

Feasibility, Acceptability, and Preliminary Effect of a Cognitive Training Intervention for Postoperative Cardiac Surgical Patients

Author: Connie Lynne Lorette Calvin

Persistent link: <http://hdl.handle.net/2345/2215>

This work is posted on [eScholarship@BC](#),
Boston College University Libraries.

Boston College Electronic Thesis or Dissertation, 2010

Copyright is held by the author, with all rights reserved, unless otherwise noted.

Boston College
William F. Connell School of Nursing

FEASIBILITY, ACCEPTABILITY, AND PRELIMINARY EFFECT OF A
COGNITIVE TRAINING INTERVENTION FOR POSTOPERATIVE CARDIAC
SURGICAL PATIENTS

a dissertation

by

CONNIE LYNNE LORETTE CALVIN

submitted in partial fulfillment of the requirements

for the degree of

Doctor of Philosophy

April 2010

© copyright by CONNIE LYNNE LORETTE CALVIN

2010

Feasibility, Acceptability, and Preliminary Effect of a
Cognitive Training Intervention for Postoperative Cardiac Surgical Patients

Connie Lynne Lorette Calvin

Dissertation Chair: Barbara E. Wolfe, PhD, RN, CS, FAAN

Abstract

Postoperative cognitive dysfunction (POCD) is characterized by a decline in cognitive performance following anesthesia and surgery and is a major cause of morbidity and mortality in the postoperative period. Moreover, studies suggest that patients who develop POCD may be at higher risk for cognitive decline later in life. POCD is of critical importance in relation to independent living, need for care, personal and economic cost, and quality of life. The majority of studies to date examine risk factors, prevalence, and complications associated with POCD. There is a lack of effective intervention strategies being developed to promote improved cognitive processing in this patient population.

The primary aim of this study was to examine the feasibility and acceptability of a cognitive training intervention (CTI) for the postoperative cardiac surgical patient. Feasibility was examined by conducting an attrition analysis to compare percent of attrition between intervention and control groups. A chi-square was conducted to answer the research question examining the difference between groups on attrition from study. Acceptability was examined by the administration of a “feasibility and acceptability” questionnaire, which was a 15-item questionnaire specific to the intervention. Fifteen one-sample *t* tests were used to determine acceptability of the intervention in the treatment population.

The secondary purpose of the study was to investigate the preliminary effect of the CTI on cognitive outcomes following cardiac surgery. A randomized controlled, single-blind, repeated measures design was used to test the hypothesis that following cardiac surgery, patients who receive a 6-week CTI when compared with those who receive usual care will demonstrate a significantly greater improvement in cognitive status when comparing discharge scores to scores at 6 weeks and 3 months postoperatively. Collection of data from 53 patients who underwent cardiac surgery was conducted from May 2008 to January 2010 at Catholic Medical Center in Manchester, NH. Factorial Analyses of Variance were conducted to answer the research question assessing the preliminary effect of a cognitive training intervention (CTI) on cognitive outcomes following cardiac surgery. Given assumptions of ANOVA were violated and non parametric statistics including two Kruskal Wallis H tests for independent samples at each assessment period as well as two Wilcoxon's signed ranks tests for related samples for each group were conducted.

The results of the chi-square were not significant, $\chi^2(1) = 0.95, p = .329$, suggesting no relationship exists between withdrawn participants and group. After Bonferroni adjustment the results of the fifteen one-sample t tests on the feasibility and acceptability questionnaire (Q1-Q15) for the intervention group reveal questions 2-8, 10, 14 and 15 have a larger mean compared to the neutral median value of 3.0, suggesting that participants tended toward a high level of acceptability over neutrality. Wilcoxon signed rank test on TICS scores by control group and time period (posttest vs. six week follow up and posttest vs. three month follow up) revealed a significant main effect by time period, $p < .01$ at both time periods. Wilcoxon signed rank test on TICS scores by

experimental group and time period (posttest vs. six week follow up and posttest vs. three month follow up) revealed a significant main effect by time period, $p < .01$ at both time periods. Kruskal Wallis test at six week follow up and three month follow up by group (control vs. experimental) was not significant, $\chi^2(1) = 0.01$, $p = .934$, and $\chi^2(1) = 0.02$, $p = .891$ respectively suggesting no statistical difference at six week follow up by group. The Wilcoxon signed rank on TICS by group and time period (six week follow up vs. 3 month follow up) was not significant ($p = .274$) and the Kruskal Wallis test at three month follow up by group (control vs. experimental) was not significant, $\chi^2(1) = 0.02$, $p = .891$, suggesting no statistical difference at three month follow up by group.

The results of this study suggest that a CTI is feasible to conduct and acceptable to patients following cardiac surgery. Results of the preliminary effect of the CTI suggest that cognitive performance improves over a six-week period following cardiac surgery independent of the CTI and there are no significant changes from the six-week to the three-month period. Preliminary findings yield further inquiry into cognitive enhancing interventions in the cardiac surgical patient.

Acknowledgements

This dissertation is dedicated to my niece Brianna Lynne Miner – you are my sunshine – you are my inspiration, and to my grandmother Dora Gaskell Firman - you live on in my heart everyday.

This dissertation would not have been possible if it were not for the collaborative efforts of many people. I would like to express my heartfelt gratitude to my dissertation committee. Dr. Barbara Wolfe acted as committee chair and provided me with exceptional support, guidance, expertise and ongoing encouragement throughout my doctoral experience. Sister Callista Roy has been an exemplary professor and scholar whose research and expertise in neuroscience as well as her theoretical contributions to nursing provided a foundation for my visions and research. Dr. Donald Likosky encouraged my intellectual curiosity. His expertise in statistics provided me with clarity and direction, which guided me through data analysis and assisted me in reporting concise research findings.

I am deeply appreciative to the American Association of Nurse Anesthetist Foundation and Boston College for providing me with doctoral fellowship funding to support my coursework and research. I am forever indebted to Cardiothoracic Surgical Associates – Dr. Yvon Baribeau, Dr. David Charlesworth, and Dr. Benjamin Westbrook – for allowing me access to their patients and providing ongoing encouragement throughout this dissertation. I am also deeply grateful to the patients for their participation in the study. To Anesthesia Care Group – Dr. Paul DelGiudice et al., for supporting my journey into academia and doctoral education, and for allowing me to continue my clinical practice on my very limited schedule. To Northeastern University

faculty and staff – Dr. Steve Alves, Dr. Jane Aroian, Janet Dewan (my greatest mentor), and Chris Litzinger – you were my coaches and my biggest cheerleaders. To my graduate assistants – Amanda Gilman, Derek Evans, Jessica Hartman, Jennifer Michael, Jessica Coxson, and Katie Fradette, - for your hard work and dedication to my dissertation.

One could not undertake the pursuit of doctoral education without the ongoing support of family and friends. My husband Dr. Rick Calvin saw me through the doctoral experience from the application process to the dissertation defense. He has provided tremendous support, insightful counsel, and unwavering dedication. To my sisters and their children for grounding me and constantly reminding me that life is so much more than homework. Finally, I am deeply grateful to my parents Robert and Carol Lorette for their unconditional love, faith, and prayers. I love you and I thank you all from the bottom of my heart.

Table of Contents

ABSTRACT.....	III
ACKNOWLEDGEMENTS.....	VI
TABLE OF CONTENTS.....	VIII
LIST OF TABLES.....	XI
LIST OF FIGURES.....	XIV
CHAPTER 1	
INTRODUCTION	1
STATEMENT OF PROBLEM	1
PURPOSE	7
BACKGROUND.....	8
SIGNIFICANCE	13
RESEARCH QUESTIONS	15
DEFINITIONS	17
ASSUMPTIONS	18
CHAPTER 2	
REVIEW OF THE LITERATURE	19
CONCEPTUAL FRAMEWORK	19
LITERATURE REVIEW	25
EPIDEMIOLOGY AND RISK FACTORS	26

CONTEXTUAL AND RESIDUAL STIMULI	30
Cognitive Processing	30
Cognitive Reserve	31
Neural Plasticity	32
The Aging Brain and Anesthesia	34
FOCAL STIMULI	36
COGNATOR	42
Cognitive Training Interventions	42
REGULATOR	54
Postoperative Cognitive Dysfunction	54
Measurements of Cognitive Function	55
Timing of Assessments	58
Criteria for Cognitive Decline in POCD	59
CHAPTER 3	
METHODS	64
RESEARCH DESIGN	64
SAMPLE	66
POWER	68
SETTING	69
DATA COLLECTION PROCEDURES	70
RANDOMIZATION	72
BLINDING	72
INSTRUMENTS	73

Demographic Questionnaire	73
Telephone Interview for Cognitive Status Questionnaire.....	73
Acceptability and Feasibility Questionnaire.....	75
Thinking Skills Workbook.....	75
PROTOCOLS.....	78
INTERVENTION GROUP.....	79
USUAL CARE GROUP	81
TIMING OF MEASUREMENTS	81
FIDELITY	82
DATA ANALYSIS	83
HUMAN SUBJECT PROTECTION	86
CONFIDENTIALITY	87
WITHDRAWAL OF PARTICIPANTS	87
PARTICIPATION PAYMENT.....	88
POTENTIAL BENEFITS	88
POTENTIAL RISKS	88
CHAPTER 4	
RESULTS	89
DESCRIPTORS AND FREQUENCIES	89
RESEARCH QUESTION 1	94
RESEARCH QUESTION 2	95
RESEARCH QUESTION 3	96

CHAPTER 5

DISCUSSION	105
REVIEW OF STUDY FINDINGS	105
Demographic Factors	105
Research Question #1	106
Research Question #2	107
Research Question #3	108
LIMITATIONS.....	111
IMPLICATIONS FOR THEORY, RESEARCH AND PRACTICE.....	113
SUMMARY	116
REFERENCES:	117
APPENDIX A INSTITUTIONAL REVIEW BOARD APPROVAL	
BOSTON COLLEGE and CATHOLIC MEDICAL CENTER.....	147
APPENDIX B PERMISSIONS	157
APPENDIX C DEMOGRAPHIC DATA INSTRUMENT	162
APPENDIX D IRB APPROVED STUDY MATERIALS.....	165
FEASIBILITY AND ACCEPTABILITY QUESTIONNAIRE	166
EXAMPLE OF ATTENTION EXERCISES.....	168
EXAMPLE OF CONCENTRATION EXERCISES.....	169
EXAMPLE OF MEMORY EXERCISES	170
APPENDIX E PATIENT CONSENT TO STUDY	175

List of Tables

Table 1. Elements of RAM and Selected Variables	22
Table 2. F tests - ANOVA: Repeated measures, within-between interaction	69
Table 3. Recruitment and Participation Rates	71
Table 4. Suggested Qualitative Interpretive Ranges for TICS Total Scores	74
Table 5. Timing of Measurements	82
Table 6. Frequencies and Percents for Gender by Group	91
Table 7. Frequencies and Percents for Age Range by Group	91
Table 8. Frequencies and Percents for Race by Group	91
Table 9. Frequencies and Percents for Marital Status	91
Table 10. Frequencies and Percents for Members of Household	92
Table 11. Frequencies and Percents for Level of Education	92
Table 12. Frequencies and Percents for Employment Status.....	92
Table 13. Frequencies and Percents for Level of Income.....	93
Table 14. Chi-Squares between Group with Demographic Variables.....	93
Table 15. Frequencies and Percents for Cognitive Decline.....	93
Table 16. Means and Standard Deviations for Declining TIC scores	94
Table 17. Cronbach's Alphas on TICS for each Assessment Period.....	94
Table 18. Chi-Square on Participants that Withdrew by Group	94
Table 19. Cronbach's Alphas for Feasibility and Acceptability Questionnaire	95
Table 20. One-Sample t-tests on the Feasibility and Acceptability Questionnaire	96
Table 21. Factorial ANOVA on TICS Scores by Group and Time Period (Posttest vs. Six Week Follow-up).....	97

Table 22. Means and Standard Deviations on TICS Scores by Group and Time (Posttest vs. Six Week Follow-up).....	98
Table 23. Wilcoxon Signed Rank Tests for each Group Comparing Posttest to Six Week Follow Up.....	99
Table 24. Kruskal-Wallis Tests for Comparing Posttest and Six Week Follow Up by Group.....	99
Table 25. Factorial ANOVA on TICS Scores by Group and Time Period (Posttest vs. Three Month Follow-up).....	100
Table 26. Means and Standard Deviations on TICS Scores by Group and Time (Posttest vs. Three Month Follow-up)	100
Table 27. Wilcoxon Signed Rank Tests for each Group Comparing Posttest to Three Month Follow Up.....	101
Table 28. Kruskal-Wallis Tests for Comparing Posttest and Three Month Follow by Group.....	101
Table 29. Factorial ANOVA on TICS Scores by Group and Time Period (Six Week Follow-up vs. Three Month Follow-up).....	102
Table 30. Means and Standard Deviations on TICS Scores by Group and Time (Six Week Follow-up vs. Three Month Follow-up).....	102
Table 31. Wilcoxon Signed Rank Tests for each Group Comparing Posttest to Three Month Follow Up.....	104
Table 32. Kruskal-Wallis Tests for Comparing Six Week Follow Up and Three Month Follow by Group	104

List of Figures

Figure 1. The Roy Adaptation Model of Nursing and Cognitive Processing.....	20
Figure 2. The Roy Adaptation Model.....	21
Figure 3. Conceptual Model for Preliminary Effect Pilot Study	23
Figure 4. Conceptual Model for Feasibility and Acceptability Study	65
Figure 5. Recruitment Protocol.....	67
Figure 6. Bar Graph of Means for Posttest, Six Week Follow Up and Three Month Follow Up.....	103

CHAPTER 1

INTRODUCTION

This chapter provides an overview of the problem of postoperative cognitive dysfunction with a specific focus on the cardiac surgical population who have undergone coronary artery bypass graft on pump or off pump and/or valve surgery. A statement of the purpose of the study is presented. The background of the problem is discussed and the significance of the study is outlined including the potential implications of the study. The chapter concludes with research questions, hypotheses, and assumptions of the study.

Statement of Problem

For more than 50 years, health care providers have acknowledged that some patients emerge from surgery and anesthesia with noted deficits in cognitive function that were not present preoperatively (Bedford, 1955). This impairment is referred to in the literature as Postoperative Cognitive Dysfunction (POCD) (Bekker & Weeks, 2003) and has been defined as a “state of cerebral cognitive alterations” (Practico et al., 2005, pp. 973). Patients undergoing cardiac surgery are reported to have a higher incidence of cognitive dysfunction than any other major surgical procedures (Shaw et al., 1987; Gau et al., 2005). The incidence of POCD in the immediate postoperative period has been reported to be as high as 80% (Arrowsmith, Grocott, Reves & Newman, 2000). Although reported as being transient, a review by Bekker and Weeks (2003) suggests that some patients may experience long-term dysfunction and this dysfunction may even become permanent. Newman and colleagues (2001) reevaluated patients 5 years after surgery and found that 42% showed decline in cognitive function from preoperative baseline assessment and decline in cognitive function in the immediate postoperative period was

predictive of long-term decline. The incidence of POCD is particularly prevalent in patients over 60 years of age (Mathew et al., 2003). More over, studies suggest (Selnes et al., 2001) that patients who develop POCD may be at higher risk for cognitive decline/dementia later in life. Longitudinal studies of normal aging without surgery suggest that any sudden decline in cognitive function leads to a loss of independence and withdrawal from society, and is an important predictor of mortality (Bosworth, Schaie, & Willis, 1999). Monk and colleagues (2008) evaluated patients one-year after surgery and reported that patients exhibiting POCD in the immediate postoperative period and 3-months after surgery had a significantly higher mortality ($p = 0.02$) than patients who did not experience POCD.

Literature suggests that age is the number one factor to be predictive of postoperative cognitive decline (Arrowsmith et al., 2000; Dodds & Allison, 1998; Quattara, Amour, & Bouzguenda, 2009). The patient population is aging and based on favorable perioperative outcomes, more high-risk patients are undergoing surgical procedures including cardiac surgery (Alexander et al., 2000). Even if the surgical procedure is uneventful, it may be followed by a decline in cognitive functional status. Cognitive function is of critical importance in relation to independent living, need for care, personal and economic cost, and quality of life. When optimizing patients for surgery, perhaps we should consider the potential for development of POCD. In doing so, perioperative management should include a long-term perspective with consideration to cognitive assessment as well as patient education regarding the potential impact of POCD.

Cognitive processing is a unique and vital human experience. From a physiologic perspective, the process of cognition is dependent in part upon the neuron, which is the functional unit of the central nervous system. Neurologic function is vital to information processing and adaptation. A classical synapse is responsible for transmitting information from a presynaptic neuron to its target cell. In contrast, the function of a neuromodulatory synapse is to transmit information that will have long-term effects on the postsynaptic neuron's activity, most importantly its response to succeeding input. Synaptic plasticity is an activity-dependent process, which involves continuous use of synaptic pathways. This process is widely believed to be elemental to learning and memory, as well as providing an important role in the development of new neural pathways (Dayan & Abbott, 2005; Singer, Lindenberger, & Baltes, 2003). To better understand the significance of neural plasticity, it is important to research the potential of modifying neuromodulatory synapses through cognitive training. Through these modifications it may be possible to promote neurogenesis, change sequences of neuronal firing, promote learning and memory, and alter behavior (Jobe et al., 2001; Crosby & Culley, 2003; Dayan & Abbott, 2005; Thompson, 2005; Olson et al., 2006).

Lezak, Howieson, and Loring (2004) defined the four main cognitive functions in terms of input, storage, processing, and output. These domains constitute comprehension, perception, integration, memory, learning, attention, concentration, and psychomotor functions. Attention, concentration, and memory are aspects of thinking that are essential in everyday life. In terms of activities of daily living (ADL), individuals need to be competent in managing finances, shopping, taking medications, transportation, and household management. Cognitive skills are learned behaviors that are acquired through

demonstration, replication, and practice. Research suggests that it is possible to improve these skills by using cognitive training techniques (Blundon & Smits, 2000; Carter, Howard, & O'Neil, 1983). Given the current state of the science, utilization of interventions designed to enhance cognitive function in the postoperative period should be considered.

Although signs and symptoms of POCD may be present in the immediate postoperative period they are most often subtle and literature suggests that it may not be detected for days or weeks postoperatively (Bekker & Weeks, 2003). Perhaps utilization of neuropsychologic evaluation in the preoperative and immediate postoperative period would assist in the identification of cognitive decline allowing for early cognitive interventions. While exact degree and magnitude of cognitive decline requires diagnosis through neuropsychological testing (Newman, 1995), one should not dismiss the fact that clinicians (e.g. nurses) and caregivers may observe changes in cognitive behavior.

The characteristics of POCD in cardiac and non-cardiac surgical patients are well documented and include but are not limited to impairment of attention, concentration, and memory (Arrowsmith et al., 2000; Rasmussen & Moller, 2000; Bekker & Weeks, 2003), which will be the cognitive domains addressed in this study. For some people these changes may simply represent a subtle annoyance while for others they may result in difficulty with social integration, loss of job, relationship issues, and loss of independence (Bekker & Weeks, 2003). Even the slightest change in cognition can negatively impact the quality of life in older adults (Mahncke et al., 2006). It is well established that POCD is associated with poor patient outcomes including longer lengths

of hospital stay, admission to long-term facilities, and increased mortality (Wu, Hsu, Richman & Raja, 2004).

Despite major improvements in surgery, anesthesia, and perfusion practice over the past 30 years, the reported incidence of POCD has not changed (Dodds & Allison, 1998; Arrowsmith et al., 2000; Newman et al., 2001). This could be the result however of a greater awareness of POCD heralding more frequent neurologic screening as well as the advances made in assessing cognitive deficits. In other words, there could be a declining incident, yet an increased number of diagnosed cases. Over the past 10 years, reports of incidence of POCD vary widely ranging from 10% to 57% of adult patients 3 to 6 months after surgery (Keith et al., 2002; Selnes et al., 2003; Selnes, Goldsborough, Borowicz & McKhann, 1999; Zimpfer et al., 2004). It is thought that this variation in reported incidence can be attributed to methodological limitations, multifarious tests used to perform cognitive evaluation, disparate criteria to define cognitive impairment, variable follow-up intervals, and diverse patient populations (Mahanna, et al., 1996; Murkin, Newman, Stump, & Blumenthal, 1995; Rasmussen et al., 2001; Symes, Maruff, & Ajani, 2000). Of note, the majority of studies to date have excluded patients with underlying cognitive disorders, psychiatric disorders or disorders of the central nervous system, and urgent or emergent surgical patients. These studies have also excluded patients who are taking psychotropic medications. While such stringent exclusion criterion avoids several confounding variables, they reduce the sample to a subpopulation of patients with limited generalizability (Ancelin et al., 2001), hence underestimating the overall incidence of POCD.

To date, the extant literature has focused almost exclusively on risk factors, incidence, and complications associated with POCD (Benoit et al., 2005; Canet et al., 2003; Sharrock et al., 2005). Although these studies provide important information, there is a dearth of studies that investigate opportunities to reverse the impact and incidence of POCD. While research suggests that cognitive activity as well as physical exercise maintain and enhance cognitive functioning in the normal aging population and in patients with traumatic brain injury (TBI), Alzheimer's disease (AD), stroke, and mild cognitive impairment (MCI) (Kramer, Erickson, & Colcombe, 2006; Olson, Eadie, Ernst, & Christie, 2006), there continues to be a gap in the literature addressing the issue of facilitating or enhancing cognitive recovery in patients with POCD. Moreover, it is unknown if a cognitive training intervention for cognitive decline is both feasible to conduct and acceptable to patient's following cardiac surgery.

The scientific community has become increasingly aware of the importance of cognitive interventions in older adults in terms of maintaining autonomy, independence, and quality of life (Ball et al., 2002). Many of the cognitive training studies that address aspects of attention and concentration are designed to restore attentional abilities through repeated practice. Results of these studies are significant for perceptual speed and selective attention (Nieman, Ruff, & Baser, 1992; Novack, Caldwell, Duke, & Berquist, 1996). It is well documented that memory training affects memory ability more than control treatments (Mohs et al., 1998; Rasmusson, Rebok, Bylsma, & Brandt, 1999). A study by Cipriani, Bianchetti, and Trabucchi (2006) utilized a computerized CTI in patients with MCI and AD. Outcome measures included the Mini Mental Status Exam (MMSE) (Folstein, Folstein, & McHugh, 1975). They reported that patients with AD

showed significant improvement ($p = 0.010$) in overall global cognitive status whereas patients with MCI showed significant improvement ($p = 0.017$) in the domain of behavioral memory. Westerberg and colleagues (2006) conducted a pilot study evaluating the use of computerized working memory training in stroke patient. They reported significant improvement ($p = 0.001$) in working memory and attention as measured by the Paced Auditory Serial Addition Task (PASAT) (Gronwall, 1977). POCD is characterized by impairment in attention, concentration, and memory (Arrowsmith et al., 2000). Therefore, the current study investigated the cognitive domains of attention, concentration and memory.

Purpose

The primary aim of the study was to investigate the feasibility and acceptability of a CTI in cardiac surgical patients, who have undergone CABG on- or off-pump and/or valve surgery, during the first 6-weeks of the postoperative recovery phase. Feasibility was determined by evaluation of the attrition rates comparing control group to treatment group. Program acceptability was determined by responses from the Feasibility and Acceptability Questionnaire. The secondary aim of this study was to conduct a preliminary investigation of the hypothesis derived from the Roy Adaptation Model of Nursing and Cognitive Processing (Roy, 2001) that following cardiac surgery, patients who receive a daily cognitive training intervention (CTI) over a period of 6 weeks will have a statistically significant improvement in cognitive function, relative to postoperative evaluation, when compared to those who receive usual postoperative cardiac care.

