[31] Complete details about the CO-OP approach have been previously published.[32] CO-OP has seven key features: cognitive strategy use, patient-chosen goals, dynamic performance analysis, guided discovery, enabling principles, parent/significant other involvement, and intervention format.[31] In the first meeting, the patient selects 3 activities to be the focus of treatment and baseline level of performance for each activity is established. In the second meeting, when CO-OP actually begins, the approach is introduced to the patient and the global cognitive strategy (GOAL-PLAN-DO-CHECK) is learned. In all subsequent sessions this strategy is used as the main problem-solving framework to facilitate skill acquisition. The patient identifies a **GOAL**, and then is guided by the therapist to develop his/her own **PLAN** to potentially achieve the goal. The client is then asked to **DO** the plan (if feasible during the therapy session otherwise asked to complete at home prior to the next treatment session), and subsequently to **CHECK** to see if the plan worked, i.e. the goal was achieved. If the goal was not achieved, as is often the case initially, the patient is guided to analyze what went wrong and modify the plan. Thereby, the lack of success is associated with the wrong plan, rather than a problem with his or her personal capacity. Throughout, the therapist actively seeks opportunities to promote generalization of skills and strategies to the natural environment and transfer to novel skills.

Behavioral Outcome Measures

All participants completed the baseline assessment (approximately 90 minutes) with a blind rater. This same assessment battery was used post-intervention. Table 1 below is an overview of all the behavioral outcome assessments. The primary outcome measures are subjective and objective measures of cognitive performance.

INSERT TABLE 1

Neuroimaging Outcome Measurement

Resting-state functional-connectivity MRI (rs-fcMRI) and anatomical images were collected using a Siemens 3T Tim Trio MRI scanner. The anatomical T1-weighted magnetization prepared rapid gradient echo (MP-RAGE) image was acquired across 176 sagittal slices (TR=2400ms; TE=3.09ms; flip angle=8°; inversion time [TI] =1000ms; 1 x 1 x 1 mm voxels). An asymmetric spin-echo echo-planar pulse sequence (EPI) (TR=2200ms, TE=27ms, flip angle=90°, 4x4x4 mm voxels) captured images of blood oxygenation level-dependent (BOLD) contrast responses across 36 odd-even, contiguously interleaved, bicommissurally aligned axial slices.[41,42] Three 164-frame (6 minute) EPI runs recorded spontaneous brain activity while participants are awake, not performing a task, with their eyes open in a darkened room.

Image Preprocessing

EPI image preprocessing started with compensation for systematic slice-dependent differences from interleaved odd-even slice acquisition and alignment of the time for each slice to the beginning of each volume acquisition using sinc interpolation. Next, corrections for intensity differences within runs utilized a whole brain mean signal intensity normalized to mode 1000. These time and intensity-adjusted slices were realigned within and across runs using rigid body correction for inter-frame head motion.[43-46] The across-run-realigned slices were resampled to $3mm^3$ voxels and registered to an atlas template by computing 12 parameter affine transforms between an average from the first frames of each EPI run and the atlas template using the individual's MP-RAGE image as an intermediary.[47] This atlas template was created using MP-RAGE structural images from 12 normal middle-age individuals (mean 48 yrs, SD $\pm$10.7) and registered to Talairach atlas space[48,49] based on spatial normalization methods.[50] Each subjects' second scan was cross-day realigned to the MP-RAGE of the first scan.

For rs-fcMRI analyses, additional preprocessing steps were applied in MATLAB (2012a, The Mathworks, Natick, MA) to reduce noise from sources unlikely to reflect neural activity.[51] These steps included demeaning and detrending each BOLD run, temporal filtering with a bandpass filter to remove frequencies <0.009Hz and >0.08Hz, and spatial smoothing with a 6 mm full width at half-maximum Gaussian kernel. Using linear regression, BOLD signal per voxel was adjusted for 24 motion-related and 6 tissue-related sources of nuisance variance. The motion regressors are the six previously computed linear corrections for head movement, their squares, and the same for the immediately preceding timepoint, as derived by Volterra expansion.[32] The tissue-related regressors were a global whole-brain signal averaged over all voxels, signals in the ventricles and white matter, and their associated temporal derivatives.[52] The subject's own anatomy, as segmented using Freesurfer version 5,[53] was used for whole-brain, ventricle, and white matter masks.[44,45,54,55] We applied a volume censoring method, [51] which removed frames of data with >.3mm of frame by frame displacement (FD), as well as episodes with fewer than 5 contiguous frames with <.3mm FD.[56] In addition, BOLD runs with fewer than 30 frames meeting these requirements were eliminated. Only the 10 subjects with 119 or more frames of good data in both scans were retained for analysis. Spatial smoothing and temporal filtering as well as nuisance variable regression were repeated on the original preprocessed data, leaving out the censored frames and interpolating across the gap.[57] Since the motion-correction parameters used are more lenient than recommended, we plotted the difference between scan days in each region pair correlation versus the distance between regions for 264 regions sampling the entire brain[16] to check for the distance-dependent artifact often caused by even sub-millimeter head motion.[51,58]

Analysis

Behavioral data analysis was conducted using SPSS version 20.[59] The data were cleaned and checked for accuracy. Distribution of the scores for each of the tests pre-intervention and post-intervention were described using median and range. The difference between pre-post test scores was calculated for each subject for each test. Median of the difference and 95% CI interval was calculated using Student version of MINITAB® Release 14.11.1. Wilcoxon signed rank test was used to test for significant differences in pre-post test scores. Non-parametric effect size (r) calculations were also performed on the behavioral data.

For neuroimaging data analysis, timecourses were calculated for each subject and each scan for the two frontoparietal control regions which showed a difference between impaired and non-impaired breast cancer survivors[20] (see eFigure 1), and also for 264 regions covering the brain.[16] Fisher z-transformed Pearson correlation coefficients calculated between two region's timecourses in a single scan serve as a measure of functional connectivity between them. The Fisher z-transform normalizes the distribution of values, to satisfy the assumptions of the Student's t-test and comparisons using the Gibbs distribution. Functional connectivity across the brain was compared between days using Object Oriented Data Analysis (OODA),[60] which uses an iterative approach and comparison to the Gibbs distribution to assess the significance of differences found in a multiple dimensional approach. Pearson correlations were also calculated to evaluate the relationship between the changes in functional connectivity in the previously reported connection[20] and changes in the behavioral outcome measures.

INSERT eFIGURE 1

Results

Participants Results

Our sample is described in the table below (see Table 2). Overall, our sample was fairly young, well-educated, mostly Caucasian, and mostly working full-time during their participation in this study. The median time duration since completion of chemotherapy was slightly less than 12 months.

INSERT TABLE 2 HERE

Behavioral Results

Table 3 displays distribution of the data for the behavioral outcome measures as well as distribution of the difference of the scores pre-intervention as compared to post intervention. The results show that CO-OP had a medium to very large effect on all the primary and secondary behavioral outcome measures in our sample (n = 14).

INSERT TABLE 3 HERE

Given the limited sample size, the individual effect of the intervention on the CFQ was also qualitatively evaluated and plotted in a bar graph in eFigure 2. As depicted in eFigure 2, there was evident variation in terms of response to the CO-OP intervention on this subjective outcome measure; however the majority of the participants had improvements on their subjective score on the CFQ (positive change on the CFQ indicated improved cognitive function).

INSERT eFIGURE 2 HERE

Neuroimaging Results

Ten of the 14 subjects had a sufficient number of good frames of MRI data in both before and after treatment scans to be analyzed further. The amount of data kept did not differ between the two scans (paired t-test p=.59). The plot of change in functional connectivity between scans vs the distance between regions for the 264 regions showed no distance dependent artifact, justifying the use of slightly relaxed motion parameters to include more subjects.