Background

Cardiac surgical procedures, including coronary artery bypass grafting and valve surgery are some of the most commonly performed procedures worldwide (Selnes et al., 1999). The fact that there have been major technical improvements in anesthesia (e.g. monitoring techniques), surgery (e.g. minimally invasive procedures), and perfusion techniques (e.g. less systemic inflammatory response), has led to a steady decline in mortality and morbidity associated with these procedures (Ivanov, Weisel, David, & Naylor, 1998). However, cognitive dysfunction continues to be a major determinant of postoperative morbidity in the cardiac surgical population (Arrowsmith et al., 2000).

The patient population is aging and people are projected to live longer. According to the most recent US census (Wan, Sengupta, Velkoff, & DeBarros, 2005), there are 35.9 million Americans age 65 and older, with a 23% increase in Americans age 75-84 and a 38% increase in Americans age 85 and older since 1990. Moreover, in the next 50 years the US population aged 65 and older is estimated to be 86.7 million and those 85 and older will increase to 20.9 million. Elderly patients are more likely to have multiple health problems and many of them will require anesthesia and surgery, including cardiac surgery. In fact, over the past several years, the average age of patients undergoing cardiac surgery has steadily increased (Rasmussen et al., 2001).

POCD following cardiac surgery is relatively common however it is seldom systematically evaluated for and receives limited consideration in the postoperative assessment (Gao et al., 2005). Although many risk factors for POCD have been identified, the specific cause remains elusive and is thought to be multifactorial. Patient risk factors for POCD identified in the literature include increased age, lower level of

education, lower socioeconomic status (Gao et al., 2005), preoperative depression and psychoactive medication use (Benoit et al., 2005), cerebral vascular disease, peripheral vascular disease, atrial fibrillation, left ventricular ejection fraction of less than or equal to 30%, preoperative cardiogenic shock, and diabetes (Bucerius et al., 2004).

Perioperative risk factors include, anesthesia, hypotension, hypoxemia, anemia, metabolic abnormalities, inhalation anesthetics (Bekker & Weeks, 2003), urgent operation, operation time of greater than or equal to 3 hours, intraoperative hemofiltration, cardiopulmonary bypass, and multiple transfusions (Bucerius et al., 2004).

Due to the subtle nature of POCD, neuropsychologic testing is helpful for its detection. Assessment includes global cognitive functioning as well as the separate domains of cognition. Specific domains defined by Lezak and colleagues (2004) include memory, verbal function and language, visuospatial functions, executive functions, speed of processing, crystallized and fluid intelligence, and motor dexterity and coordination. Neuropsychological test results are influenced by an individual's overall intelligence. In addition, there have been many propositions for the age-related effects seen among multiple cognitive variables, including 1) control and allocation of attention or executive resources; 2) quantity of attentional resources; 3) coordination or functioning of specific cortical regions, such as the prefrontal cortex; and 4) the quantity of neurotransmitters or the intactness of myelin (Salthouse & Ferrer-Caja, 2003).

Although neuropsychological testing has been used to determine changes or decline in cognition in the postoperative period the reported magnitude of these cognitive changes vary across studies (Lewis, Maruff, & Silbert, 2004). Although Murkin et al.

(1995) developed a consensus statement to establish criteria for assessing cognitive dysfunction after cardiac surgery; many studies have used several different neuropsychologic tests to quantifying POCD (Collie, Darby, Falletti, Silbert, & Maruff, 2002; Knipp et al., 2004; Lewis et al., 2004). Many of these tests are lengthy and time consuming. Given the potential for decline in cognitive domains of attention and concentration, these tests may be very daunting for the patient in the preoperative and postoperative period making routine use difficult. This study utilized the telephone interview for cognitive status (TICS) (Brandt, Spencer, & Folstein, 1988), which is a widely used test of global cognitive function that is administered over the phone and requires approximately five to ten minutes to complete. A study by Crooks, Clark, Petitti, Chui, H., and Chui, V. (2006) concluded that the TICS evaluated global cognitive function with a sensitivity of 0.83 (95% confidence interval [CI]) and the specificity was 1.0 (95% CI). Kappa was 0.89 (95% CI). In addition, specific cognitive domains were evaluated including memory, which was found to have a sensitivity of 0.38 (95% CI) and a specificity of 0.96 (95% CI). Kappa was 0.61 (95% CI). Attention, concentration and memory are the cognitive domains examined in the current study.

Timing of the cognitive testing is also an important issue. In order to evaluate changes in cognition from baseline to postoperative period, neurologic surveillance should be measured in the preoperative period (Rasmussen et al., 2001). Postoperative assessment of decline in performance has generally been measured upon discharge from hospital (between 4 and 7 days postoperatively). If assessed too early after surgery (e.g. 24 hours), some patients may exhibit postoperative delirium, which is a much more transient problem than POCD and includes fluctuations in consciousness (Bucarius et al.,

2004; Newman, Stygall, Hirani, Shaewfi, & Maze, 2007). Anesthesia, stress, fatigue and pain may also alter performance on neurocognitive tests. Murkin et al. (1995) suggests that neuropsychologic testing should be performed preoperatively to provide a baseline assessment, in the immediate postoperative period, and 3 months later. Many studies have used these suggestions they have added other time frames for neuropsychologic testing to add to the current body of knowledge. Following Murkin's suggestions, the current study conducted neurologic surveillance in the preoperative period, immediate postoperative period, and 3 months post surgery. The CTI was administered over a 6-week period; therefore an additional 6-week surveillance was conducted to evaluate potential differences in the groups following the intervention. Despite Murkin's suggestions various neuropsychological tests have been used to analyze neurocognitive function and many differing criteria have been used to define significant declines in cognition. In a review of the extant literature, there are currently no universally accepted criteria for defining incidence and severity of POCD (Keith et al., 2002; Likosky et al., 2004; Murkin et al., 1995; Rasmussen et al., 2001).

It is now accepted that cognitive decline following cardiac surgery is common (Monk et al., 2008). Despite growing recognition of POCD, there is a lack of effective intervention strategies being developed to promote improved cognitive processing after surgery. Newman et al., (2001) suggested that interventional strategies in patients with early postoperative cognitive decline might prevent late cognitive deterioration. The evolving knowledge of neural plasticity coupled with new theories of cognition have led to significant changes in the way scientists and clinicians view learning and memory. Cognitive training interventions (CTI) have been performed in several different patient

populations including; children with learning disabilities (Greydanus, Pratt, & Patel 2007), adults with age-related cognitive decline (Ball et al., 2002), stroke (Carter et al., 1983), individuals with MCI (Rapp, Brenes & Marsh, 2002), and those with AD (Cipriani et al., 2006).

Many studies have authenticated the effectiveness of CTI programs in improving cognitive function in older adults experiencing age-related cognitive decline. However, CTI was frequently reported to only be specific to the cognitive domain taught (e.g. CTI for memory is not generalizable to reasoning or spatial orientation) (Cavallini, Pagnin, & Vecchi, 2003). In a study by Ball and colleagues (2002), results supported the effectiveness and sustainability of the CTI in older adults for improving targeted cognitive abilities. Cipriani et al., (2006) evaluated cognitive outcomes of a computer-based CTI on patients with AD and MCI. The AD group showed significant improvement on the Mini Mental Status Exam (MMSE) score and in verbal production and the MCI groups showed significant improvement in behavioral memory. A study by Edwards and colleagues (2005) examined speed of processing training on older adults with baseline speed of processing difficulty. Sixty-three participants in the treatment group received ten 1-hour training sessions. Results suggested that the training not only significantly improved speed of processing ($p < 0.001$) but also a significantly improved performance on Timed Instrumental Activities of Daily Living (IADL) $p = 0.03$.

In a long-term study by Willis et al. (2006), 699 participants were randomized to receive ten 60-75-minute sessions in reasoning training. They reported that reasoning training had a significant effect on IADL with an effect size of 0.28 and a 95% confidence interval. The characteristics of POCD are reportedly similar to other

neurocognitive diagnoses (e.g. MCI, AD, TBI, and age-related cognitive decline) in terms of decline in specific cognitive domains (e.g. attention, concentration, and memory). It would stand to reason that a CTI focusing on the specific domains of attention, concentration, and memory, could be effective in the postoperative cardiac surgical patient population.

Significance

The significance of the proposed study is multifaceted. Despite progressive changes in anesthetic management with the development of new drugs and improved monitoring techniques, as well as improvements in surgical and perfusion techniques, POCD continues to be reported in the literature as one of the major morbidities following surgery and anesthesia (Bekker & Weeks, 2003). The reported incidence has varied greatly from 24% to 79% at twenty-four-hours postoperatively, and 1% to 57% several months after surgery (Newman et al., 2001; Rasmussen et al., 2001; Zimpfer et al., 2004). In addition, the patient population is aging, people are living longer and many of these patients will have multiple medical problems. It is predicted that many of these patients will undergo major surgical procedures including cardiac surgery and may be at risk for POCD (Alexander et al., 2000). POCD may complicate recovery in several ways including delayed physical and emotional rehabilitation. Longer lengths of hospital stay will lead to delayed return to work with possible loss of job and loss of independence (Dijkstra, Houx, & Jolles, 1999). Extended length of hospital stay and increased resource utilization associated with both major and minor declines in cognition has led to devastating economic as well as personal costs (Bekker & Weeks, 2003). Moreover, POCD is associated with increased morbidity and mortality in both the immediate

postoperative period as well as potential for further cognitive decline in the future (Wu et al., 2004).

In the postoperative period, many patients exhibit only subtle clinical changes, thus POCD may not be detected (Newman et al., 2001). Although clinicians should play a key role in the early recognition of cognitive decline, a study by Inouye, Forman, Mion, Katz, and Cooney (2001) concluded that clinicians often missed cognitive decline when signs and symptoms were subtle. There are several neuropsychological tests available to evaluate cognitive decline in the postoperative period that may be performed by clinicians including; 1) MMSE) (Folstein et al., 1975), and 2) Telephone Interview for Cognitive Status (TICS) (Brandt & Folstein, 1988), both of which evaluate global cognitive status. Conducting neuropsychologic testing in the postoperative period may improve the chances that POCD will be diagnosed, which will allow for early cognitive intervention.

This study explored the feasibility and acceptability of implementation of a CTI program in the postoperative recovery phase in cardiac surgical patients. The secondary aim was to evaluate the preliminary effect of a CTI on improving cognitive processing for individuals following cardiac surgery. The CTI consisted of simple tasks designed to stimulate the brain and enhance its ability to reorganize its neurons and form new neural connections, a process previously defined as neural plasticity. The study investigated the feasibility, acceptability and preliminary effect of cognitive practice simultaneously in three different domains of cognitive function (e.g., attention, concentration, and memory). These cognitive domains were chosen on the basis that they have been reported as areas of decline following cardiac surgery (Arrowsmith et al., 2000; Bekker & Weeks,

2003). In addition, these cognitive domains are associated with performance of cognitively demanding IADL that are critical for independent living (Willis, Jay, Diehl, & Marsiske, 1992; Willis, 1996). Moreover, studies suggest that these are cognitive domains that may be modified (Ball et al., 2002; Cavallini et al., 2003; Cipriani et al., 2006; & Mahncke et al., 2006).

This intervention was specifically designed to promote self-administration and practice of thinking exercises to optimize cognitive function in patients after cardiac surgery. Given the potential for significant complications of POCD following cardiac surgery and the increased personal, economic and health care cost associated with this phenomenon, interventions designed to reduce both complications and associated costs are warranted. This CTI allowed the patients to practice their cognitive skills in their homes, which frees them of the burden of attending training sessions. Implications for practice include the possible use of a CTI in association with cardiac rehabilitation to enhance cognitive processing in the cardiac postoperative period.

Research Questions

Research Question 1

RQ1: Is there a difference in the frequency of attrition across groups (control vs. experimental)?

H1_o: There is no difference in the frequency of attrition across groups (control vs. experimental).

H1_a: There is a difference in the frequency of attrition across groups (control vs. experimental).

Research Question 2

RQ2: For the intervention group, does acceptability differ significantly from the median value of 3.0 reflecting neutrality?

H2₀: For the intervention group, acceptability does not differ significantly from the median value of 3.0 reflecting neutrality.

H2_a: For the intervention group, acceptability differs significantly from the median value of 3.0 reflecting neutrality.

Research Question 3

RQ3: Following cardiac surgery, do patients who receive a 6-week CTI when compared with those who receive usual care demonstrate a significantly greater improvement in cognitive status when comparing discharge scores to scores at 6 weeks and 3 months postoperatively?

H3₀: Following cardiac surgery, patients who receive a 6-week CTI when compared with those who receive usual care do not demonstrate significantly greater improvement in cognitive status when comparing discharge scores to scores at 6 weeks and 3 months postoperatively.

H3_a: Following cardiac surgery, patients who receive a 6-week CTI when compared with those who receive usual care demonstrate significantly greater improvement in cognitive status when comparing discharge scores to scores at 6 weeks and 3 months postoperatively.

Definitions

The following operational and conceptual definitions were used for this study:

Cognitive function – For the purpose of this study cognitive function was measured by the TICS and defined as the human ability to process information in the intellectual processes of: 1) *memory*; defined as the ability to retain and recall immediate, short-term and long-term past experiences, 2) *attention and concentration*; defined as the capacity to selectively focus on one thing to the exclusion of another and be vigilant.

POCD - A state of cerebral cognitive alterations following surgery and anesthesia that is characterized by impairment of attention, concentration, and memory that may have long-term implications (Arrowsmith, et al., 2000; Rasmussen & Moller, 2000; Bekker & Weeks, 2003).

Cognitive Training Interventions – A paper and pencil thinking skills exercise booklet designed to stimulate the brain and it's ability to reorganize its neurons and form new neural connections in an adaptation process. These tasks will focus on the cognitive domains of attention, concentration, and memory.

Usual Care – For this study, usual care is defined as the postoperative care that an individual would normally receive following cardiac surgery that does not typically include a cognitive training intervention. Usual care at the study hospital consists of cardiac rehabilitation, dietary consultation, medication education, and lifestyle counseling (e.g. smoking cessation, exercise, diet and weight control).

Feasibility – For this study, feasibility assesses the ability to implement and complete a program and the degree to which the intervention addresses what is important to the participant. Feasibility will be assessed by recruitment and attrition rates.

Acceptability – For this study, acceptability assesses the ease to which the participant can use the intervention and how the participant feels that the program fits with their needs.

Acceptability will be assessed by an acceptability and feasibility questionnaire.

Assumptions

1. Age is the greatest preoperative predictor of POCD.
2. The patient population is aging and older people are more likely to have multiple health problems and it is likely that many of them will require cardiac surgery.
3. Neural plasticity continues into late old age.
4. The CTI stimulates the brain and enhances its ability to reorganize neurons and form new neural connections in an adaptive process.
5. Feasibility and acceptability are prerequisites for effective interventions.

CHAPTER 2

REVIEW OF THE LITERATURE

This chapter provides an overview of the theoretical framework that guides this study. An extant review of the literature is presented guided by the theoretical framework.

Conceptual Framework

The Roy Adaptation Model of Nursing and Cognitive Processing (figure 1) forms the theoretical framework that guides this study. The Roy Adaptation Model (figure 2) views adaptation as a constantly changing point. The stimuli that affect the individual are focal, contextual and residual. Focal stimuli are the internal and external stimuli most immediately affecting the individual. Contextual stimuli are all the other stimuli that are present and have an effect on the focal stimuli. Residual stimuli are unclear environmental factors that affect the current situation (Roy, 2009). The cognator system is “a major process involving four cognitive-emotive channels: perceptual and information processing, learning, judgment and emotion” (Roy, 2009 pp. 41). The regulator is the major biophysical coping mechanism. The combination of the cognator and regulator are what forms a method of coping. The individual then adapts through four different modes: physiological, self-concept, role function, and interdependence. When the focal and contextual stimuli promote ineffective responses from the individual, there is disruption of the integrity of the person and possible subsequent health issues (Roy, 2009).

Figure 1. The Roy Adaptation Model of Nursing and Cognitive Processing

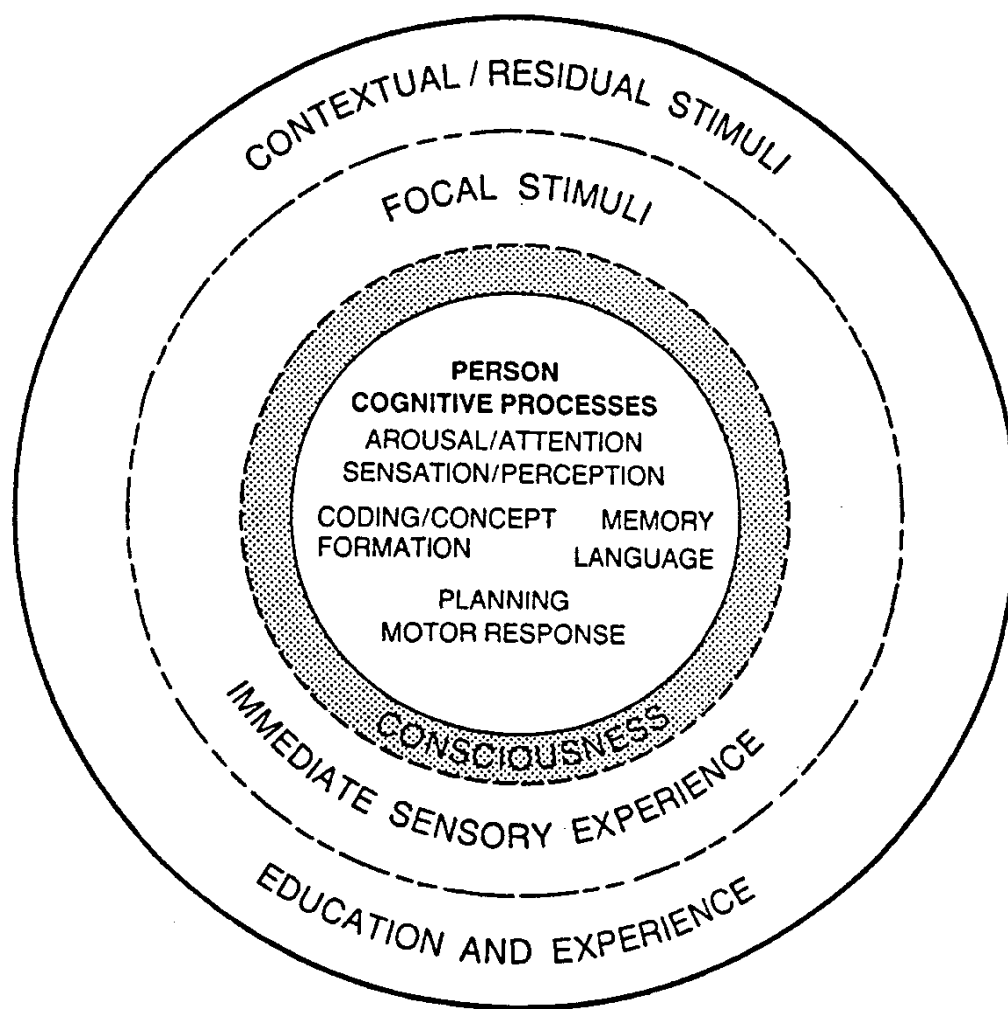
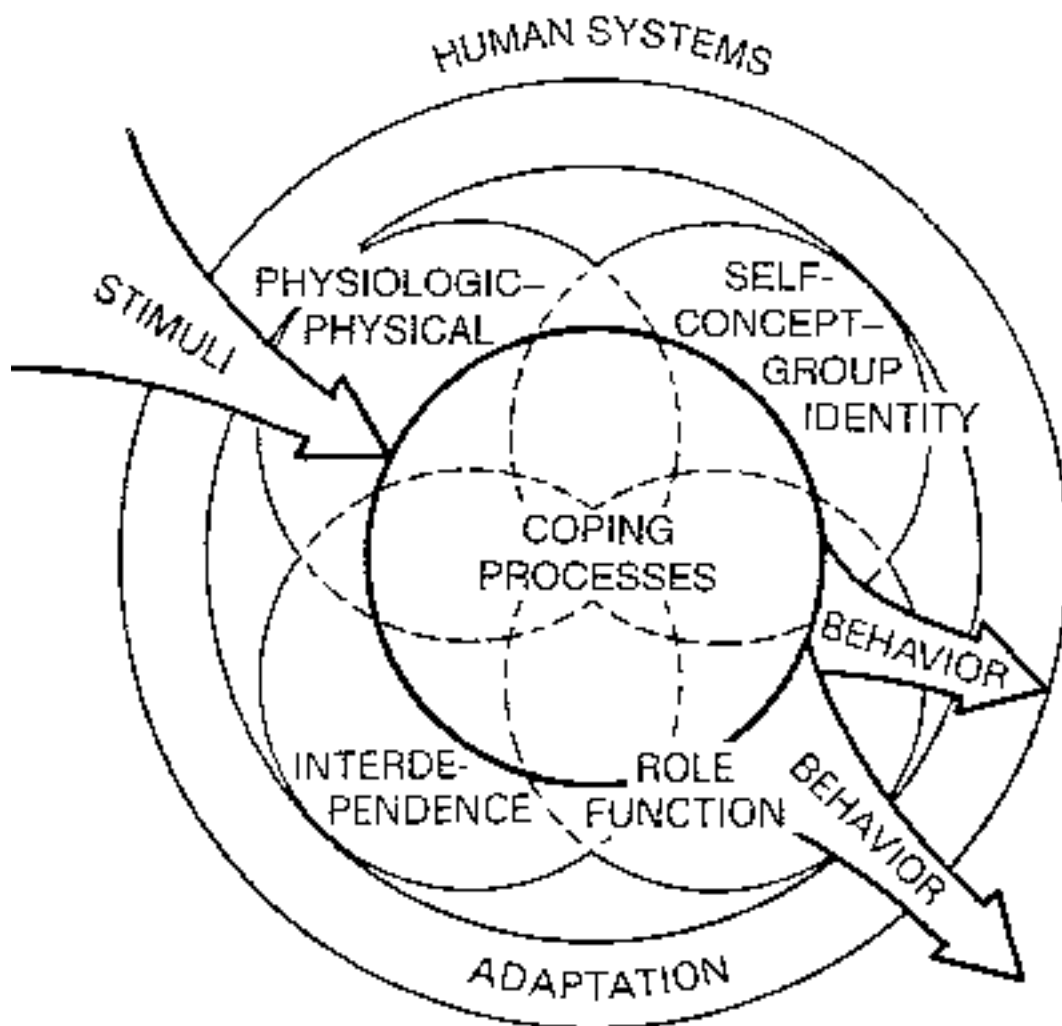


Figure 2. The Roy Adaptation Model

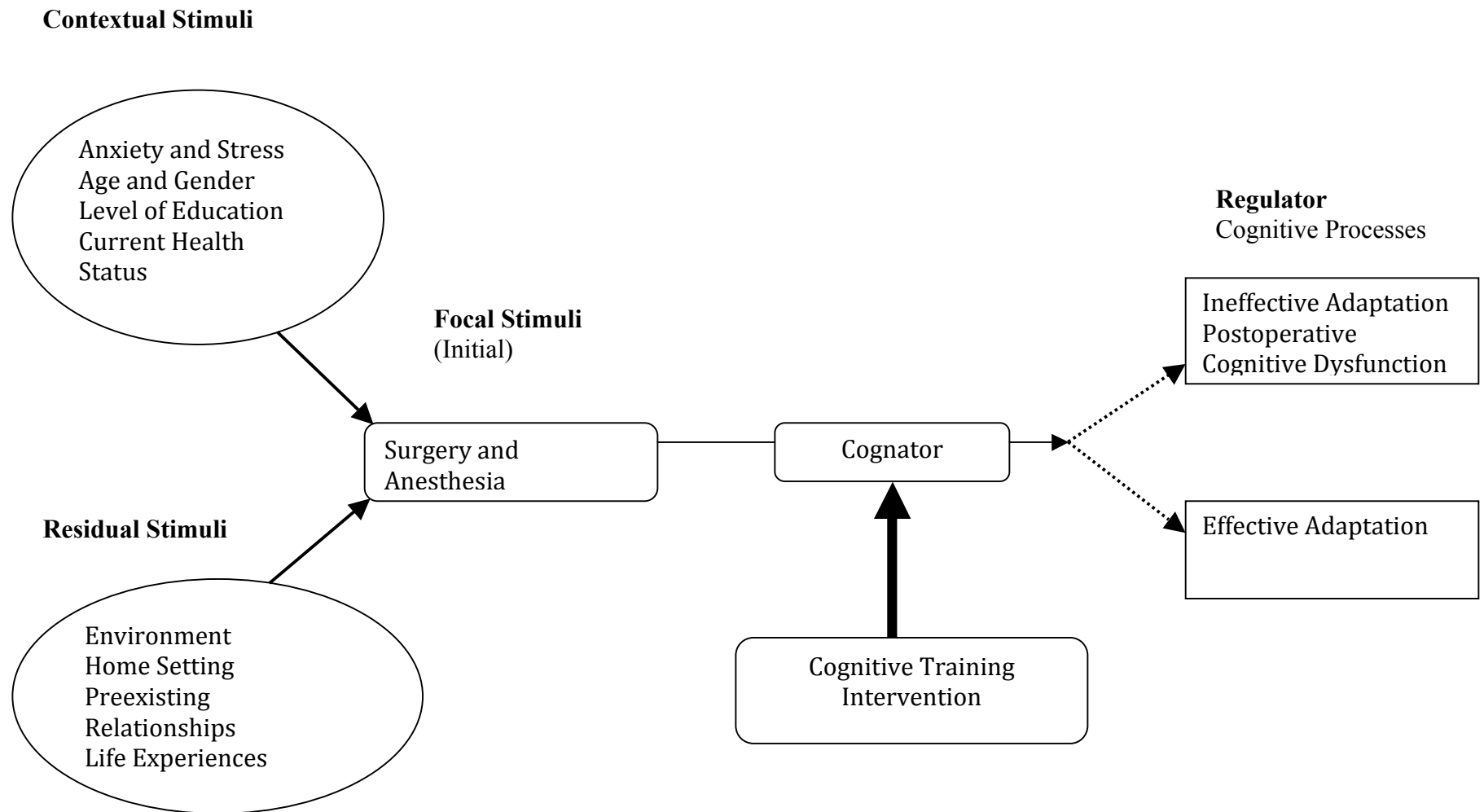


When applied to the proposed study, the elements of the model correspond to the selected variables (Table 1). The focal stimulus includes all aspects of the perioperative period. The contextual stimulus includes the patient's age, gender, level of education and overall health status as well as anxiety and stress. Finally, the residual stimuli represent the recovery trajectory, the home setting, and the pre-existing relationship between the family member and the patient as well as other environmental factors identified by the patient and family member. The cognitive processing intervention would act as the stimulus that manages the cognator (figure 3). Through this intervention, it is proposed that the nurse will affect the adaptive modes of the patient. With resources and support available for these patients, the adaptive responses that the patient makes will be effective and promote continued health.