Using object oriented data analysis (OODA)[60] for comparing subjects before and after treatment across all 264 regions was not sensitive enough to detect a difference in functional connectivity (p=.79). However, a one-tailed, paired t-test on the connection between the two frontal parietal control regions previously described[20] showed trend level significance (p=.054), demonstrating the expected increase in functional connectivity strength after treatment in 6 of the 10 subjects, and minimal decreases in 3 others (see Figure 1).

INSERT FIGURE 1

The difference, post-intervention minus pre-intervention, in two behavioral assessments correlated well with the change in connection strength between the frontal-parietal (FP) regions evaluated. The change in Personal Health Questionaire (PHQ-9), a quick screening tool for depression, explained 35% of the difference in connection strength (p=0.057), while the change in the Trailmaking subtest of the Delis-Kaplan Executive Function System (DKEFS), a measure of EF, explained 26% of the change in connection strength (p=0.108) (see Figure 2).

INSERT FIGURE 2

Discussion

The results from this study suggest that the use of CO-OP is feasible with this population and has a positive effect on improving subjective and objective cognitive performance, subjective activity performance, and quality of life. Further, we were able to detect a positive change in functional connectivity in the one frontal-parietal cognitive control brain network connection previously reported[20] and this change was correlated with changes on the behavioral measures. The results from the study are consistent with previous work using CO-OP with individuals with cognitive deficits following stroke that found positive changes in activity performance and satisfaction[25] and also changes in objective cognitive performance.[61] This study however is the first to evaluate the effect on a particular brain system, i.e., the frontal-parietal cognitive control network, of using CO-OP to address CICI. Given the limitations in how EF is often measured clinically, these data provide support for continued investigation into the use of functional neuroimaging as an objective way to assess mechanistic changes in higher-level cognitive function in women with CICI.

An important strength of the study is its repeated measures, within patient design. However, the study had several limitations. First, while a single group pre/post study was appropriate for this early-stage investigation, the lack of an active control group for comparison limits the ability to conclude the changes we observed were due to the intervention and not due to other non-specific effects of CO-OP. The next phase of this investigation should include an active control group to confirm the effects identified in this study were due to the CO-OP intervention. Second, the sample had substantial heterogeneity in terms of age, time since completion of chemotherapy, and differences in response to the intervention on both the behavioral and neuroimaging measures. As shown in Figure 1, some individuals had over a 30-point reduction in reported cognitive problems after the intervention while one person actually had a 4-point increase in reported cognitive problems. The present study provides information to inform the sample size for future studies, which must enroll sufficient number of subjects to control for resonse differences and better identify the responders vs. the non-responders to the intervention. Finally, while functional neuroimaging was able to detect a positive change in functional connectivity in 6 of the 10 subjects, the use of resting-state functional connectivity as an outcome measure was exploratory and needs considerable further investigation to evaluate its utility as a measure of the mechanistic action of CO-OP.

While there are several methodological and design limitations of this pilot study, these results do support the continued investigation of CO-OP for women with cognitive impairment after chemotherapy for breast cancer. Future studies need to investigate the findings of this study with an active control group and an attempt to control for the confounding factors, e.g., hormonal treatment, different chemotherapy treatment regimens, etc., that may have influenced the results of this study. Overall, this study found that the use of a metacognitive strategy training intervention (CO-OP) is associated with a positive effect on patient outcomes and functional connectivity in a cognitive control network previously demonstrated to be negatively impacted after chemotherapy for breast cancer.[20]

Acknowledgements

This study was funded by the McDonnell Center for Systems Neuroscience, Washington University Institute of Clinical and Translational Sciences grant UL1TR000448 from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH) and the Mallinckrodt Institute of Radiology at the Washington University School of Medicine. Research reported in this publication was also supported by the Eunice Kennedy Shriver National Institute Of Child Health & Human Development of the National Institutes of Health under Award Number U54HD087011 to the Intellectual and Developmental Disabilities Research Center at Washington University. TW received salary support from the National Center for Medical Rehabilitation Research (NCMRR) in the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) of the National Institutes of Health under award number K23HD073190. The electronic databased system used in this publication, RedCap, is also supported by the National Institutes of Health Clinical and Translational Science Award (CTSA) Grant UL1 TR000448 and Siteman Comprehensive Cancer Center and the National Cancer Institute (NCI) Cancer Center Support Grant P30CA091842. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors would also like to thank the faculty, staff, and students in the Performance, Participation, and Neurorehabilitation Laboratory.

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Table 1. Baseline Assessment Battery

Measures	Description
	Primary Outcome Measures
Cognitive Failures Questionnaire (CFQ)[33]	CFQ measures subjective lapses in motor function, memory, and perception. This questionnaire contains 25 items and scores range from 0 to 100.
Dysexecutive Questionnaire (DEX)[34]	The DEX is a subjective 20-item questionnaire that asks about behavioral changes associated with having executive dysfunction.
Delis-Kaplan Executive Function System (DKEFS)[35]	The DKEFS is the only objective scaled EF battery available. The DKEFS has 9 stand-alone tests; The Trailmaking Condition 4 subtest score was used.
	Secondary Outcome Measures
PROMIS-57 Profile v1.0[36]	The PROMIS is a patient reported outcomes measure that will be used to assess changes in physical function, fatigue, and satisfaction with social roles,
Canadian Occupational Performance Measure (COPM)[37]	The COPM is used to detect change in performance of tasks by measuring the clients' perceived performance and satisfaction with their level of participation.
Personal Health Questionnaire (PHQ-9)Depression[38]	The PHQ-9 is a quick screening tool for depression that has been used in research and clinical settings to screen for depressive symptoms.
Montreal Cognitive Assessment (MOCA)[39]	The MOCA is a publically-available cognitive screening tool to screen for dementia.
Self-Efficacy Gauge (SEG)[40]	SEG measures an individual's confidence in everyday life activities.

Table 2: Study sample characteristics (n = 14)

Variable	**Median (Min-Max) or Percentage**
Age (Years)	50.50 (36 to 65)
Time since completion of chemotherapy (months)	9.5 (7 to 34)
	n (%)
Race	
Caucasian	12 (86%)
African American	1 (7%)
Asian	1 (7%)
Highest level of education	
High School or Associate Degree	2 (14%)
Bachelor’s Degree	3 (21%)
Master’s or Doctoral Degree	9 (65%)
Work Status	
Full-time	12 (86%)
Part-time	1 (7%)
Retired	1 (7%)

Table 3: Behavioral Outcomes

Assessment	Pre-Score Median (Min-Max)	Post-Score Median (Min-Max	Median of difference (pre-post) (95%CI)	Effect size (r)[b]	Interpretation
			Primary Outcome Measures		
Cognitive Failures Questionnaire (CFQ)	50 (39-68)	36 (15-49)	15 (8.9 to 25.2)[a]	-.85	Significant decrease in subjective cognitive symptoms
Delis-Kaplan Executive Function System (DKEFS)	12 (1-13)	12 (7-14)	-1 (-2.1 to 0)[a]	-.50	Significant improvement in objective EF (cognitive flexibility)
Dysexecutive Questionnaire (DEX)	23 (3-39)	11 (0-33)	9 (4 to 16)[a]	-.75	Significant improvement in subjective executive performance
			Secondary Outcome Measures		
Montreal Cognitive Assessment (MOCA)	28 (21-30)	28 (21-30)	0(-1.05 to 0.05)	-.28	Stable general cognitive function
The Canadian Occupational Performance Measure (COPM)	4.8 (2.6-7.3)	7.7 (5.8-9.7)	-3 (-3.3 to -1.6)[a]	-.88	Significant improvement in self-rated performance of activities
	2.8 (1.4-5.5)	8.0 (3.5-10.0)	-4.5 (-5.3 to -3.3)[a]	-.88	Significant improvement in self-rated satisfaction with performance of activities
Personal Health Questionnaire (PHQ-9)-Depression	6.5 (1-13)	4.5 (0-11.0)	1.5 (0.9 to 4.1)	-.53	Decrease in depressive symptoms approaching significance
NIH-PROMIS 57-Physical Function	25.8 (20.2-37.5)	24.7 (20.2-32.7)	3.6 (2.9 to 4.8)[a]	-.88	Significant improvement in self-reported physical function
NIH-PROMIS 57-Anxiety	53.8 (37.1-61.4)	45.9 (37.1-61.4)	0 (-0.1 to 9.0)	-.65	Decrease in reported anxiety symptoms
NIH-PROMIS 57-Depression	44.7 (38.2-59.4)	44.7 (38.2-56.8)	2.3 (0 to 9.3)	-.53	Decrease in reported depression symptoms
NIH-PROMIS 57-Fatigue	51.5 (41.1-65.3)	52.0 (33.1-58.5)	7.9 (1.6 to 10.7)[a]	-.70	Significant decrease in fatigue symptoms
NIH-PROMIS 57-Sleep Function	50.2 (30.5-63.0)	49.0 (30.5-63.0)	0 (-2.9 to 5.3)	-.12	No change in sleep function
NIH-PROMIS 57-Satisfaction with Participation in Social Roles	45.3 (37.7-65.6)	53.4 (41.0-65.6)	-3.8 (-10.0 to 0)[a]	-.67	Significant improvement in satisfaction with participation
NIH-PROMIS 57-Pain Interference	48.9 (40.7-62.8)	56.6 (40.7-67.7)	-1.25 (-15.9 to 3.5)	-.30	Increase in pain interference

[a] Wilcoxon signed rank test, $p < .05$

[b] Effect Size r: .1, small effect; .3 medium effect; .5 large effect

Figure 1. Connection strength before and after treatment

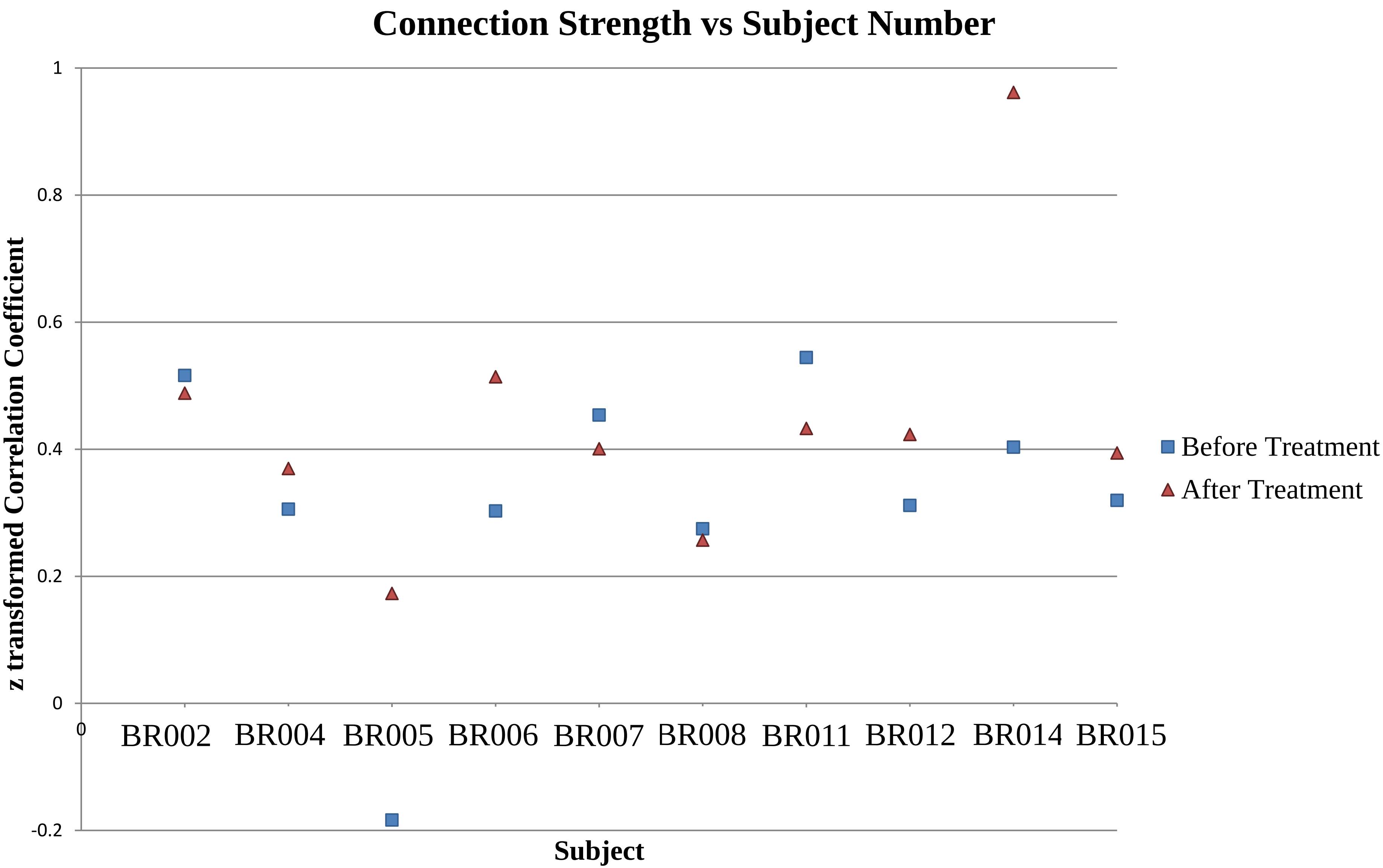
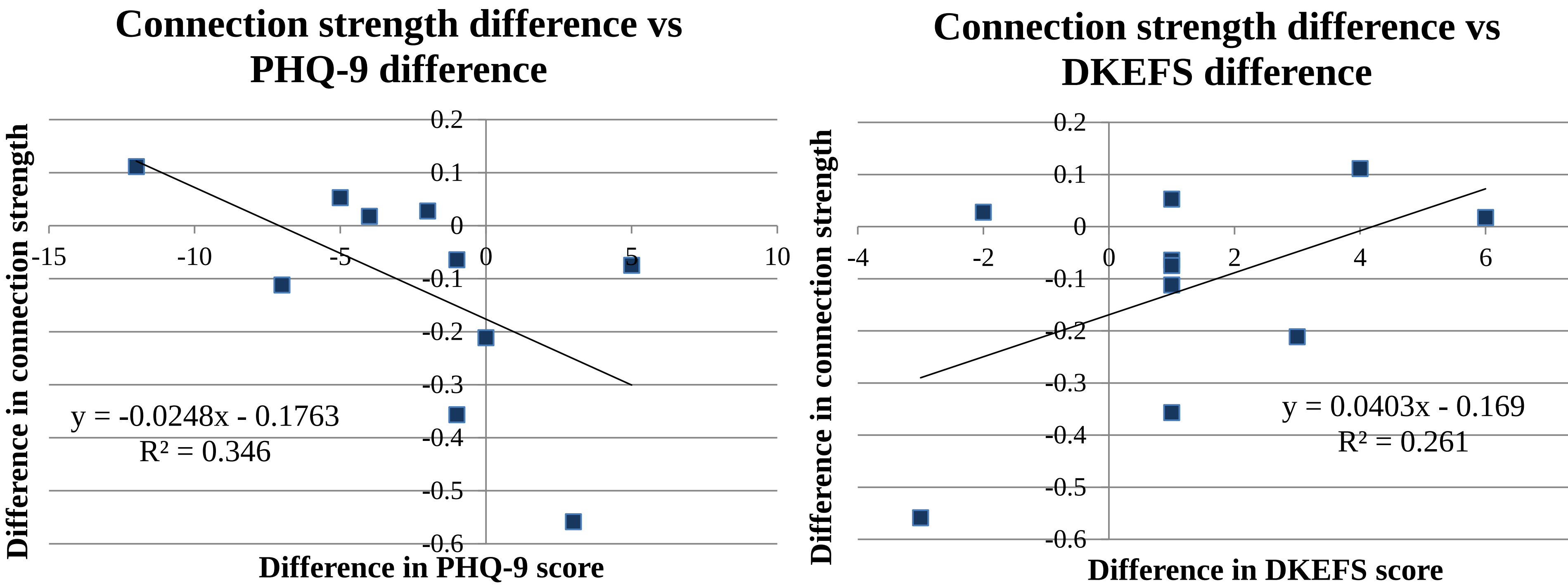
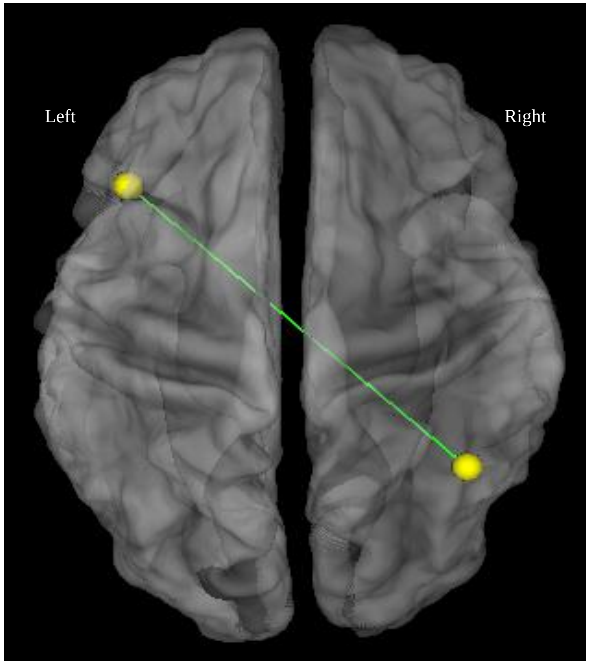
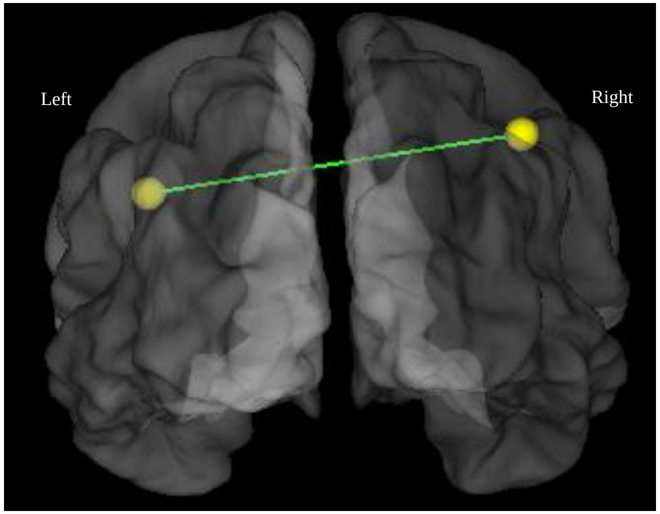