Table 1. Elements of RAM and Selected Variables

Roy Model Concept	Study Variable	Empirical Indicator
Contextual and Residual Stimuli	Age/Gender/Race	Demographic Questionnaire
	Marital Status	
	Member of Household	
	Level of Education	
	Employment Status/Income	
Focal Stimuli (Initial)	Cardiac Surgery/Anesthesia	Perioperative Record
Focal Stimuli (Intervention)	Cognitive Training Intervention	Thinking Skill Workbook
Cognator/Regulator	Cognitive Status	Telephone Interview for Cognitive Status

Figure 3. Conceptual Model for Preliminary Effect Pilot Study



Neurologic function is an essential component of a person's adaptation. In Roy's model, both the regulator and cognator subsystems are based on the processes of neurologic function (Roy, 2009). This framework includes synthesis of knowledge about integrated cerebral function and information processing theory (Das, Kirby, & Jarman, 1979; Luria, 1980). Luria (1973) described three principal functional units of cognitive function, (a) an arousal and attention unit that comprises the reticular activating system and parts of the hippocampus, limbic system and brain stem, (b) an information gathering, processing and storage unit that comprises the parietal, temporal and occipital regions of the neo-cortex and the connections to the thalamus and, (c) a programming, regulation and verification unit that includes the frontal lobe and connections to other regions of the cortex.

Roy (1999; 2001) proposed a model for nursing's view of cognitive processing (figure 1). The inner circle of the model describes cognitive process as input (arousal/attention and sensation/perception); central processing (coding/concept formation, memory and language); and output stages (planning and motor responses). These processes are enclosed within the field of consciousness. Through these cognitive processes, neural plasticity or adaptive responses occur (Roy, 2001). The circle surrounding consciousness represents what Roy refers to as the focal stimuli, which are the stimuli most immediately present in consciousness (Roy, 1984; Roy, 2009). The outer circle represents the contextual-residual stimuli, which includes the education and experiences of the person as well as the environment in which the current processing situation is embedded. The broken lines represent the interactions between the stimulus fields (Roy, 1984; Roy, 2001).

LITERATURE REVIEW

For this study, the primary searches were achieved through electronic databases Cumulative Index to Nursing and Allied Health Literature (CINHL, 1995 – 2009), Medline (1995 – 2009), PubMed (1995 – 2009), Boston College e-journal library, and the Cochran Library Databases were searched using the terms “neurologic complications after cardiac surgery”, “postoperative cognitive dysfunction”, “neurocognitive deficits”, “neuropsychological testing”, “information processing”, “neural plasticity”, “cognitive training interventions”, and “feasibility and acceptability studies”. Of the 744 citations found, 186 research reports were identified as being directly related to the topics. Abstracts were reviewed and full texts acquired if they met at least one of the following eligibility criteria, including but not limited to (1) the article was published after 1995, (2) the design was a randomized or non-randomized clinical trial, (3) patients underwent cardiac surgery (CABG on or off pump, and/or valve), (4) cognitive assessment was performed using neuropsychological instruments, (5) the study utilized a cognitive training tool, (6) the study discussed neural plasticity, and (7) the study evaluated feasibility and acceptability of an intervention. A total of 131 published studies that met criteria were selected. Each article was reviewed and data were extracted from tables or text, or extrapolated from figures. Sample demographics, research design, data collection methods, data analysis and subsequent discussions and conclusions of the studies were evaluated. This state of the science directs the decisions made regarding the design of the study.

The current review begins with the current knowledge of POCD including epidemiology and risk factors. The contextual and residual stimuli are outlined by a

discussion of cognitive processes and cognitive reserve, followed by a review of neural plasticity and the aging brain and anesthesia. The focal stimuli are comprised of events that occur during the perioperative period including immune function and biological markers of neuronal injury, and studies examining the relationship between cardiac surgery, anesthesia and POCD. The CTI is defined as the stimulus that manages the cognator. This is followed by a discussion of the regulator system in terms of adaptation including ineffective adaptation defined as POCD. Neuropsychological measurements of cognitive dysfunction are discussed including timing of assessments and criteria used to define POCD. Finally, this review identifies the gaps in the literature that require further investigation to inform nursing practice.

Epidemiology and Risk Factors

As noted, the breadth and actual incidence of POCD is unknown and reports vary widely. It is thought that this variation in reported incidence can be attributed to methodological limitations, variable neuropsychological tests performed, as well as the different criteria used to define cognitive impairment (Mahanna, et al., 1996; Murkin et al., 1995; Rasmussen et al., 2001). In a review of central nervous system complications following cardiac surgery, Arrowsmith and colleagues (2000) reported that cognitive decline was as high as 80% in the immediate postoperative period and persisted in one-third of those patients. In a longitudinal study Newman et al. (2001) evaluated neurocognitive function in patients (N = 261) who underwent CABG. Decline was defined as a decrease in scores on tests of 1 SD on any of the four cognitive domains tested. They reported cognitive decline at time of discharge to be 53%, 6 weeks post-operative at 36%, 6-month interval at 24%, and a jump to 42% after 5 years.

Stroobant, Van Nooten, Van Belleghem, and Vingerhoets (2005) conducted a prospective comparative study to evaluate the effects of on-pump ($n = 32$) and off-pump ($n = 18$) on postoperative cognitive decline. Type of surgery did not show a main effect on outcome (neuropsychological performance). They reported that 60% of the patients who underwent cardiac surgery showed evidence of POCD in the immediate postoperative period and in 24.2% of those patients, the cognitive decline was present 6 months after surgery.

In a study by Monk et al. (2008), 1,064 patients 18 years of age and older undergoing major non-cardiac surgery, completed neuropsychological evaluation at preoperative baseline, immediate postoperative period (discharge), and three-months after surgery. Participants were categorized by age; young (18-39-years), middle-age (40-59-years), or elderly (≥ 60 -years). Neuropsychological surveillance included a battery of 5 tests of memory, learning, recall, cognitive flexibility, and distractibility. Decline was defined as a z score greater than 1.96 on two individual tests. At time of discharge, all age groups were significant for decline; young (36.6%), middle-aged (30.4%), and elderly (41.4%). There was no significant difference between groups. At 3-month follow up, POCD was reported as significantly higher in the elderly group (12.7%, $p < 0.001$). Of note, the majority of studies have stringent exclusion criteria reducing the sample to a non-representative subpopulation leading to a gross underestimation of actual incidence of this phenomenon.

The literature describes preoperative, intraoperative, and postoperative variables considered to be risk factors for POCD, but as noted the exact etiology remains elusive and is thought to be multifactorial. What is known is that cognition is dependent upon the

neuron and neuronal function depends upon an adequate supply of and appropriate cell utilization of oxygen and nutrients. Unlike other cells of the body, the neuron has minimal ability for anaerobic metabolism. In addition, the neurons have a very high metabolic rate of oxygen consumption. Therefore, cessation of adequate oxygenated blood flow to the brain for as little as 15 seconds can lead to a state of unconsciousness (Guyton & Hall, 2006).

As noted in the introductory chapter, Bucerius et al. (2004) conducted a large randomized study to investigate predictors of cognitive decline on patients undergoing CABG on-pump (n=14,342) and off-pump (n=1,847). Variables associated with a high risk of cognitive decline were history of cerebrovascular diseases, atrial fibrillation, diabetes mellitus, peripheral vascular disease, left ventricular ejection fraction $\leq 30\%$, preoperative Cardiogenic shock, urgent operation, operating time ≥ 3 hours, intraoperative hemofiltration, and red blood cell transfusions ≥ 2000 ml. Other perioperative risk factors include, anesthesia, hypotension, hypoxemia, anemia, metabolic abnormalities, and inhalation anesthetics (Bekker & Weeks, 2003). Charlesworth et al. (2003) and Likosky et al. (2003) reported that cardiopulmonary bypass time ≥ 114 minutes, atrial fibrillation, intra-aortic balloon pump, and low cardiac output significantly increased the risk of a neurologic event. In a study by Boodhwani and Colleagues (2006), 448 patients undergoing CABG on-pump were evaluated to identify predictors of postoperative neurocognitive deficits. They reported that intraoperative normothermia, poor LV function, and elevated preoperative creatinine were independent predictors of postoperative neurocognitive deficits.

Patient risk factors associated with POCD have been identified in several studies. Kadoi and Goto (2006) conducted a study of eighty-eight patients who underwent elective CABG surgery. Patients were evaluated at 6 months with a battery of neuropsychological test and the incidence of cognitive decline was reported to be present in 27% of patients. Risk factors found to be significant were greater age ($p = 0.04$), renal failure ($p < 0.001$), and diabetes ($p < 0.001$). Benoit and colleagues (2005) conducted a study of 102 patients undergoing vascular surgery. They reported the incidence of cognitive dysfunction to be 33% and found a correlation between decreased level of education, preoperative depression, and greater use of preoperative psychotropic medications with cognitive decline. In addition patients who were single, divorced, or widowed were more likely to experience cognitive decline. In a large study of patients undergoing CABG surgery ($N = 937$) Ho et al. (2004) reported that patients with cerebral vascular disease ($p = 0.009$), a history of chronic disabling neurologic disorders ($p = 0.016$), and those who live alone ($p < 0.05$) were at higher risk for cognitive decline whereas number of years of education ($p < 0.001$) was inversely related to cognitive decline.

Patients with preoperative cognitive impairment have demonstrated significant decline in cognition postoperatively. A study conducted by Silverstein, Steinmetz, Reichenberg, Harvey, and Rasmussen (2007) investigated the data set of the first International Study of Postoperative Cognitive Dysfunction (ISPOCD) (Moller, et al, 1998) and reported preoperative cognitive impairment (PCI), defined as performance below 1.5 SD of the mean value, in 74 out of 1,218 patients. POCD was confirmed at the 3-month follow-up test in 15% of patients with PCI versus 9.5% of patients without PCI.

In addition, studies have suggested that a history of alcohol abuse is associated with increased incidence of POCD.

This review identifies several variables that are linked to POCD. It would stand to reason that efforts to prevent POCD or even reduce the incidence of POCD although of great importance might be unattainable. While researchers are exploring ways to prevent or reduce the incidence of POCD, the patients may benefit from a CTI designed to enhance cognitive status.

Contextual and Residual Stimuli

Contextual stimuli represent all other stimuli that are present and have an effect on the focal stimuli (Roy, 2001). For this study, contextual stimuli would comprise the recovery trajectory, home setting, and pre-existing relationship between the patient and support system. Residual stimuli are the unclear environmental factors identified by the patient and support system that may affect the current situation (Roy, 2001).

Cognitive Processing

Cognitive processing is a unique and vital human experience which encompasses the ability to use information processing to think, feel, and act. Cognitive abilities allow a person to interact with and adapt to their physical and social environments (Roy, 2009). According to Das, Naglieri, and Murphy (1995), cognitive processing is unique to human beings and consists of four functions comprising planning, arousal-attention, simultaneous, and successive (PASS) coding of information. The theory of PASS was based on Luria's (1970) classic analyses of the brain in which he defines cognitive processing as 3 functional units comprised of, 1) cortical arousal and attention, 2) information gathering, processing and storing, and 3) planning, self-monitoring, and

structuring of cognitive activities. These units relate to the function of receiving and transmitting sensory input, simultaneous and successive processing and coding of input, and integration of information for planning and decision making.

Lezak and colleagues (2004) define the four main cognitive functions in terms of input, storage, processing, and output. These domains constitute comprehension, perception, integration, memory, learning, attention, concentration, and psychomotor functions. Rietan & Wolfson (1988), described three levels of cognitive information processing, (1) attention, memory, and concentration (areas of concentration in the current study), (2) verbal skills and visual spatial skills, and (3) reasoning and logical analysis. Others define cognitive processing as memory, reasoning (executive function), and speed of processing (Jobe et al., 2001; Ball et al., 2002; Willis et al., 2006).

Yu, Kolanowski, Strumpf, & Eslinger (2006) define three broad domains of cognitive function: memory, executive function, and visuospatial functioning. Memory includes explicit, defined as recollection of previous experiences, and implicit, defined as memory that does not require conscious recollection. Executive function is defined as a group of cognitive skills that collectively promote goal-directed behavior. These skills include working memory, inhibitory control, and organization. Finally, visuospatial functioning includes perception, comprehension, and interpretation of information.

Cognitive Reserve

The concept of cognitive reserve was proposed based on the observation that the severity of brain pathology is not directly related to the degree of cognitive decline or performance (Stern, 2002). The threshold model, which revolves around the concept of cognitive reserve, suggests that there are individual differences in cognitive reserve and

that these differences may be related to brain size and number of synapses (Satz, 1993). Stern (2002) suggests that this individual variability may be genetic or may be the result of life experiences (e.g. education). The concept of cognitive reserve may provide an explanation for why older adults and those who have a lower level of education are at higher risk of developing POCD. Moreover, the concept of cognitive reserve suggests that compensation may take place in the form of reorganization of neural networks (Stern, 2003), also described in the literature as neural plasticity.

Neural Plasticity

Neurologic function is vital to information processing and adaptation. The cerebral cortex has the ability to adapt to an ever-changing environment and this modification of neurons supports cognition (Burke & Barnes, 2006). Neural plasticity refers to the neurons ability to create new connections throughout the cortex and to adapt to changes by altering roles and functional organization (Schwartz & Begley, 2002). Draganski et al. (2004) conducted a study evaluating the effects of a 3-month cognitive intervention on neural plasticity. Twenty-four homogenous volunteers were randomized to treatment or control group. Three-dimensional magnetic resonance imaging studies were completed at baseline and following the intervention. Findings indicated that learning-induced cortical plasticity is associated with anatomical changes in neural networks.

A growing body of research suggests that neural plasticity continues throughout the lifespan. Wilson and Colleagues (2002) conducted a longitudinal cohort study of 801 Catholic nuns, priests, and brothers who were without dementia at time of enrollment. They found that persons reporting frequent cognitive activity were 47% less likely to

develop AD then persons reporting infrequent cognitive activity. Verhaeghen, Marcoen, and Goossens (1992) conducted a meta-analysis of 33 studies including healthy older adults without cognitive decline who received a mnemonic intervention to improve memory. The total sample size consisted of 1,539 participants with an estimated mean age of 69.1 years. Pre-to-post-test gains in memory were found to be significantly greater in the intervention group than in both control and placebo groups. In a randomized, controlled, single-blind trial by Ball and colleagues (2002), 2,802 volunteer participants aged 65-94 years were randomly assigned to 1 of 4 groups (3 different cognitive training intervention groups and 1 control group). They reported that the cognitive training intervention significantly improved cognitive abilities in the targeted domains.

Central nervous system injury is a trigger for neural plasticity. An animal study conducted by Carmichael (2003) demonstrated that axonal sprouting occurs in the peri-infarct tissue of adult rats. Unfortunately this neural plastic mechanism may be adaptive or maladaptive. Research suggests that plasticity may be modulated and that cognitive behavioral training may contribute to adaptive plasticity after injury (Nudo, 2006). For example, Taub and Colleagues (2006) conducted a placebo-controlled clinical trial of 41 individuals with chronic stroke who were randomized to constraint-induced (CI) movement therapy (n=21) or placebo group (n=20). Results showed that after CI therapy, individuals had a significantly greater improvement in functional use of their affected arm supporting the efficacy of CI therapy in brain plasticity. These findings suggest that cognitive/neural plasticity continues into late old age and may be modulated to be adaptive in many populations. Moreover, these findings suggest that cognitive training

interventions focused on specific cognitive domains may be instrumental in enhancing plastic mechanisms within those domains.

The Aging Brain and Anesthesia

As noted, several studies reported increased age and lower level of education to be predictive of POCD (Benoit et al., 2005; Canet et al., 2003; Ho et al., 2004; Moller et al., 1998; Newman et al., 2001). General anesthesia alters several different functions of the brain including neuronal membranes, receptors, ion channels, neurotransmitters, cerebral blood flow and cerebral metabolic rate of oxygen consumption (Franks & Lieb, 1994). Perioperative hypovolemia, anemia, hypotension, and hypoxia may also lead to global neuronal injury and dysfunction (Bekker & Weeks, 2003). The aged brain is more sensitive to the effects of anesthesia with a subsequent decrease in anesthetic requirements. Moreover, there is a notable increase in the duration of action and clinical effects of anesthetic and non-anesthetic drugs in the older adult, particularly those drugs that require organ elimination (Muravchick, 2006). Regarding depth of anesthesia, Farag, Chelune, Schubert, and Mascha (2006) conducted a randomized controlled study (N=74) to lower Bispectral index (BIS) protocol (median BIS, 38.9) and higher BIS protocol (mean BIS, 50.7) and reported that deeper levels of anesthesia was associated with better recovery of cognitive function (e.g. ability to process information) 4-6 weeks postoperatively. However, a study conducted by Monk, Saini, Weldon, and Sigl (2008) reported an association between the use of volatile anesthetic agents, cumulative deep anesthesia time, and systolic hypotension and death within the first year after surgery.

Older adults are at greater risk for developing POCD for several reasons. Aging neurons decrease in size and number resulting in overall decrease in brain mass. In

addition, the complex nature of the dendritic tree is diminished along with a reduction in the number of synapses (Selkoe, 1992). During the aging process, several neurotransmitter systems are altered (Mrak, Griffin, & Graham, 1997). More specifically, there is a decrease in the level of dopamine, and the number of dopaminergic uptake sites and transporters. In the frontal lobes, dopamine controls the processing of information received from other areas of the brain (Mesulam, 2000). Dopamine is essential to the initiation of behavior such as thoughts or movements. A decrease in dopamine has the capacity to induce a decline in neurocognitive functions, most importantly memory, attention and problem solving (Houk, Davis, & Beiser, 1998). Levels of central serotonergic and gamma-Aminobutyric acid (GABA) binding sites are reduced in the aged brain (Crosby & Culley, 2003), as are markers of central cholinergic activity (Pratico et al., 2005). Serotonin plays an important role in regulation of mood, sleep, sexuality and appetite where as GABA plays an essential role in coordinating arousal, attention, mood, and motivation (Mesulam, 2000). Finally, cholinergic tracts are essential for conscious arousal, learning, memory and long-term potentiation (Woolf, 2006).

Other contextual and residual stimuli have been identified as well. Use of tobacco was associated with a significant increase in POCD (Stroobant et al., 2005). Benoit and colleagues (2005) collected demographic data on 102 patients aged 41 to 88 to identify lifestyle issues associated with POCD. The majority of patients ($n = 95$) had a history of smoking and the number of pack years smoked had a significant impact on increased incidence of POCD. Hudetz et al. (2007) conducted randomized controlled trial of male patients 55 years and older from a Veterans Administration hospital. Patients were randomized to 1 of 4 groups, self-reported alcohol abuse scheduled for surgery ($n = 14$),

self-reported alcohol abuse without surgery ($n = 14$), non-alcoholic scheduled for surgery ($n = 14$), and non-alcoholic without surgery ($n = 14$). A significant interaction was observed by ANOVA for five neurocognitive exams conducted: Visual Immediate Recall, Visual Delayed Recall and Phonemic fluency ($p < 0.05$) as well as Semantic Fluency and the Color-Word Stroop Test ($p < 0.01$). Although many of the contextual and residual stimuli may not be altered, it is imperative to have an understanding of the factors that may be predictive of POCD so that the risks and benefits of surgery and anesthesia can be evaluated.

Focal Stimuli

The focal stimuli are the internal and external factors most immediately affecting the individual (Roy, 2001). For this study, the focal stimuli would represent any factors that would be present during the perioperative period. In the preoperative period, stress would be considered a major focal stimulus. In fact the stress response is active throughout the perioperative period. Stress evokes a neuroendocrine response with stimulation of the sympathetic nervous system (Chernow et al., 1987) and is thought to play a significant role in POCD.

The effects of surgical related stress and initiation of the inflammatory process, particularly when cardiopulmonary bypass is utilized, has been well described (Shann et al., 2006). In a study by Baufreton et al. (2005) 30 patients were randomized to either standard (non-coated) or heparin coated cardiopulmonary bypass circuits. Complement activation was measured with sC5b-9 and brain injury was measured by s100beta. Outcome measure of cognitive decline was assessed using neuropsychometric tests comparing 2 week preoperative to discharge scores. They reported that s100beta and

sC5b-9 were significantly correlated ($p = 0.03$). This suggests that the inflammatory response evoked activation of the complement system and leukocytes, promotes increased capillary permeability and upregulation of protease-activated receptors, all of which may contribute to neuronal injury. Major stress evokes the release of cortisol by way of the hypothalamic-pituitary-adrenal (HPA) axis. Cortisol is thought to possess neurodegenerative properties and the cells of the hippocampus seem particularly vulnerable. The hippocampus is a brain structure vital in the conversion of short-term memory to long-term explicit memory. It also plays an integral role in the control of the HPA axis (Wolkowitz, Lupien, & Bigler, 2007). Rasmussen, O'Brien, Silverstein, Johnson, and Siersma (2005) studied 187 patients undergoing major non-cardiac surgery. Salivary cortisol levels were measured in conjunction with neuropsychologic tests preoperatively, day 1, day 7, and 3-months postoperatively. POCD was reported in 18.8% of patients at 1 week and 15.2% at 3 months. They found elevated cortisol levels to be significantly related to POCD ($p = 0.02$ for both). In addition to the inflammatory stress response of surgery, chronic low-grade inflammation accompanies aging as evidenced by increased levels of cytokines, TNF, and IL-6 (Van Zant, & Liang, 2003).