Figure 2. Change in connection strength correlates with change in behavioral measures.

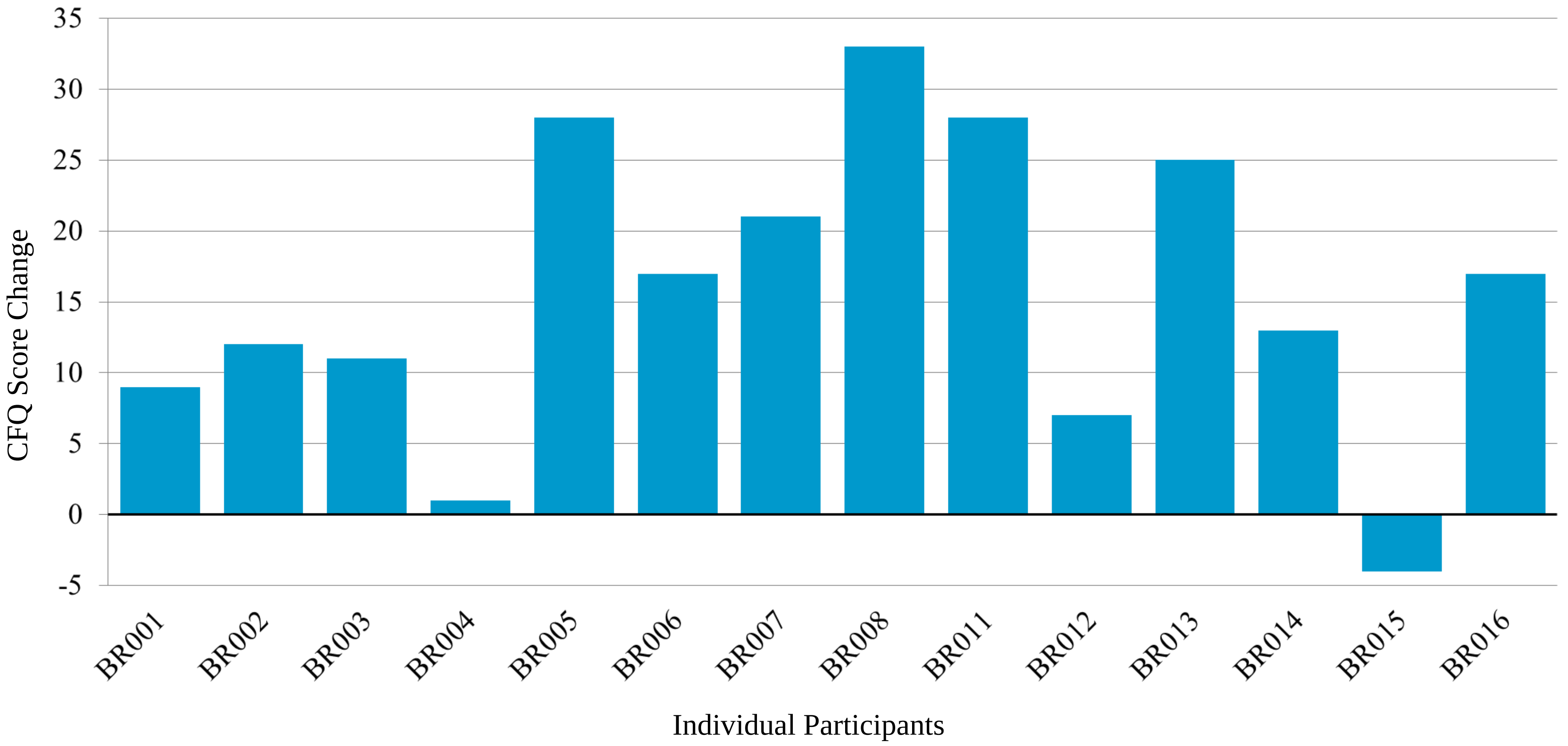


eFigure 1. Bilateral Connection between Frontoparietal Regions





eFigure 2. Change in CFQ Score Pre/Post



Measures

The following measures were used in the studies in this dissertation. These measures that have been included below are only the measures which are publically available which constitutes the vast majority of the outcome measures in this dissertation. The measures are included in alphabetical order; the information related to which measures were primary/secondary in each study can be found in the methods section.