Biochemical markers of neuronal injury have been assessed and correlated to neuropsychological testing. Iohom and colleagues (2004) conducted a study examining plasma levels of stable nitric oxide (NO) in a cohort of patients ($n = 42$) age 40 – 85 undergoing laparoscopic cholecystectomy. Spouses ($n = 13$) were used as controls. Serial measurements of serum S-100beta and Nitric oxide (NO) were performed along with neuropsychological tests preoperatively, 4-days and 6-weeks postoperatively. Cognitive decline was reported in 40% of cohort and 7% control subjects ($p = 0.01$) at 4 days

postoperatively and 53% of cohort versus 23% controls ($p = 0.03$) at 6 weeks postoperatively. Serum S-100beta was similar in both groups, but plasma NO was larger in the deficit group ($p < 0.05$ both time periods). They concluded that elevated levels of NO were associated with early POCD. An earlier study by Martens, Raabe, and Johnsson (1998) assessed the use of S-100 and neuron-specific enolase (NSE) on predicting regaining consciousness on 64 patients with acute global cerebral ischemia. They reported that serum S-100 protein and NSE were significantly higher ($p < 0.001$ for both) following global cerebral ischemia and was found to be predictive of patient outcome as measured by regaining consciousness. In a study evaluating 41 patients with a mean age of 68 resuscitated from cardiac arrest, elevated levels of S-100 were correlated ($p < 0.001$) with degree of coma suggesting that S-100 is an established marker of neuronal injury and can be used as an early prognostic indicator of short-term cognitive outcome (Rosen, Rosengren, Herlitz, & Blomstrand, 1998). Linstedt and colleagues (2002) measured serum S-100 in 120 patients undergoing vascular, trauma or abdominal surgery. Neuropsychologic tests were performed on day 1, 3, and 6 postoperatively and found significantly higher levels of serum S-100 in the group of patients ($n = 48$) that exhibited postoperative cognitive decline. Finally, Rasmussen, Christiansen, Eliassen, Sander-Jensen, and Moller (2002a) studied 15 patients undergoing CABG. They collected serum S-100beta and NSE before surgery and at 12, 18, 24, 30 and 36 hours postoperatively. Neuropsychologic tests were conducted before surgery and at time of discharge and 3 months postoperatively. They reported levels of NSE to be a significant serum marker for early detection of POCD ($p < 0.05$). This information adds to the body of knowledge that

stressful situations including surgery and anesthesia evoke a neuroendocrine response and may play a significant role in cognitive dysfunction.

There are a myriad of intraoperative stimuli including, anesthesia, hypotension, hypoxemia, anemia, metabolic abnormalities, (Bekker & Weeks, 2003), urgent operation, operation time of greater than or equal to 3 hours, intraoperative hemofiltration, cardiopulmonary bypass, and multiple transfusions (Bucarius et al., 2004). As mentioned previously, many brain functions are altered by general anesthetics including neuronal membranes, receptors, ion channels, cerebral blood flow, and cerebral metabolic rate of oxygen and glucose consumption (Franks & Lieb, 1994). In addition, it is well documented that anesthetic agents affect the release of central nervous system neurotransmitters (Bekker & Weeks, 2003; Dodds & Allison, 1998).

Acetylcholine is a one of the primary neurotransmitters involved in consciousness. The central cholinergic pathways innervate many areas of the brain and are of notable importance in regulation of memory and alertness (Tune, 2001). In fact, inhibition of cholinergic pathways during administration of anesthesia is crucial in avoiding occurrence of intraoperative memory. The long-term effects of receptor inhibition are not clear. An increase in anticholinergic activity has been associated with increased delirium (Inouye, 2006). Serotonin, which mediates several behaviors, may be altered during anesthesia. Excess levels may result in confusion and restlessness (Flacker & Lipsitz, 1999a), while reduced levels may alter cognition by decreased availability of cerebral tryptophan (Flacker & Lipsitz, 1999b). General anesthesia affects the N-methyl-D-aspartic acid (NMDA) receptors and the literature suggests that antagonism of NMDA receptors promotes mitochondrial swelling and neuronal damage (Culley, Xie, & Crosby,

2007). Alterations in other neurotransmitters (e.g. gamma-aminobutyric acid, dopamine, dopamine and glutamate) continue to be investigated as a potential source of POCD (Inouye, 2006; Wu et al., 2004).

Physiological changes during anesthesia may be contributory to POCD. In particular hyperventilation with associated hypocarbia leads to cerebral vasoconstriction and decreased cerebral perfusion. Hypotension may cause cognitive deficits secondary to overall decrease in cerebral perfusion. Hypoglycemia interrupts substrate availability to neurons while hypoxia and anemia may cause direct neuronal ischemia and death (Moller et al., 1993). As mentioned previously, Iohom and colleagues (2004) found elevated levels of plasma nitric oxide (NO) to be associated with POCD. NO promotes neuronal death by causing oxidative injury, energy depletion, inhibition of DNA synthesis, and apoptosis.

Hypoperfusion of the gut during CPB promotes translocation of bacteria from the intestinal mucosa to the blood. Mathew et al. (2003) investigated the correlation of decreased anti-endotoxin core antibody (EndoCab) and POCD in 460 patients 23 to 86-years of age undergoing elective CABG. Preoperatively levels of EndoCab were obtained and neuropsychologic evaluation was conducted preoperatively and at 6-weeks postoperatively. They reported that 36% of patients showed cognitive decline at 6 weeks follow up according to a 1-SD decline on a minimum of 1 out of 4 cognitive factors. A logistic regression demonstrated a significant correlation with EndoCab level and POCD at 6-weeks postoperatively ($p = 0.03$).

Finally, postoperative factors that may contribute to POCD have been identified. Rosenberg and Kehlet (1993) conducted a randomized study comparing patients undergoing major abdominal surgery ($n = 30$) matched with patients undergoing minor ear surgery ($n = 10$) to investigate the role of postoperative hypoxia on POCD. Oxygen saturation (SpO_2) was monitored in the preoperative and postoperative periods by pulse oximetry. Neuropsychologic evaluation was conducted preoperatively and on day 3 and day 7 in the postoperative period. The patients in the control group did not experience any hypoxic episodes whereas the patients in the major surgery group experienced several hypoxic episodes on postoperative day 2 ($p < 0.05$). In addition, cognitive decline was significant on postoperative day 3 in the same group ($p < 0.05$). Multiple regressions revealed a significant relationship ($p < 0.05$) between postoperative SpO_2 and cognitive decline.

In the ISPOCD1 study, Moller and Colleagues (1998) investigated the neurologic outcomes of patients ($N = 1,218$) undergoing major non-cardiac surgery. As noted previously neuropsychologic surveillance was conducted preoperatively and on postoperative week 1 and week 12. They reported a significant relationship between both postoperative infectious complications ($p = 0.04$) and postoperative respiratory complications ($p < 0.05$) and POCD. Wang, Sands, Vaurio, Mullen, and Leung (2007) conducted a prospective cohort study ($n = 225$) of patients' age 65 and greater that underwent non-cardiac surgery investigating the association of pain and postoperative analgesia with POCD. Neurologic surveillance was conducted using the TICS at preoperative baseline and day 1 and 2 in the postoperative period. They reported that only postoperative analgesia administered via patient controlled anesthesia (PCA) was

associated with POCD ($p = 0.02$). It is evident by the substantive published studies that the predictors, risk factors, and etiology of POCD are complex and multifarious. While current studies focused on decreasing incidence of POCD are of great importance, intervention studies designed to enhance cognitive function in the postoperative period are necessary to promote continuous improvement in patient outcomes.

Cognator

In terms of coping, the RAM encompasses the cognator and regulator subsystems. As noted earlier, the cognator subsystem is “a major process involving four cognitive-emotive channels: perceptual and information processing, learning, judgment and emotion” (Roy, 2001; pp.46). The regulator subsystem is the major biophysical coping mechanism (e.g. neuroendocrine system) that responds to the stimuli. The combination of the cognator and regulator are what forms the method of adapting (Roy, 2001). For the purpose of this study the CTI is the input that stimulates the cognator and neural plasticity as measured by enhanced global cognitive function is the regulator.

Cognitive Training Interventions

As noted, the scientific community has become increasingly aware of the importance of cognitive interventions for recovering, improving, and preserving cognitive function. A review of the published studies revealed significant disparity in the structure of CTI programs in terms of the population of patients in the studies, the nature of the interventions, duration of the program, and the outcome measures. The variation in studies implies that decline in cognition affects several different patient populations as well as many different cognitive domains. The current study will focus on the feasibility, acceptability and preliminary effect of a CTI directed at the domains of attention,

concentration and memory as they have been noted to be the cognitive domains most affected by POCD.

A study by Wadley and colleagues (2006) investigated the feasibility of the development of a self-administered cognitive intervention. A secondary aim of the study was to evaluate the interventions effectiveness. A total of 84 people aged 65 to 94 agreed to complete at least 8 out of 10 1-hour CTI sessions. A questionnaire was utilized to evaluate ease and acceptability of the CTI. Ease and acceptability were rated as high in 83% of participants ($n = 15$) with 12 or fewer years of education and 86% of participants ($n = 64$) with greater than 12 years of education. The self-administered intervention improved performance by 74% over standard laboratory training (effect size 1.74 SD). Overall results of the model showed significant effect ($p < 0.001$) of training type on pre-post difference scores on neuropsychologic surveillance.

The primary goal of cognitive interventions is to improve or maintain cognitive function. The majority of CTI studies have been conducted in healthy older adults aged 60 or older who do not exhibit signs of cognitive decline. Continuous functional decline in cognition, memory and perception are associated with the normal aging process (Mahncke et al., 2006). One such study by Gunther, Schafer, Holzner, and Kemmler (2003) investigated the effects of a computerized cognitive training intervention in 19 older adults, 75 to 91-years of age having no signs of dementia. The computer-assisted intervention consisted of one 45-minute session each week over a total of 14 weeks. Cognitive domains assessed were memory, learning and speed of processing. Neurologic outcome was measured using a battery of neuropsychologic tests for German speaking

people. They reported significant improvements in memory ($p < 0.01$) and learning ($p = 0.03$). The study was limited by sample size and it was a non-randomized trial.

One of the largest studies conducted by Ball and colleagues (2002), the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study, was a randomized controlled, single-blind design using 4 groups (ages 65-94), including a no-contact group ($n = 704$) and 3 intervention groups. The interventions groups received training in memory ($n = 711$), reasoning ($n = 705$), and speed of processing ($n = 704$). Each intervention group received ten 60- to 75-minute training sessions over 5- to 6-week interval. Cognitive outcome measures comprised a battery of neuropsychologic tests directed at the cognitive domains discussed. Each group improved in the targeted cognitive domain compared to baseline. Twenty-six percent of memory group (effect size 0.26), 74% of reasoning group (effect size 0.5), and 87% of speed of processing group (effect size -1.5) demonstrated significant improvement ($p < 0.001$ for all) immediately after the intervention period. In a five-year follow-up study of 67% of the original sample, Willis et al. (2006) reported that the improvements in cognitive function continued for 5 years following initial intervention ($p < 0.001$ for all groups).

Mohs and colleagues (1998) developed a comprehensive CTI targeting memory enhancement. Participants between the age of 60 and 90 were randomized to receive the CTI ($n = 68$) or a video control group ($n = 74$). The memory training group received nine 90-minute training sessions while the control group watched videos addressing the brain and mind over the same periods. A battery of neuropsychologic surveillance was conducted at baseline assessment and repeated immediately postintervention, 3-months and 6-months postintervention. Results revealed that the CTI group showed significant

improvement in verbal memory immediately following the intervention and at 3-months ($p < 0.03$) and mnemonic memory immediately following the intervention through the 6-month follow up ($p < 0.004$) compared to the control group.

In a repeated measures study design, Cusack, Thompson, and Rogers (2003) delivered a 1-day a week intensive CTI program administered over an 8-week period that consisted of critical thinking, learning and memory, and goal setting to participants ($n = 18$) aged 50 to 84. Mental fitness and cognition outcomes were measured with the CT-MFSS (Cusack-Thompson Mental Fitness Self-Assessment Scale) (Cusack & Thompson, 1998). Results revealed a significant effect on outcomes of creativity ($p < 0.01$), mental flexibility ($p < 0.001$), memory ($p < 0.01$), and level of mental fitness ($p < 0.01$). Although the sample size was small, the study was powered to detect significance in 9 of the 11 outcomes.

In a brain plasticity-based training study by Mahncke and colleagues (2006), 155 older adults living in the community were randomly assigned to 3 groups. One group ($n = 53$) received a computer based cognitive intervention with a focus on memory and speed of processing. The second group (matched active control group $n = 53$) viewed computer educational programs while the control group ($n = 56$) received no contact. The intervention was delivered for 1 hour a day 5 days a week for 8 to 10 weeks. Results showed that only the participants in the computer based cognitive intervention group improved on tasks of working memory ($p = 0.02$) and speed of processing ($p < 0.001$). In addition, this group improved in untrained measures of cognition, global auditory memory ($p = 0.02$) with an effects size of 0.25. Long-term changes were identified using

the digit span forward task and the improvements in these domains were significant ($p = 0.03$) at 3 months post-intervention.

As noted earlier, cognitive interventions have also been studied in adults with mild cognitive impairment (MCI) (Rapp et al., 2002) and individuals with Alzheimer's disease (AD) (Cahn-Weiner, Malloy, Rebok, & Ott, 2003; Davis, Massman, & Doody, 2001; Requena et al., 2004). Cipriani and colleagues (2006) conducted a study utilizing a computer-based cognitive training intervention. Ten AD patients aged 74.1 ± 5.6 years, 10 MCI patients aged 70.6 ± 6.0 years and 3 multiple system atrophy (MSA) patients aged 69.0 ± 9.5 years received two training programs that targeted attention, memory, perception, visuospatial, language, and non-verbal intelligence. Each training program consisted of 13-45 minute sessions held 4 days each week over a 4-week-period. There was a 6 ± 2 -week interval between the two training programs. Cognitive function was assessed at baseline and after both training programs (3-months). The neuropsychological battery included the MMSE (Folstein et al., 1975), phonemic verbal fluency (Novelli et al., 1986), semantic verbal fluency and visual search (Spinnler and Tognoni, 1987), trail making test part A and B (Giovanoli, Del Pesce, Macheroni, & Capitani, 1996), digit symbol test (Wechsler, 1981), and Rivermead behavioral memory test (RBMT) (Wilson, Cockburn, & Baddeley, 1985). The AD group showed significant improvement in MMSE scores ($p = 0.01$) ($\eta^2 = 0.66$), verbal production ($p = 0.036$) ($\eta^2 = 0.17$), and executive functions ($p = 0.05$) ($\eta^2 = 0.5$) when compared to baseline. The MCI group showed significant improvement in behavioral memory ($p = 0.01$) ($\eta^2 = 0.75$) when compared to baseline. In contrast, there were no significant improvements in the MSA group.

In a randomized controlled trial Kinsell and colleagues (2009) investigated the effects of a 5-week cognitive memory intervention on participants with MCI. The intervention was conducted for 1.5 hours each week. Neurologic surveillance was conducted at baseline, 2 weeks and 4 months post-intervention. A total of 54 patients were recruited and randomized to treatment ($n = 26$) and control ($n = 28$) groups. During the study time frame, 4 participants withdrew from the treatment group and 6 withdrew from the control group. Neurologic surveillance included the Prospective Memory Index (modified from the Rivermead Behavioural Memory Test) (Wilson, et al., 1999) and the Strategy Knowledge Repertoire (Troyer 2001). Results showed a significant ($p = 0.02$) medium size group effect ($\eta^2 = 0.14$) in performance of prospective memory and a significant ($p = 0.05$) medium size group effect ($\eta^2 = 0.14$) in performance of strategy knowledge. They concluded that early cognitive intervention for patients with MCI could assist in the cognitive domains of prospective memory and strategy knowledge.

Studies have evaluated cognitive training interventions in the population of patients with traumatic brain injury (TBI). In a feasibility study of cognitive interventions for acquired brain injury, Bergquist, Gehl, Lepore, Holzworth and Beaulieu (2008) investigated the preliminary effect of an internet-based cognitive intervention in 10 participants 20 to 56-years-old (average 45.5) with a history of moderate-to-severe brain injury and evidence of memory impairment. The participants underwent an average of 32 Internet sessions lasting 2 hours each. There was no attrition noted in the 10 participants however, 1 participant missed a single session and one participant missed 2 sessions out of the first 10 sessions. The authors reported that given the lack of attrition during the study, an internet-based CTI was feasible in individuals with TBI.

Studies have also been conducted in patients following stroke. Kaschel and colleagues (2002) conducted a randomized control-group trial comparing the effects of two training programs on memory in stroke patients. Both programs consisted of 30 sessions over a period of 10 weeks. Twenty-one patients were randomized to two different training programs. The control group ($n = 12$) received usual or pragmatic memory training whereas the experimental group ($n = 9$) received imagery-based training. Outcome measures comprised the Wechsler Memory Scale (WMS) (Wechsler, 1945), RBMT (Wilson et al., 1985), Concentration Endurance Test (Spren & Strauss, 1991) and the Memory Assessment Clinics Rating Scales (MAC-S) (Crook & Larrabee, 1990). Measurements were administered at baseline, four weeks after intervention was initiated, immediate post-training, and at three months follow-up. The WMS showed no main effect of time or group. The Concentration Endurance Test was significant ($p < 0.002$) in main effect of time but no main effect of group. The RBMT showed main effect of time ($p < 0.015$) but no group effect. Finally the MAC-S showed a main effect of time ($p < 0.001$) but no group effect. These results suggest that imagery training improves immediate and delayed verbal recall but not visual recall. It was thought that the visual test interfered with patient's own imagery.

A study conducted by Gray, Robertson, Pentland, and Anderson, (1992) evaluated the effectiveness of an attention intervention during the post-acute period of rehabilitation following brain injury (e.g. stroke or TBI). Thirty-one patients with attentional deficits following an acute brain injury, which varied widely from 7 weeks to 10 years post injury were randomized to experimental or control group. The experimental group ($n = 17$) received computerized attentional retraining and the control group ($n = 14$) received

recreational computer use. The intervention was administered in 14 sessions of 75 minutes over a 3 to 9 week period for a total of 17.5 hours of treatment. In the immediate postintervention period the treatment group scored significantly higher on 2 of the 14 outcome measures: the Wechsler Adult Intelligence Scale Revised (WAIS-R) picture completion ($p = 0.03$) (Wechsler, 1981), and PASAT ($p = 0.02$) (Gronwall, 1977). In contrast, at the 6 months follow-up the treatment group showed significant improvement in 6 of the 14 outcome measures: WAIS-R backward Digit Span ($p = 0.007$), WAIS-R Arithmetic ($p = 0.014$), PASAT ($p = 0.01$), WAIS-R Longest String ($p = 0.009$), PASAT Information Processing Rate ($p = 0.02$), and the WAIS-R Block Design ($p = 0.008$). All of these findings indicate that acquired deficits of attention and memory may be modifiable using specific cognitive skills training.

The majority of CTI studies have sought to improve memory skills (Cahn-Weiner et al., 2003; Caprio-Prevette, & Fry, 1996; Mahncke et al., 2006; Mohs et al., 1998; Singer et al., 2003), which is not surprising given that research has reported memory loss as one of the major complaints about aging (McDougall, 1999). There have also been several CTI studies focused on improving attention and speed of processing (Davis et al., 2001; Edwards et al., 2005; Wadley et al., 2006). In addition, a number of studies provide training for multiple cognitive domains (Cusack et al., 2003; Gunther et al., 2003; Loewenstein, Acevedo, Czaja, & Duara, 2004). As reported earlier, Ball and colleagues (2002) randomized patients to receive cognitive training interventions in memory, reasoning, or speed of processing domains. These cognitive domains are essential in performance of activities of daily living. Because of their importance in everyday life, attention, concentration and memory comprise the cognitive focus of the current study.

Several approaches are used for cognitive training including paper and pencil exercises and self-administered handbooks (Andrewes, Kinsella, & Murphy, 1996; Rapp et al., 2002), computerized software (Edwards et al., 2005; Gunther et al., 2003; Mahncke et al., 2006; Singer et al., 2003; Wadley et al., 2006), visual imagery (Dijkerman, Letswaartm, Johnston, & MacWalter, 2004; Kaschel et al., 2002; Page, Levine, Sisto, & Johnston, 2001), use of mnemonics (Cahn-Weiner et al., 2003; Baltes & Kliegl, 1992; Singer et al., 2003), external memory aids (e.g. notebooks, diaries, and calendars) (Koltai, Welsh-Bohmer, & Schmechel, 2001; Loewenstein et al., 2004), practice (Cahn-Weiner et al., 2003; Page, Levine, & Leonard, 2005; Taub et al., 2006), physical exercises (Kramer et al., 2006; Weuve et al., 2004; Yu et al., 2006), and group based interventions (Cusack et al., 2003; Edwards et al., 2005; Mohs et al., 1998; Rapp et al., 2002; Troyer, Murphy, Anderson, Moscovitch, & Craik, 2008). Caprio-Prevette and Fry (1996) utilized a multifactorial approach to cognitive training, as did Cavallini et al. (2003), Davis et al. (2001), and Rasmussen et al. (1999).

The current study administered exercises from The Thinking Skills Workbook (TSW) (Tondat-Ruggeri, Languirand, & Caruso, 2000). This workbook was chosen for several reasons including ease of use for older adults; exercises available in specific cognitive domains of attention, concentration and memory; exercises are geared towards everyday living; exercises are designed to gradually increase level of difficulty; and exercises have been used successfully for patients recovering from brain injury. A pilot survey study by Blundon and Smits (2000) evaluating therapeutic modalities used for patients with TBI reported that 5 of the 20 studies surveyed used the TSW. Carter and colleagues (1983) conducted a randomized control study of cognitive remediation in

acute stroke patients. Patients were randomized to intervention ($n = 16$) or control ($n = 17$) group. The groups did not differ in the cognitive skills pretest performance, or neurologic severity score. The intervention group received paper and pencil exercises from the TSW (Tondat-Ruggeri et al., 2000). The exercises were administered to each individual for 30 to 40 minutes a day, 3 days a week, for 3 weeks. The Barthel Index (Mahoney & Barthel, 1965) was the outcome measure for functional status. The intervention group had significantly higher ($p < 0.05$) pre-test to post-test scores with an effect size of 0.56 compared to the control group. The results of this study suggest that there is a relationship between improved cognitive skills and self-care skills.

The duration of programs varied significantly in terms of hours per session, days per week, number of weeks, and follow-up booster training. Mahncke et al. (2006) delivered the intervention for 60-minutes each day, 5-days each week, for 8-10 weeks. The training program designed by Singer and colleagues (2003) consisted of a total of eight 1-2 hour sessions, scheduled 1-week apart. Cusack et al. (2003) developed an intense program that consisted of eight all-day workshops for 8 continuous weeks. One of the more intensive programs developed by Baltes and Kliegle (1992), consisted of thirty-eight 1-hour sessions over a 16-month period. One of the least intensive programs developed by Andrewes and colleagues (1996) consisted of a single 30-minute session supplemented with self-study homework. In two different longitudinal study Ball et al. (2002), and Rapp and colleagues (2002) reported that booster sessions at 1 year and 3 years were instrumental to successful outcomes. The evidence remains elusive as to the appropriate duration of cognitive training interventions to provide for best outcomes.

The current study required the participants to self-administer the TSW on a daily basis for a total of 6-weeks. The intervention was expected to take between 10 and 20 minutes to complete each day. Given the fact that CTI has not been conducted in the postoperative cardiac surgical patient, the training duration for this study was based on the current literature for cognitive interventions in other cognitively impaired populations. The participants in this study were also undergoing cardiac rehabilitation which requires that they keep a log of daily items (e.g. temperature and wound assessment). Thus, it seemed logical that the TSW be implemented on a daily basis along with other routine postoperative tasks. In order to not burden or tire the recovering postoperative patient the duration of 10 to 20 minutes each day was chosen. Since the dose effect of this intervention is unknown in this population, it was proposed that participants who complete greater than 75% of the TSW were included in the analysis.

This author could not find any specific studies regarding attrition of patients who are undergoing cognitive training interventions. However, investigation of attrition was conducted by evaluating percent withdrawal of patients in treatment group versus control group. In a study by Mahncke and Colleagues (2006) evaluating memory enhancement, 15% of patients in the treatment group withdrew while 5% of patients in the control group withdrew. Rapp et al. (2001) conducted a study in which 24% of patients withdrew prior to randomization to control and treatment group. Following assignment, control (n = 9) and treatment (n = 10) no patients withdrew from the study. Gunther and Colleagues (2003) conducted a computer assisted cognitive training pilot that did not include a control group and overall attrition rate was 24%. In a large randomized, controlled study (N = 2,824) by Ball et al. (2002) patients were assigned to 4 groups (3 treatment and 1

control). Attrition rate for the 3 treatment groups were; 12.6% memory training, 11.1% reasoning training, and 10.5% speed of processing training. The attrition rate for the control group was 9.25%. It would be interesting to conduct an attrition analysis on these studies to assess the difference between study withdrawals in control versus treatment groups.

As discussed previously, a wide variety of outcomes measures have been utilized to evaluate cognitive training interventions. The majority of studies used batteries of neuropsychological tests designed to test cognitive function in the specific domains exercised. For example; Mahncke and colleagues (2006) administered the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) (Randolph, 1998), which consists of a group of 12 assessments of auditory cognition and memory, while Cusack and colleagues (2003) developed the Cusack-Thompson Mental Fitness Self-Assessment Scale. The MMSE (Folstein, Folstein, & McHugh, 1975) is widely used to assess global cognitive function (Ball et al., 2002; Edwards et al., 2002; Wadley et al., 2006). The Telephone Interview for Cognitive Status (TICS) (Brandt et al., 1988) was developed to ease the costs and time demands of person-to-person interviews particularly in large-scale studies. The TICS was chosen for this study to ease patient burden in terms of time constraints as well as the fact that it can be performed over the phone while the patient is home. It has been widely used in similar populations such as; studies with older adults (Weuve et al., 2004), patients with MCI (Lines, McCarroll, Lipton, & Block, 2003) and patients post-stroke (Barber & Stott, 2004).

In addition to neuropsychological tests, several studies have measured cognitive processes related to functional status and quality of life to determine if performance

transfers to every day function. In the ACTIVE study, Ball and colleagues (2002) utilized the ADL and IADL from the Minimum Data Set – Home Care (MDS-HC) (Morris et al., 1997). Cavallini and colleagues (2003) administered the Self-Efficacy Questionnaire (De Beni, Mazzoni, & Pagotto, 1996) to evaluate memory performance in everyday situations. Cipriani et al. (2006) measured functional status and quality of life through the advanced activity of daily living (AADL) (Reuben, Laliberte, & Hiris, 1990) and the short form health survey (SF-12) (Ware, Kosinski, & Keller, 1996). Salazar and colleagues (2000) evaluated ability to return to work and individual fitness for military duty in a cohort of traumatic brain injury patients and in a similar population, Sarajuuri et al. (2005) evaluated status of productivity defined as “working, studying, or participating in volunteer activities”. Overall, the published studies support the effectiveness of several forms of cognitive training in many different patient populations.

Regulator

Postoperative Cognitive Dysfunction

Bedford (1955) described dementia following surgery under general anesthesia. Although hypotension was noted on the anesthesia record, it was thought that the anesthetic drugs were responsible for the cognitive deficits. Studies that followed investigated the role of anesthetics in POCD, in particular the physiologic effects of anesthesia such as hypotension and hypoxia (Bekker & Weeks, 2003; Dodds & Allison, 1998; Moller et al., 1998), and specific anesthetic agents (Ancelin et al., 2001; Farag et al., 2006; Kojima & Narita, 2005; Rasmussen et al., 1999). In the 1980’s studies began to evaluate the role of catecholamines and cholinergic transmission in the central nervous system (Linstedt et al., 2002; Practico et al., 2005; Rasmussen et al., 2005). Many studies

have reported that cardiac surgery and the potential for cerebral embolism as well as use of cardiopulmonary bypass is strongly associated to POCD (Ho et al., 2004; Rubens et al., 2007; Stump, Rogers, Hammon, & Newman, 1996; Westaby et al., 2001).

The basis for POCD is a documented decline in cognitive function evaluated by repeated neuropsychological tests, although the threshold of such change has not been conclusively determined (Murkin et al., 1995). The literature suggests that POCD is difficult to evaluate based on several facts. First, neuropsychological tests should be selected based on the fact that they measure a range of cognitive functions.

Unfortunately, there are multiple batteries of tests that have very different methods. Second, the intervals between test sessions vary as does the endpoints for analysis. Third, the statistical analysis procedures are variable. Finally, the definitions used to describe neurologic deficits vary (Rasmussen et al., 2001). In addition, there has been notable discrepancy in subjective complaints versus test performance related to POCD (Dijkstra et al., 1999).

Measurements of Cognitive Function

Many instruments exist to measure cognitive functions with studies most frequently reporting use of the following: Mini Mental Status Examination (Folstein et al., 1975), Trailmaking Test Part A & B (Reitan, 1955), Rey Auditory Verbal Learning and Memory Test (Rey, 1964; Schmidt, 1996), and the Grooved Pegboard test (Klove, 1963). Other instruments used were the Stroop Color Word Interference Test (Stroop, 1935; Jensen & Rohwer, 1966), Digit Span and Digit Symbol subtest of the WAIS-R (Wechsler, 1981), California Verbal Learning Test (Delis, Kramer, Kaplan, & Ober, 2000), Controlled Oral Word Association (Benton & Hamsher, 1989; Strauss, Sherman,

& Spreen, 1998), Wisconsin Card Sorting Test (Grant & Berg, 1948), Randt Memory Test (Randt & Brown, 1986), Wechsler Memory Test (Wechsler, 1945; Wechsler, 1997), Benton Visual Retention (Sivan, 1992), Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983; Goodglass & Kaplan, 2001), Short Orientation Memory Concentration Test (Leshner & Whelihan, 1986), and the Bells Cancellation Task (Gauthier, Dehaut, & Joannette, 1989). Some of the studies included measurements of depression and anxiety including, Hospital Depression and Anxiety Scale (Zigmond & Snaith, 1983), Epidemiological Studies Depression Scale (Radloff, 1977), as well as the Health Complaints Scale (Eriksen, Ihlebaek & Ursin, 1999), and the Functional Status Questionnaire (Jette et al., 1986).

As noted, the number of neuropsychologic batteries administered to categorize POCD has varied greatly. Some researchers suggest that there is an increase risk of a type I error when more tests are used in the test batteries (Newman et al., 2001; Selnes et al., 2001). According to consensus statements, a wide range of cognitive function should be assessed by neurologic surveillance (Murkin et al., 1995). However, consideration of clinical constraints, medical management, and limited availability for assessment is necessary. For the current investigation several considerations occurred in selecting the tool for which to measure cognitive function. The majority of the patients recruited for this study were consented either over the phone the evening before surgery or on admission, the morning of surgery. The TICS (Brandt et al., 1988) can be administered over the phone or in person. It takes approximately 10 minutes to complete which decreases patient burden and allows the preoperative staff the time necessary to prepare the patient for surgery. In the postoperative period, patients are potentially experiencing

fatigue and pain. The brief duration for administration of the TICS makes it feasible to conduct during postoperative recovery. Finally, the patients do not need to come in to the hospital or be burdened by a visit to their homes for the 6-week and 3-month follow up. After close evaluation of the different neuropsychological tests available for examining cognitive behavior, the TICS was chosen as the best fit for this study.

The TICS was designed to be administered via telephone or face-to-face and is indicated when clinical follow up is burdensome to participants. In addition, it is a test of global cognitive status. The test includes 11 items assessing orientation to time and place, respective and expressive language functions, short-term verbal memory (recall), calculation and verbal extraction. The total number of correctly answered items is used as the overall score with a maximum total score of 41 (Brandt et al., 1988). A study by Crooks, et al., (2006) concluded that the TICS evaluated global cognitive function and was sensitive to distinctive cognitive domains including memory and attention, which are the cognitive domains requiring evaluation in the current study. The TICS and TICS-modified (M) were found to be practical and valid for use of assessing cognitive function in community outpatients following stroke (Barber & Stott, 2004). De Jager, Budge, and Clarke (2003) reported that when comparing the TICS-M with the MMSE and the Cambridge Cognitive Examination (CAMCOG) (Huppert, Brayne, Gill, Paykel, & Beardsall, 1995), the TICS was less constrained by a ceiling effect. They concluded that the TICS-M is a reliable instrument in the assessment of global cognitive function in both research and clinical practice.

Timing of Assessments

All of the POCD studies reviewed assessed neurologic function at baseline prior to surgical procedure and at regular intervals following surgery. The majority of the studies assessed patients 5 to 7 days postoperatively or upon discharge from the hospital, and 3 months after surgery (Rubens et al., 2007; Rasmussen et al., 2001; Selnes et al., 2003; Silbert et al., 2006; Westaby et al., 2001). Other studies assessed patients at 6 weeks, 4 months, 6 months, and 3 years after surgery (Grimm et al., 2003; Ho et al., 2004; Selnes et al., 2005; Stroobant et al., 2005; Zimpfer et al., 2004). Three studies conducted longitudinal assessment that followed patients for 5 years after surgery. A study by van Dijk and Colleagues (2007) compared off-pump (n = 123) versus on-pump (n = 117) patients and reported that 50.4% of both groups had cognitive decline 5 years after coronary artery bypass graft (CABG) surgery. Selnes et al. (2001) reported a significant decline over a one to five-year period following CABG surgery in all cognitive domains with the exception of attention and executive function. Newman et al. (2001) assessed patients at 6 weeks, 6 months, and 5 years after CABG surgery and results suggest that there is a pattern of early recovery at 6 months followed by a later decline at 5 years.

The timing of assessments is an important issue. Preoperative neuropsychological assessment is crucial to obtain baseline cognitive function status. Early postoperative assessment allows for early diagnosis and immediate intervention. Postoperative assessment of decline in performance has generally been measured upon discharge from hospital (between 4 and 7 days postoperatively). If assessed too early after surgery (e.g. 24 hours), some patients may exhibit postoperative delirium, which as noted is a much

more transient problem than POCD (Bucerius et al., 2004; Newman et al., 2007). In addition, anesthesia, stress, fatigue and pain may alter performance on neurocognitive tests. Consensus groups suggest that neuropsychologic testing should be performed preoperatively to provide a baseline assessment, in the immediate postoperative period, and 3 months later (Murkin et al., 1995). For the purpose of this study, neuropsychologic testing was assessed in accordance with Murkin and Colleagues (1995) consensus with an addition of a 6-week test to assess potential immediate effect of the CTI.

Criteria for Cognitive Decline in POCD

To date, studies have used different criteria to diagnose cognitive decline. Mathew et al. (2003) and Newman et al. (2001) defined cognitive decline to be significant if there was a decrease in one standard deviation (SD) from pre-operative to postoperative results on 1 of 4 cognitive factors. In two separate studies; Rasmussen and colleagues (2002a) and Rasmussen, Sperling, Abildstrom, and Moller (2002b) cognitive decline was defined as combined z-scores of 1.96 or more; or if two z-scores in individual tests were 1.96 or more. Both studies by Selnes and colleagues (2003; 2005) defined cognitive decline as a negative change in SD by 0.5 in one or more cognitive domains; if any of the three cognitive tests showed a negative change in SD by 1; or if there was a 20% negative change in any of the neurologic tests. Other studies used the following criteria; (1) a 20% decrease from baseline in two or more test (Stroobant et al., 2005), (2) a 20% decrease from baseline on 20% of the test scores (Thorton et al., 2005), and (3) greater than 1 SD deterioration from baseline (Zimpfer et al., 2004). Five of the studies did not define the criteria used to assess cognitive decline.

As noted, the choice of neuropsychological tests accounts for some of the variation in reported incidence of POCD. Additional variation can be attributed to the statistical methods chosen for evaluating cognitive changes. The two major methods for evaluating cognitive changes are group comparisons or individual variation. Consensus groups prefer the use of individual variation in POCD research because it allows for a more accurate account of the incidence of POCD by detecting change in individuals and not groups (Murkin, Stump, Blumenthal, & McKhann, 1997). In addition, the statistical analysis relating to criteria used to define cognitive decline varies. Mahanna et al. (1996) utilized several different criteria on the same subjects test results and reported a range of POCD from 20 to 70%. Statistical analysis used to determine cognitive decline should be based on the following factors: 1) the psychometric properties of the neuropsychologic tests and 2) the methodological design of the study (Collie et al., 2002).

The majority of the studies revealed significant decline in cognitive function 5 to 7 days following surgery. Newman and Colleagues (2001) assessed cognitive decline after CABG (n = 261) and found the incidence of decline to be 53% at discharge. In a randomized, double-blind study conducted by Rubens et al. (2007) patients were randomized to control group, which received unprocessed blood (n = 134) versus treatment group, which received cardiectomy blood (n = 132). At time of discharge the incidence of POCD was 45.3% for the treatment group and 39% for the control group. As noted earlier, Stroobant and Colleagues (2005) reported an incidence of 60% cognitive decline 6 days after CABG surgery in a sample of 63 patients. Two studies were significant for cognitive decline in 36% of patients 6 weeks after surgery (Mathew et al., 2003; Newman et al., 2001). Other studies showed statistically significant cognitive

decline in patients following CABG surgery at different follow-up intervals ranging from 15.9% at 3 months (Rubens et al., 2007) to 48.8% at 4 months (Zimpfer et al., 2004). Grimm and Colleagues (2002) reported a statistically significant increase in cognitive decline in patients receiving a mechanical valve replacement (n = 20) versus mitral valve repair (n = 20). The study by Stroobant et al. (2005) reported that cognitive impairment persisted at 6 months follow-up in 31.1% of the patients in the on-pump group (n = 32) and 9.1% of the patients in the off-pump group (n = 18). In a much larger study (n = 939), Ho and Colleagues (2004) reported a significant cognitive decline in 36.6% of patients 6 months following CABG surgery.

In the longitudinal studies conducted, Zimpfer, Czerny, Kilo, Kasimir, and Madl (2002) reported a statistically significant cognitive impairment in patients who received a biological aortic valve at 7 days 4 months (n = 30) as compared to age-matched controls (n = 30) undergoing CABG. In a follow-up study, Zimpfer, Czerny, Schuch, Fakin, and Madl (2006) reported no long-term effects (3 years after surgery) on neurocognitive function in patients who received an AVR compared to age-matched non-surgical controls. In contrast, Zimpfer et al. (2004) reported significant neurocognitive deficits in 50% of CABG patients at a 3-year follow up. Van Dijk and Colleagues (2007) conducted a multicenter randomized controlled trial comparing cognitive decline 5 years after off-pump (n = 142) versus on-pump (n = 139) CABG surgery and found 50.4% decline in both groups. In addition, Newman et al. (2001) found cognitive decline in 42% of patients 5 years after surgery.

In summary, the literature suggests that POCD is difficult to evaluate based on several facts. First, neuropsychological tests should be selected based on the fact that they

measure a range of cognitive functions. Unfortunately, there are multiple batteries of tests that have very different methods. Second, the intervals between test sessions vary as does the endpoints for analysis. Third, the statistical analysis varies. Finally, the criteria for defining neurologic deficits vary greatly among studies (Rasmussen et al., 2001). Moreover, there has been a notable discrepancy in subjective complaints versus test performance related to POCD (Dijkstra et al., 1999). For this study the TICS neurologic surveillance was chosen because of its ability to measure global cognitive function as well as ease of use. The intervals between test sessions were based on consensus (Murkin et al., 1995). Finally a within-subjects and between-subjects analysis was chosen to evaluate individual changes and group differences.

Cognitive training studies demonstrate tremendous potential for cognitive improvement. As noted, researchers use a vast armamentarium of cognitive training interventions to address the specific needs of the population studied. In addition, the Internet and advances in computer technology, has created new possibilities for advanced intervention. However, advances in technology may create several challenges for older adults and patients with cognitive impairment. Many of these studies have limitations for usefulness, more specifically the need for educators, classrooms, computers and other training materials. The TSW (Tondat-Ruggeri et al., 2000) has the advantage of providing for a self-administered, paper and pencil, practice approach to cognitive interventions.

As noted, the majority of studies focus on training a single ability. However, in order to maximize patient potential particularly in terms of ADL, it would seem that multiple domains should be intervened. Because persons with POCD exhibit cognitive

impairments in different domains, it is imperative to continually evaluate cognitive enhancing interventions that are specific to the effected domains as well as the complex interactions of cognitive function.

CHAPTER 3

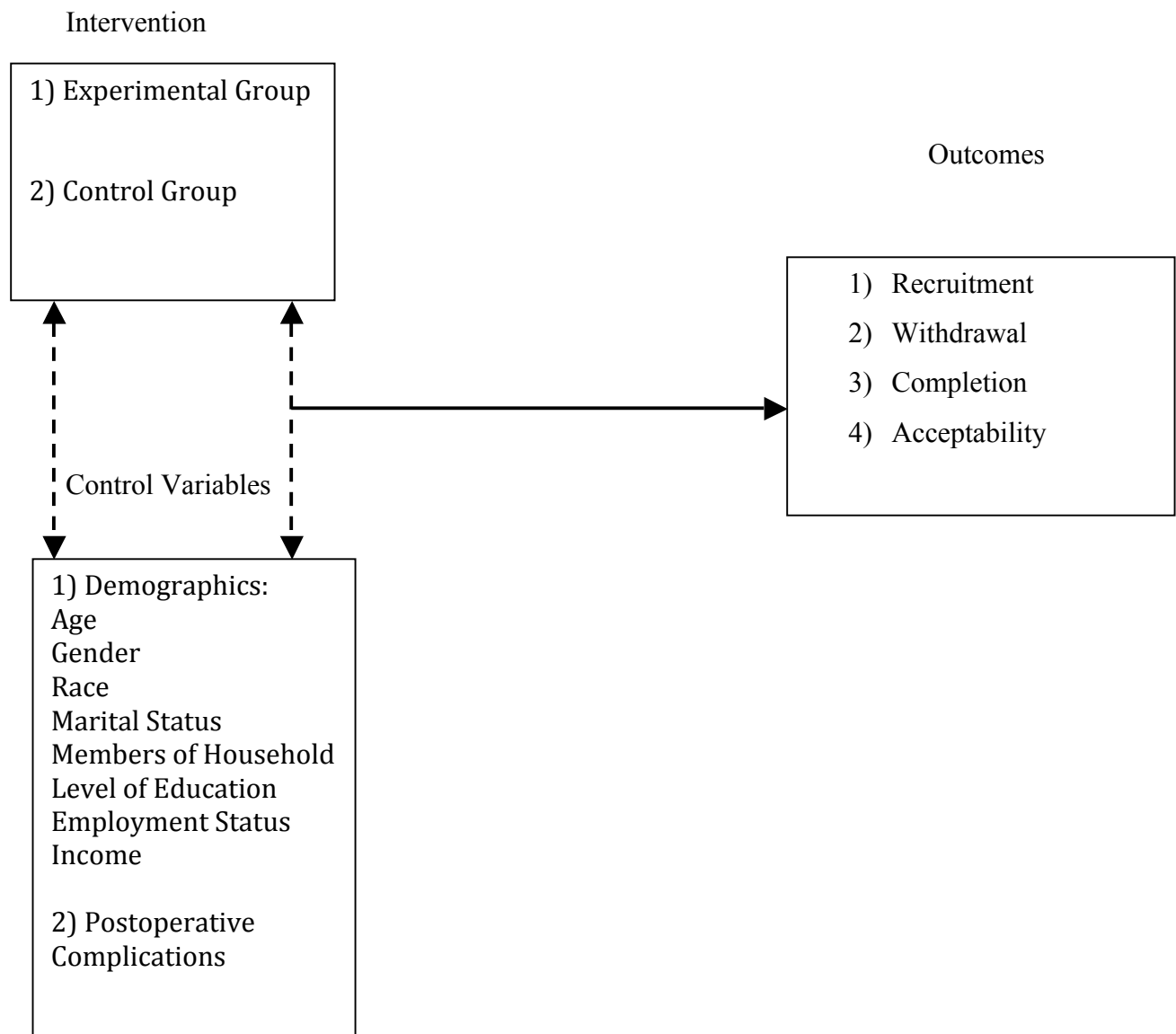
METHODS

This chapter provides an overview of the design, sample, setting, and testing procedures used in the current investigation. The data collection instruments and CTI are presented with a discussion of psychometrics as appropriate. The study protocol is presented followed by a discussion of the data analyses. The chapter concludes with a statement of human subject protection, confidentiality, withdrawal of participants, participant payment, and potential benefits and risks posed by this investigation.

Research Design

The primary aim of this study was to examine the feasibility and acceptability of a CTI for postoperative cardiac surgical patient. Feasibility was examined by conducting an attrition analysis to compare percent of attrition between groups. A one-group post-test design was used to examine the feasibility and acceptability of a six-week CTI in postoperative cardiac surgical patients (see Figure 4). The secondary aim was to pilot test the preliminary effect of the CTI. A repeated measures, randomized controlled, single-blind design was used to test the hypothesis that following cardiac surgery, patients who receive a 6-week CTI when compared with those who receive usual care will demonstrate a significantly greater improvement in cognitive status when comparing discharge scores to scores at 6 weeks and 3 months postoperatively.