Action Arm Research Test (ARAT)

Participant ID # ____________ Test Time ___________ Tester Initials ___________

Date ___________

ACTION RESEARCH ARM TEST								
	Left				Right			
A. Subtest Grasp								
1. 4” block (if score is 3 then score 3 throughout subtest)	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
2. 1” block (if 0 on #1 & 0 here, score 0 throughout)	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
3. 2” block	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
4. 3” block	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
5. 3” ball	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
6. Stone	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
TOTAL FOR GRASP								
B. Subtest Grip								
1. Pour water glass to glass (if a score of 3 is obtained then score 3 throughout)	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
2. 1” tube	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
3. 1 cm tube	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
4. washer over bolt	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
TOTAL FOR GRIP								
C. Subtest Pinch								
1. Lift ball bearing with ring finger and thumb (if a score of 3 is obtained, score 18 for that UE)	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
2. Lift marble with index finger and thumb	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
3. Lift ball bearing with long finger and thumb	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
4. Lift ball bearing with index finger and thumb	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
5. Lift marble with ring finger and thumb	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
6. Lift marble with long finger and thumb	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
TOTAL FOR PINCH								
D. Subtest Gross Movement								
1. Place hand behind head (if score a 3 on this item, a total score of 9 is given)	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
2. Place hand on top of head	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
3. Bring hand to mouth	0 ☐	1 ☐	2 ☐	3 ☐	0 ☐	1 ☐	2 ☐	3 ☐
TOTAL FOR GROSS MOVEMENT								
TOTAL ARA SCORE								

3: Performs test normally
2: Completes test but has great difficulty, does not apply coordinated movement pattern
1: Performs test partially
0: Cannot perform any part of the test

Cognitive Failures Questionnaire (CFQ)

Cognitive Failures Questionnaire

Participant Study ID ______________________

Do you read something and find you haven't been thinking about it and must read it again?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you find you forget why you went from one part of the house to the other?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you fail to notice signposts on the road?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you find you confuse right and left when giving directions?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you bump into people?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you find you forget whether you've turned off a light or a fire or locked the door?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you fail to listen to people's names when you are meeting them?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you say something and realize afterwards that it might be taken as insulting?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you fail to hear people speaking to you when you are doing something else?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you lose your temper and regret it?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you leave important letters unanswered for days?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you find you forget which way to turn on a road you know well but rarely use?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you fail to see what you want in a supermarket (although it's there)?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you find yourself suddenly wondering whether you've used a word correctly?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you have trouble making up your mind?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you find you forget appointments?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you forget where you put something like a newspaper or a book?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you find you accidentally throw away the thing you want and keep what you meant to throw away - as in the example of throwing away the matchbox and putting away the used match in your pocket?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you daydream when you ought to be listening to something?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you find you forget people's names?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you start doing one thing at home and get distracted into doing something else (unintentionally)?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you find you can't quite remember something although it's "on the tip of your tongue'?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you find you forget what you came to the shops to buy?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you drop things?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

Do you find you can't think of anything to say?

☐ Very often ☐ Quite often ☐ Occasionally ☐ Very rarely ☐ Never

---

Global Rating of Cognition When answering this next question think how things are now compared to before you started chemotherapy.

Many cancer patients who receive chemotherapy experience changes in thinking, memory, and/or decision making. When thinking back to before you had chemotherapy, please indicate how much you think chemotherapy has affected your ability to function from day-to-day.
(select the answer that best describes you the last two weeks.)

☐ Not at all
☐ Slightly
☐ Moderately
☐ Strongly
☐ Extremely

Community Participation Indicators (CPI)

Community Participation Indicators

This survey is voluntary. If you choose to participate, your information will be kept private. Your name will never be linked to any of the information you share.

Shade circles like this: ●
Not like this:

The statements below describe many of the ways that people participate in society. For each item, tell us:

1) How often you do the activity,
2) If the activity is important to you, and
3) If you feel you are doing the activity enough, too much, or not enough.

1. How often? --> 2. Important? --> 3. Doing enough?

In a typical week, how many days do you:	None	1-2 Days	3-4 Days	5-6 Days	7 Days	Is this activity important to you? No	Yes	Are you doing this activity: Enough	Not Enough	Too Much
Get out and about	○	○	○	○	○	○	○	○	○	○
Spend time with family	○	○	○	○	○	○	○	○	○	○
Keep in touch with family by phone or Internet	○	○	○	○	○	○	○	○	○	○
Spend time with friends	○	○	○	○	○	○	○	○	○	○
Keep in touch with friends by phone or Internet	○	○	○	○	○	○	○	○	○	○
Go to parties, out to dinner, or other social activities	○	○	○	○	○	○	○	○	○	○
Spend time with a significant other or intimate partner	○	○	○	○	○	○	○	○	○	○

33968

Community Participation Indicators

CaseId #

Shade circles like this: ●
Not like this: ⊠ ⊘

For each item, tell us:

1) How often you do the activity,
2) If the activity is important to you, and
3) If you feel you are doing the activity enough, too much, or not enough.

1. How often? --> 2. Important? --> 3. Doing enough?

In a typical week, how many hours do you:	None	1-4 Hours	5-9 Hours	10-19 Hours	20-34 Hours	35 or more Hours	Is this activity important to you? No	Yes	Are you doing this activity: Enough	Not Enough	Too Much
Work for money	O	O	O	O	O	O	O	O	O	O	O
Cook, clean, and look after your home	O	O	O	O	O	O	O	O	O	O	O
Manage household bills and expenses	O	O	O	O	O	O	O	O	O	O	O
Look after children or provide care for a loved one	O	O	O	O	O	O	O	O	O	O	O
Go to classes or participate in learning activities	O	O	O	O	O	O	O	O	O	O	O
Volunteer	O	O	O	O	O	O	O	O	O	O	O

33968

Shade circles like this: ●
Not like this:

For each item, tell us:

1) How often you do the activity,
2) If the activity is important to you, and
3) If you feel you are you are doing the activity enough, too much, or not enough.