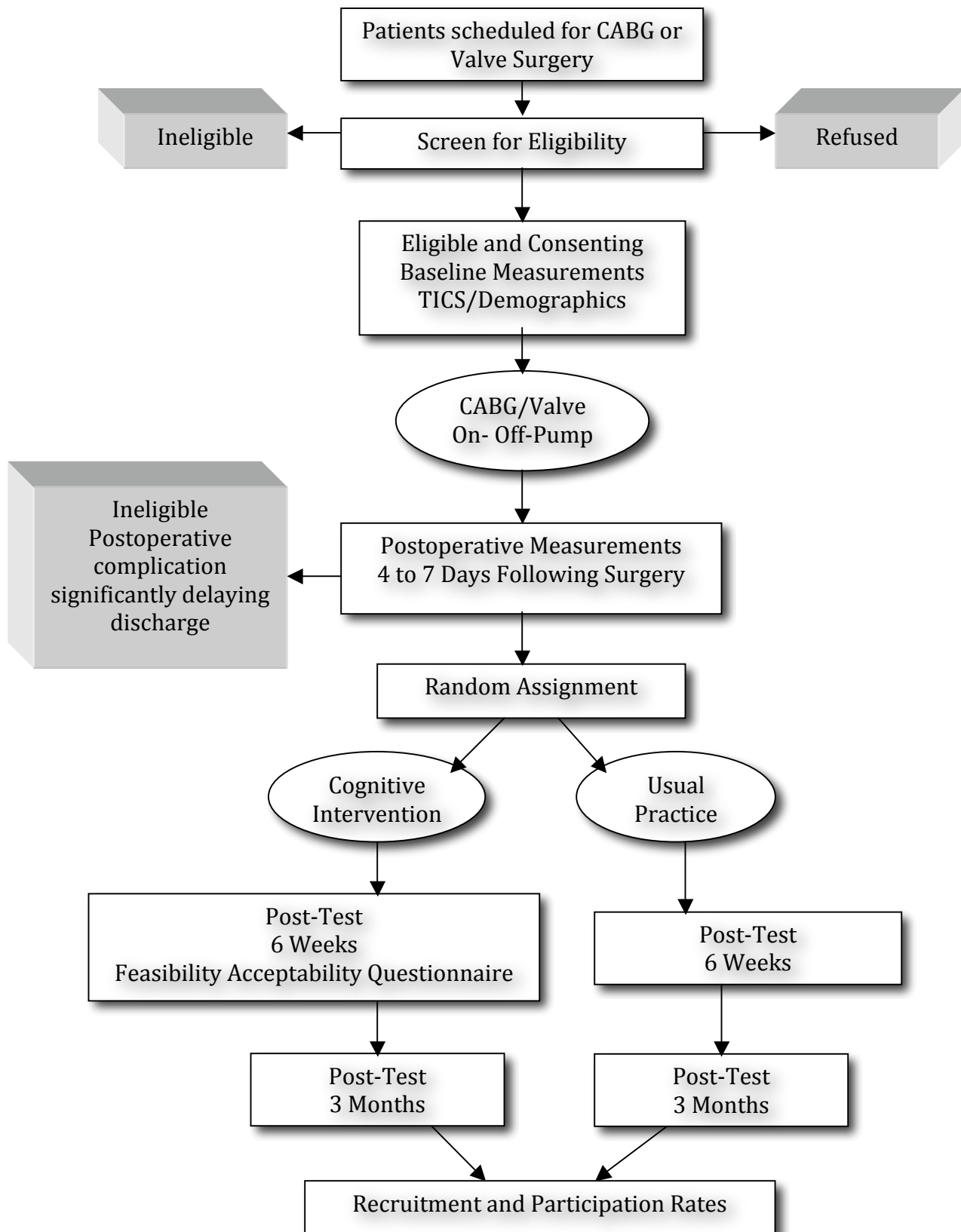
Figure 4. Conceptual Model for Feasibility and Acceptability Study



Sample

Subjects were recruited from a clinical site involved in a larger prospective study of neuromonitoring and cognitive outcomes. The target population for the study was patients undergoing cardiac surgery (valve or coronary artery bypass graft as well as on pump or off pump). Patients who were willing to participate in the sub-study were chosen if they meet inclusion criteria and were randomly assigned to experimental or control group. Subject inclusion criteria were: 1) English-speaking patients, 2) greater than 40 years of age, 3) undergoing general anesthesia for cardiac surgery and, 4) willing to participate in the study. Exclusion criteria were: 1) severe auditory or visual disturbances, 2) poor English comprehension, 3) physiologic disorders of the CNS (e.g. AD, Parkinson's disease, Multiple Systems Atrophy) that would limit the patient's ability to participate, 4) patients who reported having participated in a prior cognitive training study and, 5) patients whose discharge date was significantly delayed (greater than 2 weeks) secondary to postoperative complication. Patients who were readmitted to the hospital during the intervention phase secondary to postoperative complications were withdrawn from the study (figure 5).

Figure 5. Recruitment Protocol



Power

Estimate of required sample size was based on previous studies of cognitive training (Carter et al., 1983; Mahncke et al., 2006) and studies examining the effects of extended practice on cognitive performance (Baltes, Kliegl, & Dittmann-Kohli, 1988; Baltes, Sowarka, & Kliegl, 1989), which found an effect size ranging from 0.5 to 1.0. The initial power analysis was conducted when it was thought that the study would be utilizing a mixed model ANOVA with repeated measures and within-between interaction. Given the four measurement time points and 2 groups, the minimum sample size needed to achieve a power of 0.80 with an alpha of 0.05, a medium effect size of 0.5, and a minimum correlation among repeated measures of 0.5, was estimated to be 42 (Maxwell & Delaney, 2004, pp 641). Previous studies examining POCD in the cardiac population have an estimated attrition rate of 15% and previous studies examining CTI in the aging adult population have an estimated attrition rate of 16%. Based on previous studies in both of these populations, it was anticipated that there would be an attrition rate of up to 20%. The sampling plan included an over-sampling of 20% to ensure adequate power at each of the data collection points, resulting in a target sample of Fifty-three participants. Given assumptions of ANOVA were violated, non parametric statistics including two Kruskal Wallis *H* tests for independent samples at each assessment period and two Wilcoxon signed ranks for related samples for each group were also conducted. The study was not powered to detect statistically significant results increasing the risk of a Type II error however the primary focus of the study was to assess the feasibility and acceptability of a theory-based CTI.

Post hoc analysis revealed an effect size of 0.15 and a power analysis was conducted using G*Power 3.1 (Erdfelder, Faul & Buchner, 1995). Given the four measurement time points and 2 groups, the minimum sample size needed to achieve a power of 0.80 with and alpha of 0.05, a small effect size of 0.15, and a minimum correlation among repeated measures of 0.5, was estimated to be 62 (see Table 2). The sampling plan would include an over-sampling of 20% to ensure adequate power at each of the data collection points, resulting in a target sample of Seventy-Five participants.

Table 2. F tests - ANOVA: Repeated measures, within-between interaction

Analysis: Post hoc: Compute achieved power			
Input:	Effect size f	=	0.15
	α err prob	=	0.05
	Total sample size	=	62
	Number of groups	=	2
	Number of measurements	=	4
	Corr among rep measures	=	0.5
	Nonsphericity correction ϵ	=	1
Output:	Noncentrality parameter λ	=	11.1600000
	Critical F	=	2.6547918
	Numerator df	=	3.0000000
	Denominator df	=	180
	Power (1- β err prob)	=	0.8007043

Setting

Recruitment took place at a community hospital in Northern New England. The site was selected based on the number of potential participants and the support of Cardiothoracic Surgical Associates, Northern New England Cardiovascular Disease Study Group (NNECDSG) and the Agency for Healthcare Research and Quality

(AHRQ). Data from the admissions office indicated that there would be a sufficient volume of patients having cardiac surgery to achieve the desired number of patients for the study. Eligibility screening, baseline neuropsychological assessment and discharge neuropsychological testing was conducted on site. The patient received instructions on how to complete the CTI and a practice session was conducted prior to discharge. The CTI was then self administered at the patient's home and mailed to the investigator. The feasibility and acceptability questionnaire was completed by the patient at the completion (6 weeks) of the CTI and mailed to the investigator along with the final CTI module. Follow-up neuropsychological assessments were conducted via telephone at the designated time.

Data Collection Procedures

This study was a sub-study (part B) to an ongoing prospective trial of neuromonitoring and cognitive outcomes. The primary study is titled Redesigning Cardiac Surgery to Reduce Neurologic Injury. During surgery, cerebral blood flow is monitored by transcranial Doppler and embolic events are documented. All study data (e. g. neurologic surveillance) was the same for both studies and there is no indication that the primary study affected the outcomes of this study. General overviews of enrollment and study design are as follows. Participants were identified by the cardiac surgical office staff in coordination with the surgeon of record. The surgeon introduced the primary study (part A) to each patient and the study coordinators discussed the study (part A and part B) in detail. The patients chose to participate in part A, part B, or both components of the study. The participants who meet eligibility criteria were consented and enrolled by the PI of this study in coordination with the study coordinators. A total of 53 patients

consented to be in the study. After obtaining informed consent, the demographic questionnaire and the preoperative baseline TICS were administered. Following surgery the postoperative discharge TICS was administered between 4 and 7 days and the patients were randomized to intervention group or usual care group. The participants randomized to the intervention group, received the cognitive training intervention, a set of instructions regarding the intervention, feasibility and acceptability questionnaire, 6 addressed stamped envelopes, and a form to complete scheduling of a practice session, follow-up telephone calls (~ once a week) and 2 follow-up tests points. The participants randomized to the usual care group, received information to complete scheduling for the 2 follow-up tests points. Table 3 displays recruitment and attendance rates.

Table 3. Recruitment and Participation Rates

	N	% rate
Invitations to participate in the study	68	100
Participants excluded (Did not meet criteria for the study)	4	6
Signed consent forms	53	83
Participants withdrawn after first assessment	1	2
Participants who completed the 6-week CTI	23/27	85
Participants who completed 6-week assessment	44	83
Participants who completed 3-month assessment	45	85
Participants who completed Feasibility and Acceptability Questionnaire (Treatment group)	23/27	85
Participants excluded from final results secondary to death	2	4

Randomization

In order to ensure random assignment and equal numbers of participants in each group, blocked randomization was conducted. Blocked randomization is typically used to ensure close balance of the numbers of participants in each group at any given time during the study while continuing to conceal treatment allocation from the observer. The block size must be divisible by the number of groups in the study (Saghaei, 2004). For this study the blocks were in groups of 4 to balance assignment at frequent intervals. The blocked assignments were generated on paper in advance and accessible to the researcher who was responsible for administering the intervention. An excess number of assignments were generated and used sequentially. Sixty sequentially numbered envelopes were prepared. Each participant recruited was given the next sequential number, and the envelope was opened to determine his or her allocation.

Blinding

At preoperative baseline (pretest) and postoperative discharge (posttest), prior to randomization, the study coordinators and/or the principle investigator performed the neuropsychologic surveillance. The principle investigator was aware of treatment allocation. The patients were also aware of treatment allocation therefore it was not possible to blind them. The study coordinators and research assistants were blinded to treatment allocation and were therefore responsible for conducting the 6-week and 3 month follow up neuropsychologic surveillance. The participants were instructed to not reveal the treatment allocation to which they were assigned. The participants all followed through on this request.

Instruments

Demographic Questionnaire

An 8 item demographic questionnaire (Appendix C) was used to collect data on the following variables: age, gender, race, education level, marital status, members of household, employment status, and level of income. On a separate page, participants were asked to include a telephone number and convenient calling time in the event that the principle investigator or research assistants needed to contact them with questions about missing or unclear data and for follow up neurologic surveillance.

Telephone Interview for Cognitive Status Questionnaire

The TICS is a widely used standardized test of global cognitive function that is easy to administer and score (Brandt et al., 1988). The TICS can be administered via telephone or in person by either a qualified and appropriately credentialed professional or a professional that has been trained and supervised by an appropriately credentialed professional. The TICS is indicated when clinical follow up is burdensome to participants. The test includes 11 items assessing orientation to time and place, respective and expressive language functions, short-term verbal memory (recall), calculation and verbal extraction. The total number of correctly answered items is used as the overall score with a maximum score of 41 (Brandt et al., 1988).

Internal consistency yielded a reliability coefficient of 0.75 (Black et al., 2003). Brandt and Colleagues (1988) reported a test-retest reliability coefficient of $r = 0.97$ in a study examining AD patients. The TICS strongly correlated with the MMSE covering similar cognitive domains with a greater sensitivity in the assessment of memory (Lezak

et al., 2004). In a study of 16 AD patients and 33 controls, Brandt et al. (1988) reported a sensitivity of 94%, a specificity of 100% and high concurrent validity ($r = 0.94$).

Qualitative interpretation of the TICS scores is presented in Table 4. TICS scores higher than 33 indicate that cognitive impairment is unlikely whereas scores less than 25 indicate cognitive impairment. For the participants that scores fall between 26 and 32, cognitive impairment may or may not be present.

Table 4. Suggested Qualitative Interpretive Ranges for TICS Total Scores

Qualitative interpretive range	TICS Total score range
Non-Impaired range – Cognitive impairment is unlikely	33-41
Ambiguous range- Cognitive impairment may or may not be present, depending on examinee's age education, history, etc.	26-32
Mildly Impaired range	21-25
Moderately to Severely Impaired range	≤ 21

Note. The interpretation of a Telephone Interview for Cognitive StatusTM (TICS)TM Total score (or any cognitive test score) must consider the person's prior and current levels of functioning. Screening tests for cognitive impairment, including the TICS and the Mini-MentalTM State Examination (MMSETM), are sensitive to age, education, sensory impairment, motor deficits, etc. These interpretive guidelines must be used with caution and should not override professional judgment.

Reproduced by special permission of the Publisher, Psychological Assessment Resources, Inc., 16204 North Florida Avenue, Lutz, Florida 33549 from the Telephone Interview for Cognitive Status by Jason Brandt, Ph.D. and Marshal F. Folstein, M.D., Copyright 1987, 2003. Further reproduction is prohibited without permission of the Publisher.

Acceptability and Feasibility Questionnaire

There are no specific rules to guide measurement of feasibility and acceptability of modified interventions (Vandelandotte & De Bourdeaudhuij, 2003). However, in a report of measuring outcomes by Andrews, Peters, and Teeson (1994), feasibility was defined as having 3 dimensions: 1) applicability is the degree to which the intervention addresses what is important to the participant, 2) acceptability assesses the ease to which the participant can use the intervention and, 3) practicality, which includes the costs of implementation of the intervention. For the purpose of this study feasibility was assessed using recruitment and participant withdrawal versus completion rates at the different time frames of the study. Feasibility and acceptability of the intervention was evaluated using quantitative feedback on the Feasibility and Acceptability Questionnaire (Appendix D). The questionnaire consists of 15 items related to the cognitive intervention and is based on a 5 point Likert scale (Likert, 1932) in which an attitude scale is provided for participants to select an option from a specific range (e.g. 1 = ‘strongly disagree’ to 5 = ‘strongly agree’). Questions 3-8 pertain to acceptability, questions 9-10 pertain to feasibility, questions 1, 11-13 pertain to perceived benefit, questions 2 and 14 pertain to satisfaction and question 15 is an overall evaluation.

Thinking Skills Workbook

The cognitive training intervention utilized for this study consisted of assigned modules from *The Thinking Skills Workbook: A Cognition Skills Remediation Manual for Adults* (Tondat-Ruggeri et al., 2000). The workbook was created to assist adults with alterations in cognitive function including; cognitive dysfunction from stroke, traumatic brain injury or disease processes. It has also been used in normal aging populations. The

cognitive domains of attention, concentration and memory are affected in these populations as well as in the population of patients with POCD. Research suggests that cognition may be enhanced by utilization of the procedures as outlined by the text in particular, by utilization of demonstration, repetition, and practice (Carter et al., 1983; Carter, Oliveira, Duponte, & Lynch, 1988). Exercises were chosen for the specific cognitive domains affected by POCD including: 1) attention, 2) concentration, and 3) memory. The cognitive skills that are provided in this workbook range in difficulty from simple tasks to more complex tasks.

Attentional behavior exercises began with letter-by-letter focusing and left to right eye movements, and progressed to more difficult visual performance tasks such as word and number finding. Attention must be coupled with the ability to concentrate. To improve concentration skills the exercises began by focusing on simple and familiar details and progressed to very complex designs. Memory exercises began with item recognition and short recall lists that progressed to longer, more complex lists and paragraphs.

Attention

The attention exercises began with scanning and matching (Appendix D). The initial exercises have bold margins, which assists the reader to move in a left to right manner. There is a single letter or number at the top of the page with rows and columns of letters or numbers beneath it. The participant was to identify all other letters or numbers on the page that corresponded to the target letter or number. The participant was asked to start with the left-hand margin and read across the page to the right-hand margin so that no target letter or number would be missed. As the exercises increased in

difficulty the margins were removed to evaluate whether the participants could scan from left to right without assistance. The next level of difficulty was word finding. The participant was to locate a target word or words in a group of words. This exercise increased in complexity as the participant was given a group of words and was asked to locate the words in a paragraph.

Concentration

The initial exercises allowed the participant to concentrate on broad visual details and progress to finer details (Appendix D). Exercises began with matching objects. There was a single object at the top of the page with a set of objects below it. The participants were instructed to find and circle each of the objects that matched the one at the top. The exercise progressed in difficulty as objects that match the one at the top were positioned differently. The more complex exercises required the participant to apply advance visual concentration by completing pictures, copying, and finding map locations. For picture completion the participant was given a pair of pictures in which one picture was complete and the other was missing a part and the participant was instructed to draw-in the missing detail. The participant was then given a page of shapes and was instructed to copy the shapes. Finally, the participant was asked to find locations on a map. A map was presented to the participant along with directions (e.g. How would you get from Mountain View Rd. to Roy Rd.?) and the purpose of the exercise was to draw the shortest possible path between the two points.

Memory

Memory exercises began with picture recognition (Appendix D). The participant was asked to look at a picture for 5-10 seconds (later exercises required more time) and

was instructed to turn the page over and identify the picture from an assortment of pictures provided. The exercises increased in difficulty with the addition of words and numbers instead of pictures. Memory recall was exercised as the participant observed a page of pictures for 30 seconds, then the participant turned the page over and wrote down what he/she had recalled. These exercises became more complex with the introduction of words and numbers.

Protocols

All eligible participants received routine preoperative and postoperative care provided by the study site. All participants were offered enrollment in the in-hospital Phase I Cardiac Rehabilitation Program (CRP). A common set of discharge criteria were used to determine the patient's readiness for discharge with the fourth to seventh postoperative day targeted as the day of discharge. All patients undergoing cardiac surgery received the same postoperative educational activities and materials from the study site. The content of the postoperative education program includes specific information related to the surgical procedure, immediate postoperative needs and introduction to cardiac risk factor modification. This included assumption or maintenance of heart healthy behaviors such as diet, exercise, stress management, medications, and smoking cessation. Education was provided in the hospital via a video program and companion booklet. The nursing staff of the cardiac surgical unit provided the patient with discharge instructions and individual educational sessions. Families were invited to attend the Family Resource Group, a discussion and information providing session offered by the cardiac rehabilitation department.

Intervention Group

Participants randomized to the intervention group received the routine postoperative care, patient education, and support as described above. Their contact with study personnel occurred at enrollment, postoperative discharge, and scheduled phone calls (~ once a week) during the intervention phase. In addition, follow-up phone calls were conducted at 6 weeks and 3 months to complete the neurologic surveillance.

The participants assigned to receive the CTI were given a TSW, which includes exercises and instructions to allocate which exercises were to be performed on each day. The PI guided the participant through an example workbook, thoroughly explaining the instructions for self-administration of each of the exercises in each of the cognitive domains (e.g. attention, concentration, and memory). Participants then practiced self-administration of the daily exercises in each domain under the supervision of the PI who provided immediate feedback.

After the participants successfully reviewed the modules and questions were addressed, they received an educational booklet, which also offered guidelines for timing of CTI (Appendix D). Each module was to be completed in the early morning when patients are most likely to be rested and alert (Edwards, Waterhouse, & Reilly, 2007; Lezak et al., 2004). One module was completed each day for 6 consecutive weeks. Each module takes approximately 10 to 20 minutes to complete. The level of difficulty and duration of the CTI is based on the effects found in previous research (Ball et al., 2002; Cahn-Weiner et al., 2003; Davis et al., 2001). All modules are to be completed by the participant with no outside assistance. The participants signed a “declaration of non-collaboration” on the first page of each module to verify this (Appendix D). At the end of

each week, the completed modules were mailed to the project office using self-addressed envelopes with prepaid postage. Since the dose effect of this intervention is unknown in this population, it was proposed that participants who complete greater than 75% of the TSW would be included in the analysis. Of the treatment group ($n = 24$), $n = 22$ participants completed the TSW, $n = 1$ participant completed 75%, and $n = 1$ participant did not complete any of the workbooks.

After the guidelines were reviewed, each participant received a TSW divided into daily modules for each week along with instructions. The modules were clearly marked with the corresponding date for completion. Each participant in the intervention group received the TSW and the order of administration of the modules was uniform. The participants mailed the completed modules in the envelopes provided, to the PI each week. Upon weekly receipt of the participant's modules the material was evaluated to determine if they were being completed correctly. If a pattern of errors was identified, the participant was contacted by phone to determine if additional clarification of the instructions was needed.

During the 6-week intervention the PI attempted to contact participants via telephone approximately once a week on the dates that were decided upon at time of discharge. Contact was made to assure that all questions or concerns regarding the TSW were addressed and to prompt the participants to complete and mail the modules. In addition, the participants received day and evening contact numbers for the PI in the event that they had questions or concerns regarding the study.

Usual Care Group

Patients randomized to the usual care group received the routine postoperative care, cardiac rehabilitation, and patient education and support as previously described. Contact with study personnel occurred at time of enrollment, postoperative discharge, and during follow-up phone calls at 6 weeks and 3 months. The participants were asked if they had received any additional cognitive rehabilitation interventions during this time frame and if so, were withdrawn from the study. All participants denied receiving any additional cognitive training, rehabilitation, or interventions, therefore no participants were withdrawn from the study for this reason.

Timing of Measurements

Table 5 list the measures included in the study and the administration schedule. After determining eligibility for the study and obtaining consent, all participants received the demographic questionnaire and the baseline (pretest) TICS prior to surgery. Posttest TICS was administered after surgery upon discharge (4-7 days) and patients were randomized to intervention or control group. A follow up TICS was administered at Six-weeks and for the intervention group, the feasibility and acceptability questionnaire was completed. The final follow up TICS was administered at three-months postoperatively.

Table 5. Timing of Measurements

Measure	Pretest Baseline	Posttest Discharge	6 weeks	3 months
Demographic Questionnaire	X			
Telephone Interview For Cognitive Status	X	X	X	X
Feasibility and Acceptability Questionnaire (Intervention Group)			X	

Fidelity

For quantitative studies the issue of intervention integrity is fundamental to the indication of validity (Santacroce, Maccarelli, & Grey, 2004). Integrity is defined as the extent to which the intervention is utilized as it was designed (Burns & Grove, 2005). In order to maintain the integrity of this intervention study, the principal investigator (PI) administered the instructions and assessed and evaluated the appropriate utilization of the intervention as outlined above. The PI noted the process surrounding the implementation of the intervention such as; did the participants complete the workbooks as instructed.

The outcome measures (TICS) were administered by study personnel who were trained and supervised by a designated credentialed professional. Administration of the TICS was guided by the most recent edition of *Standards for Educational and Psychological Testing* (Arrasmith, Sheehan, & Grobe, 1986). The designated credentialed professional was the principle investigator of this study. The designated study

coordinators and research assistants were randomly evaluated to ensure appropriate administration of the test. The PI was available for consultation during the study.

Data Analysis

All study data was first entered into the Statistical Package for the Social Sciences (SPSS) (International Business Machines, Chicago, Illinois) version 16 for Windows (Microsoft Corporation, Redmond, Washington). Descriptive statistics including frequencies, percentages, means and standard deviations were computed on study variables for all data collection points. Frequency and proportions were conducted on all categorical data and tests of means and ranks were conducted on all continuous data depending on its distribution. Continuous data were examined to determine the presence of marked skewed data, outliers and systematic missing data. For interval/ratio data, means and standard deviations were conducted. Cronbach's alpha internal consistency reliability coefficients were run on all study instruments and all potential confounders were determined. All independent variables were assessed for a relationship with the dependent variable. If a significant relationship was reported, the independent variable was entered as a covariate. Shapiro-Wilk's test was conducted to assess the assumption of normality and Levene's test was conducted to examine baseline homogeneity of participants (Hazard Munro, 2005).

Research Question 1

RQ1: Is there a difference in the frequency of attrition across groups (control vs. experimental)?

H1_o: There is no difference in the frequency of attrition across groups (control vs. experimental).

H1_a: There is a difference in the frequency of attrition across groups (control vs. experimental).

To examine research question 1, a chi-square was conducted. Chi-square is a test of the association between two variables (Hazard Munro, 2005). In this analysis, the frequency of withdrawal was compared between groups (control vs. experimental). Withdrawal only occurred at the 6-week time frame therefore only one chi-square was conducted. Frequency of withdrawal (within the first 6 weeks vs. completed 6 weeks) was compared between groups (control vs. experimental).

Research Question 2

RQ2: For the intervention group, does acceptability differ significantly from the median value of 3.0 reflecting neutrality?

H2_o: For the intervention group, acceptability does not differ significantly from the median value of 3.0 reflecting neutrality.

H2_A: For the intervention group, acceptability differs significantly from the median value of 3.0 reflecting neutrality.

To examine research question 2, fifteen one-sample *t* tests were conducted to compare the intervention group to a hypothesized median value of 3.0. The one-sample *t* test is used to determine whether the population mean (experimental group) is equal to a hypothesized value and is appropriate to use when data are available from a single random sample (Triola, 2008). A Bonferroni adjustment was made to reduce the chance

of a Type 1 error. For this analysis, Acceptability was determined with the Acceptability and Feasibility Questionnaire, a 15 item 5-point Likert scale. All items were summed up in each subscale and divided by the total number of items to calculate composite scores. The median value of 3.0 was used as a comparison to determine whether or not the intervention group mean composite scores differ from the hypothesized mean.

Research Question 3

RQ3: Following cardiac surgery, do patients who receive a 6-week CTI when compared with those who receive usual care demonstrate a significantly greater improvement in cognitive status when comparing discharge scores to scores at 6 weeks and 3 months postoperatively?

H3_o: Following cardiac surgery, patients who receive a 6-week CTI when compared with those who receive usual care do not demonstrate significantly greater improvement in cognitive status when comparing discharge scores to scores at 6 weeks and 3 months postoperatively.

H3_a: Following cardiac surgery, patients who receive a 6-week CTI when compared with those who receive usual care demonstrate significantly greater improvement in cognitive status when comparing discharge scores to scores at 6 weeks and 3 months postoperatively.

In order to determine whether the CTI improved performance on the TICS, 3 factorial (mixed model) Analyses of Variance (ANOVAs) were conducted. Factorial ANOVA's are used in research when one wants to test two independent groups using repeated measures, where one factor is a between subjects variable and the other is a

within subjects variable. (Tabachnick & Fidell, 2007). TICS scores were compared by group (control vs. experimental) and 3 time periods (posttest vs. six week follow-up), (posttest vs. three month follow-up), and (six week follow-up vs. three month follow-up).

The significance level for hypothesis testing was set at 0.05. After accounting for the degrees of freedom, if the observed F -value exceeded the critical F -value the null hypothesis (H_0) was rejected (Maxwell & Delaney, 2004). The results of the factorial ANOVA are presented in the form of main effects and the interactions among study variables. Post hoc analyses consisting of sequential independent t -tests were conducted if a significant interaction was revealed.

The assumptions of normality and homogeneity of variance were assessed. Normality is the assumption that all variables are equally distributed (Tabachnick & Fidell, 2007) and was assessed using the one-sample Shapiro-Wilk test. Homogeneity of variance assumes that the variances of the observations in individual groups are equal (Burns & Grove 2005) and was assessed using Levene's test. Assumptions of ANOVA were violated therefore nonparametric statistics were also conducted. Kruskal Wallis H tests for independent samples were run at each assessment period and Wilcoxon signed ranks test for related samples for each group was also conducted.

Human Subject Protection

This research study involves human subjects therefore Institutional Review Board (IRB) approval was obtained from both Catholic Medical Center and Boston College (Appendix A) prior to any data collection. The consent explains the details of the study, its goals, protection of confidential information, potential benefits, and any potential risks (Appendix E). There was no fee to participate in the study. Costs not related to the study

were charged to the participant or insurance carrier as though the patient were not participating in the study. The alternative to participating in this study was to not participate. It was explained to the participants that they had the right to withdraw from the study at anytime and it would not affect their care.

Confidentiality

A HOGBEN code, which consisted of the first 3 letters of the participant's last name followed by the first letter of their given name followed by their date of birth, replaced all identifying information on the data forms. A master code chart linking the identification numbers of the participants with their name, was kept in a secure location and only accessible by the principal investigator and study coordinator. Upon completion of the primary study, the master list will be destroyed. Copies of all materials were housed at Catholic Medical Center and an additional copy sent to the Data Center at Dartmouth College. The research project was performed under the guidelines of the National Institute of Health Office for Protection from Research Risks for the Protection of Human Rights.

Withdrawal of Participants

Participation is voluntary and participants could withdraw from the study at any time for any reason if they wished to do so without any consequences. Participants would have been provided with any significant new findings had any developed during the course of the research. The investigator could withdraw a participant from the study if they did not follow instructions, if the study was canceled secondary to staffing or equipment issues, or for medical reasons (e.g. readmission during the intervention phase).

Participation Payment

Patients eligible for the research study, having signed the consent form, and having completed the study (e.g. both groups completing the TICS at baseline, 6 weeks and 3 months and termination questionnaire – intervention group completing the TSW) were compensated with a \$50.00 gift card for their time and travel expenses.

Potential Benefits

There were no known direct benefits to participants in this study. The potential benefit exists for one of the first effective cognitive interventions for patients who experience cognitive decline following cardiac surgery

Potential Risks

This study presented minimal risk to participants, as the intervention is an educational one. There were no invasive interventions, nor any untested experimental measurements used. There was the potential for a small burden placed on the participant, as they were undertaking tasks that were timed. They were asked to answer questions and fill in a termination questionnaire. The risks faced by participants were no greater than the risks they face during routine cardiac rehabilitation.

CHAPTER 4

RESULTS

The current study investigated the feasibility, acceptability and preliminary effect of a cognitive training intervention in the postoperative cardiac surgical population. The study enrolled 53 patients who underwent elective cardiac surgery defined as CABG on or off pump and/or valve surgery. Patients excluded from the analysis were (n = 6) withdrawn from the study, and (n = 2) participants died in the postoperative period. Data were analyzed on (n = 24) experimental and (n = 21) control participants. All data were entered into SPSS (International Business Machines, Chicago, Illinois) version 16 for Windows (Microsoft Corporation, Redmond, Washington).

Descriptors and Frequencies

Fifty-three individuals participated in the demographic survey 40 (75.5%) were male and 13 (24.5%) were female (see Table 6). Frequencies and percents for age are presented in Table 7, where the largest proportion of participants 23 (43.4%) were between ages 60 to 69. Fifty-two (98.1%) participants were Caucasian and 1 (1.9%) responded other (see Table 8). Frequencies and percents for marital status are presented in Table 9, where the majority of participants 38 (71.7%) were married/living with partner. Frequencies and percents for members of household are presented in Table 10, where the majority of participants 32 (60.4%) were living with their spouse/partner. Frequencies and percents for level of education are presented in Table 11, where the largest proportion of participants 16 (30.2%) were high school graduates. Frequencies and percents for employment status are presented in Table 12, where the largest proportion of participants 26 (49.1%) was retired. Frequencies and percents for level of

income are presented in Table 13. There were no differences between groups on the following variables: age, race, marital status, members of household, and employment status. There was a statistically significant difference ($p = 0.03$) between groups on the variable of gender (see Table 14).

Cognitive decline was defined as a negative change from baseline on TICS scores. Forty-five (86.5%) of participants had a decline from pretest (baseline) to posttest (immediate postoperative period) and 7 (13.5%) did not. Data was lost to follow up on 1 patient. At the 6-week time period 6 (30%) of 20 control participants had decline from pretest while 5 (20.8%) of 24 intervention participants had decline. A total of 11 (25%) of participants had a decline from pretest and 33 (75%) did not. Data was not available for 9 participants ($n = 4$ control participants and $n = 2$ treatment participants withdrew from the study, $n = 1$ treatment participant died and $n = 2$ lost data). At the 3-month time period 7 (33%) of 21 control participants had decline from baseline while 4 (16.6%) of 24 intervention participants had decline. A total of 11 (24.4%) of participants had a decline from pretest and 34 (75.6%) did not. Data was not available for 8 participants ($n = 4$ control participants and $n = 2$ treatment patients withdrew, $n = 2$ patients died). Frequencies and percents for cognitive decline are presented in Table 15. Means and standard deviations for declining TIC scores by assessment period are presented in Table 16. Cronbach's alphas for TIC scores for each assessment period are presented in Table 17.

Table 6. Frequencies and Percents for Gender by Group

Gender	Control		Experimental	
	Frequency	Percent	Frequency	Percent
Male	23	88.5	17	63.0
Female	3	11.5	10	37.0

Table 7. Frequencies and Percents for Age Range by Group

Age Range	Control		Experimental	
	Frequency	Percent	Frequency	Percent
40 to 49	2	7.7	2	7.4
50 to 59	3	11.5	6	22.2
60 to 69	12	46.2	11	40.7
70 to 79	8	30.8	7	25.9
80 to 89	1	3.8	1	3.7

Table 8. Frequencies and Percents for Race by Group

Race	Control		Experimental	
	Frequency	Percent	Frequency	Percent
Caucasian	26	100	26	96.3
Other	0	0.0	1	3.7

Table 9. Frequencies and Percents for Marital Status

Marital Status	Control		Experimental	
	Frequency	Percent	Frequency	Percent
Single, Never Married	2	7.7	3	11.1
Married/Living with Partner	20	76.9	18	66.7
Separated/Divorced	3	11.5	4	14.8
Widowed	1	3.8	2	7.4

Table 10. Frequencies and Percents for Members of Household

Members of Household	Control		Experimental	
	Frequency	Percent	Frequency	Percent
Spouse/Partner	19	73.1	15	55.6
Parents	1	3.8	0	0.0
Children	4	15.4	0	0.0
Friends	0	0.0	1	3.7
Other	2	7.7	1	3.7
Live Alone	2	7.7	8	29.6

Table 11. Frequencies and Percents for Level of Education

Level of Education	Control		Experimental	
	Frequency	Percent	Frequency	Percent
Less than/Some High School	5	19.2	11	40.7
High School Graduated	6	23.1	2	7.4
Trade School	1	3.8	6	22.2
Some College	6	23.1	5	18.5
College/Graduate Degree	8	30.7	4	14.8

Table 12. Frequencies and Percents for Employment Status

Employment Status	Control		Experimental	
	Frequency	Percent	Frequency	Percent
Employed Full Time	7	26.9	4	14.8
Employed Part Time	3	11.5	5	18.5
Student	0	0.0	0	0.0
Homemaker	0	0.0	1	3.7
Unemployed	1	3.8	6	22.2
Retired	15	57.7	11	40.7

Table 13. Frequencies and Percents for Level of Income

Level of Income	Control		Experimental	
	Frequency	Percent	Frequency	Percent
Less than \$10,000	0	0.0	2	7.4
\$10,000 to \$20,000	2	7.7	3	11.1
\$21,000 to \$35,000	2	7.7	0	0.0
\$36,000 to \$50,000	2	7.7	1	3.7
\$51,000 to \$65,000	1	3.8	3	11.1
Over \$65,000	7	26.9	7	25.9
Decline to Respond	12	46.2	9	40.7

Table 14. Chi-Squares between Group with Age, Gender, Race, Marital Status, Members of Household, Education, Employment Status and Income

	χ^2	df	p
Age * Group	1.09	4	.896
Gender * Group	4.65	1	.031
Race * Group	0.98	1	.322
Marital * Group	0.76	3	.858
Members of Household * Group	8.04	6	.235
Education * Group	4.57	6	.600
Employment * Group	6.49	4	.166
Income * Group	5.57	7	.591

Table 15. Frequencies and Percents for Cognitive Decline

Cognitive Decline	Control		Treatment		Total	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Postoperative TICS	20	78	25	92.5	45	86.5
6-week TICS	6	30	5	20.8	11	25
3-month TICS	7	33	4	16.6	11	24.2

Table 16. Means and Standard Deviations for Declining TIC scores for each Assessment Period by Group

Assessment Period	Control		Experimental	
	M	SD	M	SD
Δ at Posttest	-4.10	4.13	-3.40	2.06
Δ at Six Week Follow Up	-2.36	1.29	-1.88	1.02
Δ at Three Month Follow Up	-3.29	2.75	-2.59	1.97

Table 17. Cronbach's Alphas on TICS for each Assessment Period

Assessment	α	Items
TICS Pretest	.586	11
TICS Posttest	.642	11
TICS Six Week Follow Up	.660	11
TICS Three Month Follow Up	.602	11

Research Question 1

To examine research question 1, a chi-square was conducted for the six-week follow-up to assess if there was a statistically significant difference between participants that withdrew by group (control vs. experimental). The results of the chi-square were not significant, $\chi^2(1) = 0.95$, $p = .329$, suggesting no relationship exists between withdrawn participants and group. The results of the crosstabs are presented in Table 18.

Table 18. Chi-Square on Participants that Withdrew by Group

χ^2	p	Control		Experimental	
		Withdrew	Did Not Withdraw	Withdrew	Did Not Withdraw
0.95	0.33	4	20	2	24

Research Question 2

To examine research question 2, fifteen one-sample *t* tests were conducted to assess if differences exist on the Feasibility and Acceptability questionnaire (Q1-Q15) for the intervention group compared to the median value of 3.0 reflecting neutrality. A Bonferroni adjustment was made to reduce the chance of a Type 1 error. This adjustment was calculated by dividing alpha .05 by the number of bivariate analyses ($p = .003$). Cronbach's alpha for the acceptability and feasibility questionnaire was .883 and is presented in Table 19. The results of the *t* tests are presented in Table 20 and reveal questions 2-8, 10, 14 and 15 have a larger mean compared to the neutral median value of 3.0 suggesting that participants tended toward a high level of acceptability over neutrality.

Table 19. Cronbach's Alphas for Feasibility and Acceptability Questionnaire

Assessment	α	Items
Feasibility and Acceptability	.883	15

Table 20. One-Sample t-tests on the Feasibility and Acceptability Questionnaire

	<i>t</i>	Sig.	M	SD
This program has been helpful to me (Q1)	2.6	.016	3.4	0.7
I was satisfied with the information provided (Q2)	6.3	.001	3.8	0.6
I think the workbooks had clear instructions (Q3)	7.9	.001	4.2	0.7
I think the workbooks are logical (Q4)	4.5	.001	3.1	0.7
I think the workbooks are user friendly (Q5)	10.1	.001	4.1	0.5
I think the workbooks are easy to read (Q6)	13.3	.001	4.4	0.5
I think the workbooks are easy to complete (Q7)	13.3	.001	4.4	0.5
I think the workbooks are interesting (Q8)	3.7	.001	3.6	0.8
I think there were too many exercises (Q9)	2.0	.059	3.4	0.9
I think the time requirements to complete the workbooks are reasonable (Q10)	8.7	.001	4.2	0.7
I think the workbooks are personally relevant (Q11)	2.3	.030	3.4	0.9
I would recommend this program to a friend (Q12)	2.7	.013	3.5	0.9
I would be interested in continuing a program like this one (Q13)	-1.5	.148	2.7	1.0
I am satisfied that I took part in the program (Q14)	7.8	.001	4.1	0.7
Overall how would you rate the CTI program (Q15)	5.1	.001	3.8	0.7

Research Question 3

To examine research question 3, three factorial analyses of variance were conducted to assess if differences exist on TICS scores by group (control vs. experimental) and among three time periods (posttest vs. six week follow-up), (posttest vs. three month follow-up) and (six week follow-up vs. three month follow-up). Preliminary analysis, six Shapiro-Wilk tests were conducted to assess the assumption of normality, the results revealed that at posttest the control group was not normally distributed; however, Maxwell and Delaney (2004 p. 112) states “ANOVA is generally robust to violations of the normality assumption, in that even when data are non-normal, the actual Type I error rate is usually close to the nominal (i.e. desired) value”. Levene’s test of equality of variance was conducted to assess homogeneity of variance and

revealed that at posttest there was a significant difference between groups suggesting the assumption was violated. However, Maxwell and Delaney (2004 p. 112) states that “ANOVA is generally robust to moderate violations of homogeneity of variance as long as the sample sizes in each group are equal to each other and are not unreasonably small (e.g. less than five per group)”.

The ANOVA on TICS scores by group and time period (posttest vs. six week follow-up) revealed a significant main effect by time period, $F(1, 42) = 32.24, p < .001$, with the posttest having a smaller mean ($M = 30.57, SD = 4.63$) compared to the six week follow-up ($M = 34.05, SD = 3.90$). The interaction of group and time period was not significant, $F(1, 42) = 0.18, p = .678$, suggesting that no differences exist between groups on TICS scores by time period once group is entered into the equation. The results of the ANOVA are summarized in Table 21 and means and standard deviations are presented in Table 22.

Table 21. Factorial ANOVA on TICS Scores by Group and Time Period (Posttest vs. Six Week Follow-up)

Source	df	<i>F</i>	Sig.	Partial η^2	Power
Time Period	1	32.24	.001	0.43	0.99
Time Period * Group	1	0.18	.678	0.00	0.07
Error	42	(8.07)			

Table 22. Means and Standard Deviations on TICS Scores by Group and Time (Posttest vs. Six Week Follow-up)

Time Period	Group	M	SD
Posttest	Control	30.55	5.80
	Experimental	30.58	3.50
	Total	30.57	4.63
Six Week Follow-up	Control	33.75	4.78
	Experimental	34.29	3.07
	Total	34.05	3.90

Given assumptions of ANOVA were violated nonparametric statistics including two Kruskal Wallis H tests for independent samples at each assessment period and two Wilcoxon signed ranks tests for related samples for each group were also conducted. The Wilcoxon signed rank test for the control group was significant, $z = -2.73, p < .01$, with the posttest having a smaller mean rank compared to the six week follow up. The Wilcoxon signed rank test for the experimental group was significant, $z = -3.74, p < .001$, with the posttest having a smaller mean rank compared to the six week follow up (see Table 23). The Kruskal Wallis test at posttest by group (control vs. experimental) was not significant, $\chi^2(1) = 0.25, p = .620$, suggesting no statistical difference at posttest by group. The Kruskal Wallis test at six week follow up by group (control vs. experimental) was not significant, $\chi^2(1) = 0.01, p = .934$, suggesting no statistical difference at six week follow up by group (see Table 24).

Table 23. Two Wilcoxon Signed Rank Tests for each Group Comparing Posttest to Six Week Follow Up

Source	z	p	Negative Ranks	Positive Ranks	Ties
Control Group	-2.73	.006	4 ^a	14 ^b	2
Experimental Group	-3.74	.001	1 ^a	22 ^b	1

Note. ^a six weeks < posttest, ^b six weeks > posttest.

Table 24. Two Kruskal-Wallis Tests for Comparing Posttest and Six Week Follow Up by Group

Source	χ^2	df	p	Control Mean Rank	Experimental Mean Rank
Posttest	0.25	1	.620	27.58	25.50
Six Week	0.01	1	.934	22.68	22.35

The ANOVA on TICS scores by group and time period (posttest vs. three month follow-up) revealed a significant main effect by time period, $F(1, 43) = 37.66, p < .001$, with the posttest having a smaller mean ($M = 30.69, SD = 4.28$) compared to the three month follow-up ($M = 34.62, SD = 3.49$). The interaction of group and time period was not significant, $F(1, 43) = 0.55, p = .461$, suggesting that no differences exist between groups on TICS scores by time period once group is entered into the equation. The results of the ANOVA are summarized in Table 25 and means and standard deviations are presented in Table 26.

Table 25. Factorial ANOVA on TICS Scores by Group and Time Period (Posttest vs. Three Month Follow-up)

Source	df	<i>F</i>	Sig.	Partial η^2	Power
Time Period	1	37.66	.001	0.47	0.99
Time Period * Group	1	0.55	.461	0.01	0.11
Error	43	(9.06)			

Table 26. Means and Standard Deviations on TICS Scores by Group and Time (Posttest vs. Three Month Follow-up)

Time Period	Group	M	SD
Posttest	Control	30.81	5.11
	Experimental	30.58	3.50
	Total	30.69	4.28
Three Month Follow-up	Control	34.24	4.09
	Experimental	34.96	2.93
	Total	34.62	3.49

Given assumptions of ANOVA were violated non parametric statistics including two Kruskal Wallis *H* tests for independent samples at each assessment period and two Wilcoxon signed ranks tests for related samples for each group were also conducted. The Wilcoxon signed rank test for the control group was significant, $z = -2.99$, $p < .01$, with the posttest having a smaller mean rank compared to the three month follow up. The Wilcoxon signed rank test for the experimental group was significant, $z = -4.18$, $p < .001$, with the posttest having a smaller mean rank compared to the three month follow up (see Table 27). The Kruskal Wallis test at posttest by group (control vs. experimental) was not significant, $\chi^2(1) = 0.25$, $p = .620$, suggesting no statistical difference at posttest by group. The Kruskal Wallis test at three month follow up by group (control vs.

experimental) was not significant, $\chi^2 (1) = 0.02, p = .891$, suggesting no statistical difference at three month follow up by group (see Table 28).

Table 27. Two Wilcoxon Signed Rank Tests for each Group Comparing Posttest to Three Month Follow Up

Source	z	p	Negative Ranks	Positive Ranks	Ties
Control Group	-2.99	.003	2 ^a	15 ^b	4
Experimental Group	-4.18	.001	1 ^a	22 ^b	1

Note. ^a three month < posttest, ^b three month > posttest.

Table 28. Two Kruskal-Wallis Tests for Comparing Posttest and Three Month Follow by Group

Source	χ^2	df	p	Control Mean Rank	Experimental Mean Rank
Posttest	0.25	1	.620	27.58	25.50
Three Month	0.02	1	.891	22.71	23.25

The ANOVA on TICS scores by group and time period (six week follow-up vs. three month follow-up) revealed no significant main effect by time period, $F(1, 41) = 1.23, p = .274$, suggesting that no difference exists from six week follow-up compared to the three month follow-up. The interaction of group and time period was not significant, $F(1, 41) = 0.65, p = .425$, suggesting that no differences exist on TICS scores by group or time period. The results of the ANOVA are summarized in Table 29 and means and standard deviations are presented in Table 30. Bar Graph of Means for Posttest, Six-Week Follow Up and Three-Month Follow Up is presented in Figure 6.

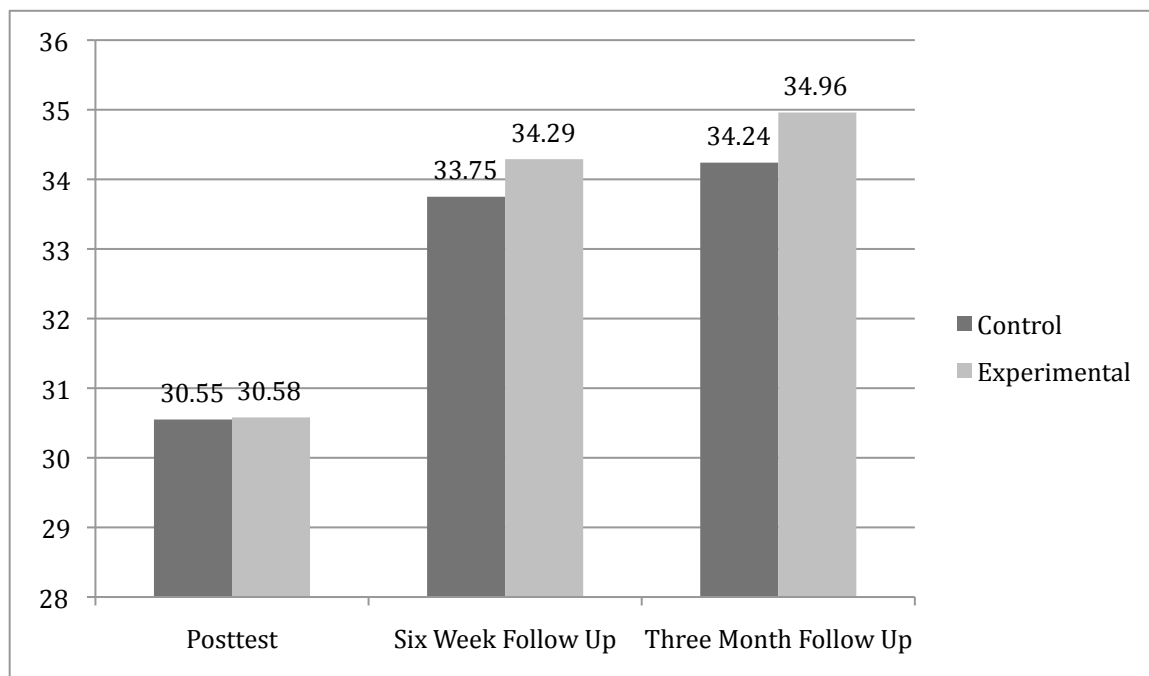
Table 29. Factorial ANOVA on TICS Scores by Group and Time Period (Six Week Follow-up vs. Three Month Follow-up)

Source	df	<i>F</i>	Sig.	Partial η^2	Power
Time Period	1	1.23	.274	0.03	0.19
Time Period * Group	1	0.65	.425	0.02	0.12
Error	41	(2.58)			

Table 30. Means and Standard Deviations on TICS Scores by Group and Time (Six Week Follow-up vs. Three Month Follow-up)

Time Period	Group	M	SD
Six Week Follow-up	Control	34.53	3.37
	Experimental	34.29	3.07
	Total	34.40	3.17
Three Month Follow-up	Control	34.63	3.82
	Experimental	34.96	2.93
	Total	34.81	3.31

Figure 6. Bar Graph of Means for Posttest, Six Week Follow Up and Three Month Follow Up



Given assumptions of ANOVA were violated non parametric statistics including two Kruskal Wallis H tests for independent samples at each assessment period and two Wilcoxon signed ranks tests for related samples for each group were also conducted. The Wilcoxon signed rank test for the control group was not significant, $z = -0.16$, $p = .875$, suggesting no statistical difference comparing six week follow up to the three month follow up. The Wilcoxon signed rank test for the experimental group was not significant, $z = -1.44$, $p = .151$, suggesting no statistical difference comparing six week follow up to the three month follow up (see Table 31). The Kruskal Wallis test at six week follow up by group (control vs. experimental) was not significant, $\chi^2(1) = 0.01$, $p = .934$, suggesting no statistical difference at six week follow up by group. The Kruskal Wallis

test at three month follow up by group (control vs. experimental) was not significant, $\chi^2(1) = 0.02, p = .891$, suggesting no statistical difference at three month follow up by group (see Table 32).