1. How often? --> 2. Important? --> 3. Doing enough?

In a typical month, how many times do you:	None	Once	2 Times	3 Times	4 Times	5 or More Times	Is this activity important to you? No	Yes	Are you doing this activity: Enough	Not Enough	Too Much
Participate in religious or spiritual activities	○	○	○	○	○	○	○	○	○	○	○
Go to support groups or self-help meetings	○	○	○	○	○	○	○	○	○	○	○
Engage in hobbies or leisure activities	○	○	○	○	○	○	○	○	○	○	○
Go to movies, sporting events or entertainment events	○	○	○	○	○	○	○	○	○	○	○
Exercise, participate in sports or active recreation	○	○	○	○	○	○	○	○	○	○	○
Participate in community clubs or organizations	○	○	○	○	○	○	○	○	○	○	○
Participate in civic or political activities	○	○	○	○	○	○	○	○	○	○	○

33968

Shade circles like this: ●
Not like this:

Please mark the choice that most closely reflects your opinion:

	All the time	Frequently	Sometimes	Seldom	Almost never
1. I live my life the way that I want	○	○	○	○	○
2. People try to put limits on me	○	○	○	○	○
3. I participate in a variety of activities	○	○	○	○	○
4. I am uncomfortable participating in community activities	○	○	○	○	○
5. I spend time doing things that improve my community	○	○	○	○	○
6. I participate in activities that I choose	○	○	○	○	○
7. I spend time helping others	○	○	○	○	○
8. I count as a person in society	○	○	○	○	○
9. I have the freedom to make my own decisions	○	○	○	○	○
10. I live my life fully	○	○	○	○	○
11. I regularly seek out new challenges	○	○	○	○	○
12. I have reliable access to a telephone	○	○	○	○	○
13. I have a say on decisions in my community	○	○	○	○	○
14. I have choices about the activities I do	○	○	○	○	○
15. I actively pursue my dreams and desires	○	○	○	○	○
16. I do things that are important to me	○	○	○	○	○
17. People have high expectations of me	○	○	○	○	○
18. I am able to go out and have fun	○	○	○	○	○
19. I contribute to society	○	○	○	○	○
20. I have opportunities to make new friends	○	○	○	○	○
21. I speak up for myself	○	○	○	○	○
22. People speak to me disrespectfully	○	○	○	○	○
23. I take responsibility for my own life	○	○	○	○	○
24. I have good job opportunities	○	○	○	○	○
25. People underestimate me	○	○	○	○	○

CaseId #

Shade circles like this:
Not like this:

Please mark the choice that most closely reflects your opinion:

	All the time	Frequently	Sometimes	Seldom	Almost never
26. I assume leadership roles in organizations	○	○	○	○	○
27. I am welcome in my community	○	○	○	○	○
28. I am treated equally	○	○	○	○	○
29. I have reliable access to community services	○	○	○	○	○
30. I do important things with my life	○	○	○	○	○
31. My community respects me the way that I am	○	○	○	○	○
32. I have influence in my community	○	○	○	○	○
33. I am in control of my own life	○	○	○	○	○
34. I am ignored	○	○	○	○	○
35. I feel safe participating in community activities	○	○	○	○	○
36. I am treated as a valued member of society	○	○	○	○	○
37. People see my potential	○	○	○	○	○
38. I have access to reliable transportation	○	○	○	○	○
39. I have reliable access to the Internet	○	○	○	○	○
40. I have control over how I spend my time	○	○	○	○	○
41. People listen to what I say	○	○	○	○	○
42. I participate in activities when I want	○	○	○	○	○
43. I am uncomfortable participating in public meetings	○	○	○	○	○
44. I am treated like a human being	○	○	○	○	○
45. People count on me	○	○	○	○	○
46. I contribute to the well-being of my community	○	○	○	○	○
47. I am actively involved in my community	○	○	○	○	○
48. It is hard for me to get information about community services	○	○	○	○	○

25944

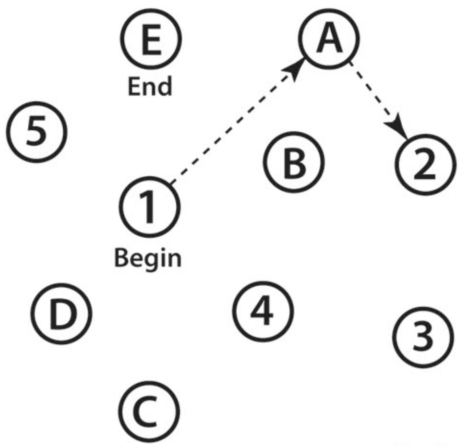
Montreal Cognitive Assessment (MOCA)

NAME :
Education : **Date of birth :**
Sex : **DATE :**

MONTREAL COGNITIVE ASSESSMENT (MOCA)

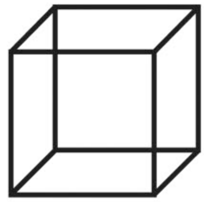
Version 7.1 Original Version

		POINTS
VISUOSPATIAL / EXECUTIVE		



[ ]

Copy cube



[ ]

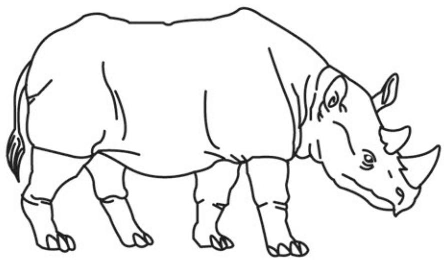
Draw CLOCK (Ten past eleven)
(3 points)

[ ] Contour [ ] Numbers [ ] Hands

___/5

NAMING

[ ]



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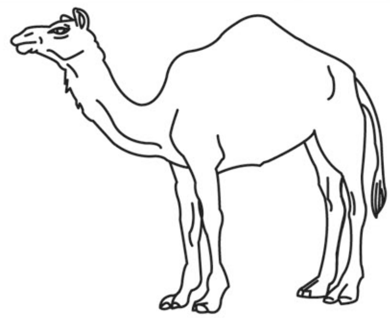

[ ]

___/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2

___/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

___/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

___/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ]

___/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

___/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

___/2

DELAYED RECALL	Has to recall words **WITH NO CUE**	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only	___/5
Optional	Category cue							
	Multiple choice cue							

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

___/6

 www.mocatest.org Normal ≥26 / 30

TOTAL ___/30

Add 1 point if ≤ 12 yr edu

Administered by: ______________________________

Participation Strategies Self-Efficacy Scale (PS-SES)

4. Participation Strategies

This questionnaire is designed to help us get a better understanding of how confident you are in strategizing your participation in home, community, and work activities.

Not at all confident | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Totally confident

Home	
Using a scale of 1 to 10, how confident are you that you…	**Confidence**
1. can stay in your home as you age and prevent nursing home placement.	
2. can adapt your home environment to stay safe and active in it. (e.g., modifying your bathroom, installing grab bars, avoiding clutter)	
3. can access and use adaptive equipment. (e.g., getting a tub bench, using a reacher)	
4. can adapt home activities so you can do what you want/need to. (e.g., prioritizing, organizing, scheduling)	
5. can access and use resources/ information to stay in your home and living in the community of choice. (e.g., resources for home modification)	
6. can access services to help you stay in home. (e.g., home maker, meals on wheels, personal assistant)	
7. can strategize long term income support. (e.g., SSI, SSDI, work compensation)	
8. can organize and keep track of finances and bill payments.	
9. can use strategies to keep track of appointments or to remember to do things. (e.g., using calendars or daily weekly planners, using timers or alarms, to-do lists, or post notes)	
10. can use strategies to find things easier in your home (e.g., labeling, putting things back where they were)	
11. create a home workstation to be organized	
12. can deal with changes in your health or life. (e.g., another stroke, new conditions, moving)	
Community Participation	
13. keep participating in activities of choice as you age.	
14. feel comfortable with going to places you want to go.	
15. can plan ahead to do what you want to do in the community.	
16. can arrange transportation options. (e.g., adaptive driving, private/public transportation, paratransit)	
17. can strategize falling or fear of falling in the community.	
18. can strategize fatigue and find your way to save your energy.	
19. can handle issues as they happen in the community.. (e.g., dealing with weather, crowd, emergency)	
can find your way around in the community. (e.g., using a map)	

Using a scale of 1 to 10, how confident are you that you…	Confidence
20. can access services or agencies to help you participate in the community.	
21. can ask for ways to make your community accessible to you. (e.g., talking to store/restaurant manager and request accessible entrances)	
Work/Volunteer	
22. can find new or alternative job/volunteer opportunities that match your strengths and interest.	
23. Identify what you need in order to go back to work/ volunteer.	
24. can identify disability issues and handle those when you apply for your job or volunteer position. (e.g., disclose your disability, know what can/can't be asked)	
25. can identify essential job functions	
26. can identify ways to modify your work setting so you can do your job effectively. (e.g., making an accessible work station, using equipment or software)	
27. can identify ways to adapt policies so you can do your job. (e.g., scheduling breaks, job sharing, telecommuting)	
28. can request and negotiate reasonable accommodations.	
Communication	
29. can effectively communicate with someone.	
30. can ask for help from family/friends without feeling like a burden.	
31. can speak up for yourself when communicating with family/friends.	
32. can communicate your concerns with family/friends who overprotect you.	
33. can deal with someone who disrespects you.	
34. can advocate for yourself so that people don't take advantage of you.	
35. feel comfortable communicating with people in public. (e.g., order from a menu, ask for directions)	
36. can set up strategies for other people to check on you and for you to check on others.	

Patient Health Questionnaire 9-item (PHQ-9)

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME: ____________________ DATE: ____________

Over the last *2 weeks,* how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so figety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3
	add columns	____ +	____ +	____

(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card). TOTAL: ____________

10. If you checked off *any problems,* how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all ________ Somewhat difficult ________ Very difficult ________ Extremely difficult ________

A2663B 10-04-2005

PHQ-9 Patient Depression Questionnaire

For initial diagnosis:

1. Patient completes PHQ-9 Quick Depression Assessment.
2. If there are at least 4 ✓s in the shaded section (including Questions #1 and #2), consider a depressive disorder. Add score to determine severity.

Consider Major Depressive Disorder

- if there are at least 5 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Consider Other Depressive Disorder

- if there are 2-4 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Note: Since the questionnaire relies on patient self-report, all responses should be verified by the clinician, and a definitive diagnosis is made on clinical grounds taking into account how well the patient understood the questionnaire, as well as other relevant information from the patient.
Diagnoses of Major Depressive Disorder or Other Depressive Disorder also require impairment of social, occupational, or other important areas of functioning (Question #10) and ruling out normal bereavement, a history of a Manic Episode (Bipolar Disorder), and a physical disorder, medication, or other drug as the biological cause of the depressive symptoms.

To monitor severity over time for newly diagnosed patients or patients in current treatment for depression:

1. Patients may complete questionnaires at baseline and at regular intervals (eg, every 2 weeks) at home and bring them in at their next appointment for scoring or they may complete the questionnaire during each scheduled appointment.
2. Add up ✓s by column. For every ✓: Several days = 1 More than half the days = 2 Nearly every day = 3
3. Add together column scores to get a TOTAL score.
4. Refer to the accompanying **PHQ-9 Scoring Box** to interpret the TOTAL score.
5. Results may be included in patient files to assist you in setting up a treatment goal, determining degree of response, as well as guiding treatment intervention.

Scoring: add up all checked boxes on PHQ-9

For every ✓ Not at all = 0; Several days = 1;
More than half the days = 2; Nearly every day = 3

Interpretation of Total Score

Total Score	Depression Severity
1-4	Minimal depression
5-9	Mild depression
10-14	Moderate depression
15-19	Moderately severe depression
20-27	Severe depression

A2662B 10-04-2005

Patient Reported Outcomes Measurement Information System-57 item (PROMIS-57)

PROMIS–57 Profile v1.0

Please respond to each question or statement by marking one box per row.

		Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
1	Are you able to do chores such as vacuuming or yard work?..........................	☐	☐	☐	☐	☐
2	Are you able to go up and down stairs at a normal pace?	☐	☐	☐	☐	☐
3	Are you able to go for a walk of at least 15 minutes?	☐	☐	☐	☐	☐
4	Are you able to run errands and shop?.......	☐	☐	☐	☐	☐
		Not at all	**Very little**	**Somewhat**	**Quite a lot**	**Cannot do**
5	How much do physical health problems now limit your usual physical activities (such as walking or climbing stairs)?.........	☐	☐	☐	☐	☐
6	Does your health now limit you in doing moderate work around the house like vacuuming, sweeping floors or carrying in groceries?	☐	☐	☐	☐	☐
7	Does your health now limit you in lifting or carrying groceries?...............................	☐	☐	☐	☐	☐
8	Does your health now limit you in doing heavy work around the house like scrubbing floors, or lifting or moving heavy furniture?.......................................	☐	☐	☐	☐	☐
	In the past 7 days…	**Never**	**Rarely**	**Sometimes**	**Often**	**Always**
9	I felt fearful..	☐	☐	☐	☐	☐
10	I found it hard to focus on anything other than my anxiety	☐	☐	☐	☐	☐
11	My worries overwhelmed me....................	☐	☐	☐	☐	☐
12	I felt uneasy	☐	☐	☐	☐	☐
13	I felt nervous...	☐	☐	☐	☐	☐
14	I felt like I needed help for my anxiety	☐	☐	☐	☐	☐
15	I felt anxious...	☐	☐	☐	☐	☐

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	In the past 7 days…	Never	Rarely	Sometimes	Often	Always
16	I felt tense	☐	☐	☐	☐	☐

	In the past 7 days...	Never	Rarely	Sometimes	Often	Always
17	I felt worthless	☐	☐	☐	☐	☐
18	I felt helpless	☐	☐	☐	☐	☐
19	I felt depressed	☐	☐	☐	☐	☐
20	I felt hopeless	☐	☐	☐	☐	☐
21	I felt like a failure	☐	☐	☐	☐	☐
22	I felt unhappy	☐	☐	☐	☐	☐
23	I felt that I had nothing to look forward to	☐	☐	☐	☐	☐
24	I felt that nothing could cheer me up	☐	☐	☐	☐	☐

	In the past 7 days…	Not at all	A little bit	Somewhat	Quite a bit	Very much
25	I feel fatigued	☐	☐	☐	☐	☐
26	I have trouble starting things because I am tired	☐	☐	☐	☐	☐
27	How run-down did you feel on average?	☐	☐	☐	☐	☐
28	How fatigued were you on average?	☐	☐	☐	☐	☐
29	How much were you bothered by your fatigue on average?	☐	☐	☐	☐	☐
30	To what degree did your fatigue interfere with your physical functioning?	☐	☐	☐	☐	☐

	In the past 7 days…	Never	Rarely	Sometimes	Often	Always
31	How often did you have to push yourself to get things done because of your fatigue?	☐	☐	☐	☐	☐
32	How often did you have trouble finishing things because of your fatigue?	☐	☐	☐	☐	☐

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	In the past 7 days…	Very poor	Poor	Fair	Good	Very good
33	My sleep quality was.................................	☐	☐	☐	☐	☐

	In the past 7 days…	Not at all	A little bit	Somewhat	Quite a bit	Very much
34	My sleep was refreshing............................	☐	☐	☐	☐	☐
35	I had a problem with my sleep	☐	☐	☐	☐	☐
36	I had difficulty falling asleep	☐	☐	☐	☐	☐
37	My sleep was restless	☐	☐	☐	☐	☐
38	I tried hard to get to sleep..........................	☐	☐	☐	☐	☐
39	I worried about not being able to fall asleep...	☐	☐	☐	☐	☐
40	I was satisfied with my sleep.....................	☐	☐	☐	☐	☐

	In the past 7 days…	Not at all	A little bit	Somewhat	Quite a bit	Very much
41	I am satisfied with how much work I can do (include work at home)	☐	☐	☐	☐	☐
42	I am satisfied with my ability to work (include work at home)…………………	☐	☐	☐	☐	☐
43	I am satisfied with my ability to do regular personal and household responsibilities...	☐	☐	☐	☐	☐
44	I am satisfied with my ability to perform my daily routines	☐	☐	☐	☐	☐
45	I am satisfied with my ability to meet the needs of those who depend on me………	☐	☐	☐	☐	☐
46	I am satisfied with my ability to do household chores/tasks………………….	☐	☐	☐	☐	☐
47	I am satisfied with my ability to do things for my family……………………………	☐	☐	☐	☐	☐
48	I am satisfied with the amount of time I spend performing my daily routines…….	☐	☐	☐	☐	☐

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	In the past 7 days…	Not at all	A little bit	Somewhat	Quite a bit	Very much
49	How much did pain interfere with your day to day activities?	☐	☐	☐	☐	☐
50	How much did pain interfere with work around the home?.....................................	☐	☐	☐	☐	☐
51	How much did pain interfere with your ability to participate in social activities?	☐	☐	☐	☐	☐
52	How much did pain interfere with your enjoyment of life?.....................................	☐	☐	☐	☐	☐
53	How much did pain interfere with the things you usually do for fun?	☐	☐	☐	☐	☐
54	How much did pain interfere with your enjoyment of social activities?..................	☐	☐	☐	☐	☐
55	How much did pain interfere with your household chores?.....................................	☐	☐	☐	☐	☐
56	How much did pain interfere with your family life?..	☐	☐	☐	☐	☐

	In the past 7 days…											
57	How would you rate your pain on average?...	☐ 0 **No pain**	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10 **Worst imaginable pain**

Performance Quality Rating Scale (PQRS)

Performance Quality Rating Scale: 10 point rating scale

Name ____________________

Therapist ____________________

Date – Pre ____________ **Date – Post** ____________

Goal	Very poor									Very good	Comment
1. ________	1	2	3	4	5	6	7	8	9	10	________
2. ________	1	2	3	4	5	6	7	8	9	10	________
3. ________	1	2	3	4	5	6	7	8	9	10	________

Figure 25

Stroke Impact Scale (SIS)

Participant ID # ____________ Test Time ___________ Tester Initials ___________

Date ___________

STROKE IMPACT SCALE (SIS)

These questions are about the physical problems that may have occurred as a result of your stroke.

1.	**In the past week, how would you rate the strength of your…**	A lot of strength	Quite a bit of strength	Some strength	A little strength	No strength at all
a.	Arm that was **most affected** by your stroke?	5	4	3	2	1
b.	Grip of your hand that was **most affected** by your stroke?	5	4	3	2	1
c.	Leg that was **most affected** by your stroke?	5	4	3	2	1
d.	Foot/ankle that **most affected** by your stroke?	5	4	3	2	1

2.	**In the past week, how difficult was it for you to…**	Not difficult at all	A little difficult	Somewhat difficult	Very difficult	Extremely difficult
a.	Remember things that people just told you?	5	4	3	2	1
b.	Remember things that happened the day before?	5	4	3	2	1
c.	Remember to do things (e.g. keep scheduled appointments or take medication)?	5	4	3	2	1
d.	Remember the day of the week?	5	4	3	2	1
e.	Concentrate?	5	4	3	2	1
f.	Think quickly?	5	4	3	2	1
g.	Solve everyday problems?	5	4	3	2	1

3.	In the past week, how often did you…	None of the time	A little of the time	Some of the time	Most of the time	All of the time
a.	Feel sad?	5	4	3	2	1
b.	Feel that there is nobody you are close to?	5	4	3	2	1
c.	Feel that you are a burden to others?	5	4	3	2	1
d.	Feel that you have nothing to look forward to?	5	4	3	2	1
e.	Blame yourself for mistakes that you made?	5	4	3	2	1
f.	Enjoy things as much as ever?	5	4	3	2	1
g.	Feel quite nervous?	5	4	3	2	1
h.	Feel that life is worth living?	5	4	3	2	1
i.	Smile and laugh at least once a day?	5	4	3	2	1

Participant ID # ____________ Test Time ___________ Tester Initials ___________

Date ___________

4.	**In the past week, how difficult was it to…**	Not difficult at all	A little difficult	Somewhat difficult	Very difficult	Extremely difficult
a.	Say the name of someone who was in front of you?	5	4	3	2	1
b.	Understand what was being said to you in a conversation?	5	4	3	2	1
c.	Reply to questions?	5	4	3	2	1
d.	Correctly name objects?	5	4	3	2	1
e.	Participate in a conversation with a group of people?	5	4	3	2	1
f.	Have a conversation on the telephone?	5	4	3	2	1
g.	Call another person on the telephone, including selecting the correct phone number and dialing?	5	4	3	2	1

5.	**In the past 2 weeks, how difficult was it to…**	Not difficult at all	A little difficult	Somewhat difficult	Very difficult	Could not do at all
a.	Cut your food with a knife and fork?	5	4	3	2	1
b.	Dress the top part of your body?	5	4	3	2	1
c.	Bathe yourself?	5	4	3	2	1
d.	Clip your toenails?	5	4	3	2	1
e.	Get to the toilet on time?	5	4	3	2	1
f.	Control your bladder (not have an accident)?	5	4	3	2	1
g.	Control your bowels (not have an accident?	5	4	3	2	1
h.	Do light household tasks/chores (e.g. dust, make a bed, take out garbage, do the dishes)?	5	4	3	2	1
i.	Go shopping?	5	4	3	2	1
j.	Do heavy household chores (e.g. vacuum, laundry or yard work)?	5	4	3	2	1

6.	**In the past 2 weeks, how difficult was it to…**	Not difficult at all	A little difficult	Somewhat difficult	Very difficult	Could not do at all
a.	Stay sitting without losing your balance?	5	4	3	2	1
b.	Stay standing without losing your balance?	5	4	3	2	1
c.	Walk without losing your balance?	5	4	3	2	1
d.	Move from a bed to a chair?	5	4	3	2	1
e.	Walk one block?	5	4	3	2	1
f.	Walk fast?	5	4	3	2	1
g.	Climb one flight of stairs?	5	4	3	2	1
h.	Climb several flights of stairs?	5	4	3	2	1
i.	Get in and out of a car?	5	4	3	2	1

Participant ID # ____________ Test Time ___________ Tester Initials ___________

Date ___________

7.	**In the past 2 weeks, how difficult was it to…**	Not difficult at all	A little difficult	Somewhat difficult	Very difficult	Could not do at all
a.	Carry heavy objects (e.g. bag of groceries)?	5	4	3	2	1
b.	Turn a doorknob?	5	4	3	2	1
c.	Open a can or jar?	5	4	3	2	1
d.	Tie a shoelace?	5	4	3	2	1
e.	Pick up a dime?	5	4	3	2	1

8.	**During the past 4 weeks, how much of the time have you been limited in…**	None of the time	A little of the time	Some of the time	Most of the time	All of the time
a.	Your work (paid, voluntary or other)?	5	4	3	2	1
b.	Your social activities?	5	4	3	2	1
c.	Quiet recreation (crafts, reading)?	5	4	3	2	1
d.	Active recreation (sports, outings, travel)?	5	4	3	2	1
e.	Your role as a family member and/or friend?	5	4	3	2	1
f.	Your participation in spiritual or religious activities?	5	4	3	2	1
g.	Your ability to control your life as you wish?	5	4	3	2	1
h.	Your ability to help others?	5	4	3	2	1

9.	**Stroke Recovery**	On a scale of 0 to 100, with 100 representing full recovery and 0 representing no recovery, how much have you recovered from your stroke?__________