Table 31. Two Wilcoxon Signed Rank Tests for each Group Comparing Posttest to Three Month Follow Up

Source	z	p	Negative Ranks	Positive Ranks	Ties
Control Group	-0.16	.875	9 ^a	7 ^b	3
Experimental Group	-1.44	.151	6 ^a	10 ^b	8

Note. ^a three month < six weeks, ^b three month > six weeks.

Table 32. Two Kruskal-Wallis Tests for Comparing Six Week Follow Up and Three Month Follow by Group

Source	χ^2	df	p	Control Mean Rank	Experimental Mean Rank
Six Week	0.01	1	.934	22.68	22.35
Three Month	0.02	1	.891	22.71	23.25

In this chapter, findings of the doctoral dissertation research were presented. Data was collected from May 2008 to January 2010 and was used to answer the research questions. Chapter 5 will discuss these results in detail.

CHAPTER 5

DISCUSSION

The purpose of this chapter is to provide a review of the findings of the study with an interpretation of those findings. This study addressed two research questions about the feasibility and acceptability of a CTI for postoperative cardiac surgical patients and one question addressed the preliminary effect of a CTI delivered to postoperative cardiac surgical patients. This will be followed by a discussion of how these findings are similar to or different from the current literature. Implications for theory, research and practice will be offered followed by a discussion of the limitations of the study. Finally directions for future research will be suggested.

Review of Study Findings

The specific aims of this study were to examine the hypotheses that 1) There is a difference in attrition across groups, 2) for the intervention group, acceptability differs significantly from a median value of 3.0, and 3) following cardiac surgery, patients who receive a 6-week CTI when compared with those who receive usual care demonstrate significantly greater improvement in cognitive status when comparing discharge scores to scores at 6 weeks and 3 months postoperatively.

Demographic Factors

The study sample was primarily white and male. The largest proportion of participants was between the ages of 60 to 69. The majority of participants were married or living with a partner, which also followed that the participants were primarily living with their spouse or partner. The largest portion of participants were high school graduates. The participants were primarily retired and a large percentage declined to a

respond to income. While other studies have suggested that lower socioeconomic status is a predictor of POCD (Gao et al., 2005), no correlation with socioeconomic status and POCD could be made in this study. There was no statistically significant difference between groups in any of the following demographic variables; age, race, marital status, members of household, or employment status. The groups did not differ in level of education with the largest percent of patients having a high school education. Benoit and colleagues (2005) suggested that POCD was inversely related to level of education. Association of level of education and cognitive outcomes was not within the scope of this study. However, the data provided from this study could be utilized in a secondary analysis to answer such questions.

A total of 86.5 percent of participants experienced cognitive decline in the immediate postoperative period. Data was lost on 1 participant who withdrew because the caregiver decided that the study would be too burdensome for the patient. Decline was present in 25 percent of participants at the 6-week interval. Data were lost on 2 control participants, 3 control participants withdrew, 2 treatment participants withdrew, and 1 treatment participant died. Finally, 24.2 percent of participants had decline at the 3-month testing interval with one death in the control group.

Research Question #1

The number of patients that withdrew from the control group ($n = 4$) and from the experimental group ($n = 2$) was not found to be significant therefore the null hypothesis was accepted. This data suggests that patients are not more likely to withdraw from a study when randomized to receive the cognitive intervention. Additional information obtained from the recruitment and retention table reported that 78% of patients recruited

for the study signed consent to participate in the study and of those participants, 85% completed the study. In addition, 85% of the participants in the treatment group completed the treatment. Thus suggesting that the intervention is feasible to administer in the postoperative cardiac recovery period. This data is similar to other cognitive studies that found attrition rates to be less than 15% (Ball et al., 2002; Mahncke et al., 2006) in both the treatment and control groups. It would be interesting to conduct an attrition analysis to investigate whether the participants who withdrew from the study differed at pretest (TICS) and/or pre-intervention difference score, from those who completed the study.

Research Question #2

As reported in chapter 4, the majority of questions on the feasibility and acceptability questionnaire were significant suggesting that participants tended to agree on the 5-point Likert scale more than the median neutral value of 3.0. For questions 2-8, 10, 14 and 15 the null hypothesis was rejected. For questions 1, 9, and 11-13, the null hypothesis was accepted. This suggests that participants were satisfied with the information provided by study personnel (3.78 ± 0.60). The participants found the workbooks to have clear instructions (4.14 ± 0.72) and agreed that they were logical (3.61 ± 0.66), interesting (3.61 ± 0.78), user friendly (4.09 ± 0.51), and easy to read and complete (4.35 ± 0.49). The participants felt that the amount of exercises were reasonable (3.39 ± 0.94) and they were given adequate time to complete the exercises (4.22 ± 0.67). Finally the participants were satisfied that they took part in the program (4.09 ± 0.67) and rated the program higher than the neutral median value of 3.0 (3.78 ± 0.74) suggesting that participants tended toward a high level of acceptability over neutrality.

There are a limited number of acceptability and feasibility studies investigating cognitive training interventions. One study conducted by Vandelandotte and De Bourdeaudhuij (2003) evaluated difference in feasibility and acceptability between groups (e.g. age, gender, education level) of a computer activity and reported very few significant differences. The information provided by this questionnaire suggests that the CTI is acceptable to cardiac patients in the postoperative period. The questions in which the null hypotheses were accepted suggest that although the program was feasible and acceptable, the participants did not perceive a benefit from the program. Perhaps a secondary analysis of the data would reveal a specific subgroup (e. g. age, level of education) that did not perceive a benefit from the CTI.

It would also be interesting to conduct a qualitative study to address what is important for each individual therefore, gearing an intervention to individual needs. After completion of the study, the PI had opportunity to speak with the individuals from the treatment group. One participant stated, “After the first few weeks, I became very bored with the exercises”. This individual had a college education. Another participant stated, “Some of the exercises were hard”. This individual had less than a high school education. There are many different levels of difficulty to the TSW and perhaps tailoring the intervention to level of education as well as individual likes (e.g. verbal vs. mathematical problems) would create even greater acceptance as well as a perceived benefit of a cognitive program.

Research Question #3

As reported in chapter 4, the ANOVA on scores by group and time period (posttest vs. six week follow-up) and (posttest vs. three month follow-up) revealed a

significant main effect by time period, but the interaction of group and time period was not significant. The ANOVA on scores by group and time period (six week follow-up vs. three month follow-up) revealed no significant main effect by time period or interaction of group and time period. These findings were consistent with the findings from the Kruskal Wallis H and Wilcoxon signed ranks, which revealed that in the immediate postoperative period (posttest) both groups had a smaller mean rank compared to the six-week and three-month follow up. Wilcoxon signed rank test for both groups comparing six-week follow up and three-month follow up were not significant. Kruskal Wallis H suggested no statistical difference at posttest, six-week, or three-month follow up by group.

These findings suggest that patients' cognitive performance improves from the immediate postoperative period to the six-week follow-up postoperative period and that cognitive performance improvement is sustainable at the three-month follow-up postoperative period. The fact that interaction of group revealed no significant main effect suggests that the CTI was not significant in improving cognitive performance in the postoperative period and the null hypothesis was accepted. Although this analysis did not prove to be statistically significant, the overall mean of the treatment group (34.29) was greater than that of the control group (33.75).

The current study reported cognitive decline to be greatest during the immediate postoperative period (86.5%). The majority of studies reviewed found POCD to be greatest in the immediate postoperative period (53% to 80%) (Arrowsmith et al., 2000; Newman et al., 2001; Stroobant et al., 2005). The current study also revealed cognitive decline to be between 21% (treatment) to 30% (control) at the six-week testing period.

This finding is similar to other studies that reported cognitive decline to be 36% at six-week follow-up (Mathew et al., 2003; Newman et al., 2001). Finally, the current study reported cognitive decline to be present in 16.6% (treatment) to 33% (control) at the three-month follow up. This finding is similar to other studies that reported cognitive decline to be 10 – 37% (Selnes et al., 2003; Zimpfer et al., 2004; Yin, Luo, Guo, Li, & Huang, 2007). Regarding preliminary effect of the CTI, findings shared similarities to a study by Cipriani and colleagues (2005) comparing a cognitive intervention in patients with AD and MCI. Results suggest that the patients with AD who received a CTI showed statistically significant improvement ($p < 0.01$) in MMSE scores while patients with MCI showed no significant improvements. This study also did not have enough power ($N=20$) to achieve significant results.

In contrast to other studies (Carney et al., 1999; Kaschel et al., 2002; Prigatano, 1997; Sarajuuri et al., 2005) that found cognitive training interventions to be effective in improving memory and other cognitive functions in different population of patients (e.g. stroke, TB), the current study did not show that the CTI had a significant impact on cognitive performance. This could be attributed to the many issues including; different populations of patients (i.e. TBI and stroke vs. postoperative cardiac surgical patients), length of CTI (6 weeks vs. other, daily vs. other), time spent performing exercises (10 minutes vs. other), different exercises (attention, concentration, and memory vs. speed of processing, perception, language and visuospatial cognition), modes of exercises used (paper and pencil vs. computer) and self administered training vs. facilitated training.

Perhaps the CTI would be effective in a sub group of the study (e. g. age, level of education), by type of surgery, or with pretest and/or posttest scores in certain ranges.

The data provided by this analysis suggests future research on cognitive enhancing interventions be conducted, in particular research that focuses on developing effective strategies including; investigation of specific cognitive domains and directing interventions to enhance those affected, evaluation of dose effect for a particular population (e.g. cardiac surgical patients), modification of intervention focusing on level of education and intellectual abilities, and utilization of computer interventions.

Limitations

There are some important limitations of this study that may account for the fact that intervention was not significant in regards to the study outcome (TICS). One limitation of the current study is sample size. The number of participants did not provide enough power for a medium to small effect size. It is possible that some of the nonsignificant findings of this study are due to Type II error. This study was intended primarily as an evaluation of the feasibility and acceptability of a CTI and preliminary investigation of the effect of the program was a secondary aim. Therefore, exploratory evaluation of the effectiveness of the intervention should be interpreted with caution. The lack of a statistically significant effect may not necessarily be attributed to a lack of intervention effectiveness. The data analysis conducted provided the researcher with an effect size from which to draw a power analysis for future studies.

Another limitation is the homogeneity of the sample. The majority of participants were Caucasian and male. In addition, the majority of participants were between the ages of 60 to 69 and there were not a proportionate number of individuals from other age groups. Thus the sample was not diverse with respect to race, gender, and age, limiting generalizability of the study to other populations.

Inherent to interventional research using a self-administered tool, is the reliance on self-reporting for adherence. The focus of the intervention was to complete exercises on a daily basis to provide daily cognitive stimulation. Participants completed the TSW in their homes without supervision from a proctor therefore it is difficult to ascertain if they completed the workbooks as instructed (e.g. correct day, time of day). Even though the participants were instructed to complete the TSW without help and signed a “declaration of non-collaboration”, they may have received coaching from an outside source. However, the benefit of providing cardiac surgical patients with the opportunity to potentially enhance cognition following surgery outweighs the limitations noted.

A final limitation of the study pertains to practice effect when repeated measures are used. The participants received the TICS evaluation at 4 different time periods. Their performance may improve as they become familiar with the questions on the neurologic surveillance. Unfortunately practice effects almost always affect repeated measures designs. Perhaps utilization of additional neurologic outcome measures would attenuate this effect. In addition, the TICS neurologic surveillance is administered over the telephone without direct supervision from a testing proctor. Participants could be prepared with paper and pencil when being instructed to repeat the list of 10 words by memory, or a calculator for the mathematical questions. One of the major strengths of the TICS design is that it decreases patient burden (i.e. it is delivered over the phone at the patients home). This is particularly important in a longitudinal study when the participants may be living at different locations (e. g. winters in Florida) during the study. The TICS has proven to be valid and reliable and it is more efficient and cost effective than other more sophisticated neurologic batteries.

Implications for Theory, Research and Practice

The present study adds to the emerging literature on enhancing cognition in the postoperative cardiac surgical patient. The CTI approached the challenges inherent in the process of integrating cognitive enhancing strategies into the postoperative cardiac surgical rehabilitation phase. The selected theoretical framework determined the construct validity of the CTI. As mentioned previously, the Roy Adaptation Model of Nursing and Cognitive Processing formed the theoretical framework that guided this study. The model was derived from knowledge of neuroscience and clinical practice (Roy, 2009). When applied to the study, the elements of the model correspond to the selected variables. An integral component of this model is the process of neural plasticity, which is known to be the adaptive capacity of the central nervous system (CNS).

Although the interaction of the CTI was not found to be significant in this analysis, there was a significant improvement in cognition when comparing the immediate postoperative TICS scores with the six-week TICS scores. Therefore the results of the current study support the theoretical framework, most importantly the adaptive capacity of the CNS.

While the current study will add to the body of knowledge regarding the nature of POCD, it has also provided insight into new avenues of research. Given that the current study supports the hypotheses that a CTI in the postoperative cardiac surgical patient is both feasible and acceptable, along with the literature that supports the effectiveness of CTI in other populations, further research examining the utilization of a CTI in the postoperative cardiac surgical patient is warranted. One avenue of research is to investigate the types of exercises administered to the patient. The goal of CTI in the older adult is to improve cognitive function in skills and strategies of everyday activities. The

current study utilized exercises in the cognitive domains of attention, concentration and memory. While these are domains that are essential for activities of daily living (ADL), it may be useful to develop exercises within these domains that are more specific for ADLs.

In addition, another potential influence of the intervention is the presence of ceiling and floor effects. During discussion with participants, it was noted that some participants considered the exercises to be too simple, while others commented that they were too difficult. If the intervention were adapted to level of education, perhaps there would be greater gains in performance and cognitive outcome.

Although self-administration of an intervention is an ideal tool in terms of resource utilization and cost, it limits the control of time, dose, and potential for collaboration. A study that includes guidance from a proctor would help assure that the intervention is being used as it was designed. This would also allow for evaluation of individual abilities and implementation of exercises of appropriate level. Inclusion of additional measures (e.g. depression, quality of life, self efficacy) would also add important information regarding patients' overall functional status.

Another avenue of research is to examine the dose effect of a CTI in the postoperative cardiac surgical population. From a methodological perspective, future randomized studies would benefit from a larger sample size not only increasing the statistical power but also allowing patients to be randomized to several treatment groups receiving different doses of the intervention as well as a control group. Moreover, a larger sample size from more than one institution in different geographic areas would decrease the homogeneity of the sample and create a more generalizable study. As in the current study, use of repeated measures will allow for continued measurement at different time

periods to better understand time related changes. Perhaps utilization of a battery of neuropsychological exams that measure the same cognitive domains will decrease the likelihood of practice effect. Given that the literature suggests that patients who develop POCD may be at higher risk for cognitive decline later in life (Selnes et al., 2001), a long-term follow-up study may be indicated.

From a practice perspective, the findings of this study along with a majority of studies, suggests that assessment of cognitive function in the preoperative and postoperative period may be beneficial to help guide postoperative care. Even though the results of this analysis did not reveal that the CTI was significant in improving cognitive status, there continues to be a need for patient education regarding the potential issues surrounding POCD. Current programs spend a significant amount of time and energy focusing on improving patient outcomes in the perioperative period. Knowledge of what to expect when considering cognitive function can only improve upon those outcomes. Clinicians also need to develop an understanding of POCD and the effects that it may have on patient care and outcomes. As noted previously, nurses and other allied health professionals do not always notice the subtle changes present in POCD (Inouye, 2001). A study to measure the impact of a clinical-based educational intervention on the ability of the postoperative cardiac nurses to identify cognitive decline at the bedside would be another avenue of research.

Given that patients' subjective complaints do not always mirror the neurologic surveillance outcome a mixed method study using a qualitative approach would help provide additional subjective information. The major goal for such a program of research would be to create a change in the current practice environment that would take into

consideration the lived experience of the patient and promote early detection and appropriate management for patients experiencing POCD.

Summary

Utilization of evidence based and knowledge based practice is essential to move towards continual improvement in patient care. Conducting intervention studies is an important mechanism to attain this goal. This is the first study conducted to evaluate the feasibility, acceptability and preliminary effect of a cognitive training intervention in the postoperative cardiac population. The current study adds to the body of knowledge encompassing POCD. The study revealed that there was not a significant attrition rate between the treatment and control group. Most importantly the study demonstrated that a CTI is both feasible and acceptable for the postoperative cardiac surgical patient. Although there were no significant differences in this analysis, this data may still yield further understanding of the effects of a CTI in postoperative cardiac surgical patients. Specific areas for program improvement were identified. The knowledge of neural plasticity provides another avenue for research and practice in the area of promoting adaptation with patients experiencing cognitive decline in the postoperative period. Finally, the findings of this study add to the empirical foundation of the Roy Adaptation Model of Nursing and Cognitive Processing and demonstrates potential for advancement of its use in research surrounding POCD.

References:

- Alexander, L. P., Anstrom, K. J., Muhibaier, L. H., Grosswald, R. D., Smith, P. K., Jones R. H., & Peterson E. D. (2000). Outcomes of cardiac surgery in patients ≥ 80 years: Results from the National Cardiovascular Network. *Journal of the American College of Cardiology*, 35(3), 731-738.
- Ancelin, M. L., DeRoquefeuil, G., Ledesert, B., Bonnel, F., Cheminal, J.C., & Ritchie, K. (2001). Exposure to anaesthetic agents: Cognitive functioning and depressive symptomatology in the elderly. *British Journal of Psychiatry*, 178, 360-366.
- Andrews, G., Peterson, L., & Teeson, M. (1994). *The measurement of consumer outcome in mental health: A report to the National Mental Health Information Strategy Committee*. Sydney: Australian Government Publishing Service.
- Andrews, D. G., Kinsella, G., & Murphy, M. (1996). Using a memory handbook to improve everyday memory in community-swelling older adults with memory complaints. *Experimental Aging Research*, 22(3), 305-322.
- Arrasmith, D. G., Sheehan, D. S., & Grobe, R. P. (1986). (Review of) Standards for Educational and Psychological Testing by the American Educational Research Association, the American Psychological Association, and the National Council on Measurement in Education. *Journal of Educational Measurement*, 22(1), 83-86.
- Arrowsmith, J. E., Grocott, H. P., Reves, J. G, & Newman, M. F. (2000). Central nervous system complications of cardiac surgery. *British Journal of Anaesthesia*, 84, 378-393.

- Ball, K., Berch, D. B., Helmers, K. F., Jobe, J. B., Leveck, M. D., Marsiske M., et al. (2002). Effects of cognitive training interventions with older adults. *JAMA*, 288(18), 2271-2281.
- Baltes, P.B., & Kliegl, R. (1992). Further testing of limits of cognitive plasticity: Negative age differences in mnemonic skill are robust. *Developmental Psychology*, 28(1), 121-125.
- Baltes, P. B., Kliegl, R., & Dittmann-Kohli, F. (1988). On the locus of training gains in research on the plasticity of fluid intelligence in old age. *Developmental Psychology*, 28, 121-125.
- Baltes, P. B., Sowarka, D., & Kliegl, R. (1989). Cognitive training research on fluid intelligence in old age: What can older adults achieve by themselves? *Psychology and Aging*, 4, 217-221.
- Barber, M., & Stott, D. J. (2004). Validity of the Telephone Interview for Cognitive Status (TICS) in post-stroke patients. *International Journal of Geriatric Psychiatry*, 19, 75-79.
- Baufreton, C., Allain, P., Chevailler, A., Etcharry-Bouyx, F., Corbeau, J. J., Legall, L., et al. (2005). Brain injury and neuropsychological outcome after coronary artery surgery are affected by complement activation. *Annals of Thoracic Surgery*, 79(5), 1597-1605.
- Bedford, P. D. (1955). Adverse cerebral effects of anaesthesia on old people. *Lancet*, 269(6884), 259-263.
- Bekker, A. Y., & Weeks, E. J. (2003). Cognitive function after anaesthesia in the elderly. *Best Practice and Research*, 17(2), 259-272.

- Benoit, A. G., Campbell, B. I., Tanner, J. R., Staley, J. D., Wallbridge, H. R., Biehl, D. R., et al. (2005). Risk factors and prevalence of perioperative cognitive dysfunction in abdominal aneurysm patients. *Journal of Vascular Surgery*, 42(5), 884-890.
- Benton, A. L., & Hamscher, K. (1989). *Multilingual Aphasia Examination*. Iowa City: AJA Associates.
- Black, B. S., Kasper, J., Brandt, J., Shore, A. D., German, P., Burton, L., et al. (2003). Identifying dementia in high-risk community samples: The Memory and Medical Care Study. *Alzheimer's Disease and Related Disorders*, 17, 9-18.
- Blunden, G., & Smits, E. (2000). Cognitive rehabilitation: A pilot survey of therapeutic modalities used by Canadian occupational therapists with survivors of traumatic brain injury. *Canadian Journal of Occupational Therapy*, 67(3), 184-196.
- Boodhwani, M., Rubens, F. D., Wozny, D., Rodriguez, R., Alsefaou, A., Hendry, P. J., et al. (2006). Predictors of early neurocognitive deficits in low-risk patients undergoing on-pump coronary artery bypass surgery. *Circulation* 114(I Supple), 1461-1466.
- Bosworth, H. B., Schaie, K. W., & Willis, L. L. (1999). Cognitive and sociodemographic risk factors for mortality in the Seattle Longitudinal. *Journal of Gerontology: Psychological Sciences* 54(B), 273-282.
- Brandt, J., Spencer, M., & Folstein, M. (1988). The telephone interview for cognitive status. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology*, 1, 111-17.

- Bucerius, J., Gummert, J. F., Borger, M. A., Walther, T., Doll, N., Falk, V., et al. (2004). Predictors of delirium after cardiac surgery: Effect of beating-heart (off pump) surgery. *Journal of Thoracic and Cardiovascular Surgery*, 127, 57-64.
- Burke, S. N., & Barnes, C. A. (2006). Neural plasticity in the ageing brain. *Nature Reviews Neuroscience*, 7, 30-40.
- Burns, N., & Grove, S. K. (2005). *The Practice of Nursing Research: Conduct, Critique, and Utilization* (5th ed.). St. Louis, MO: Elsevier Saunders.
- Cahn-Weiner, D. A., Malloy, P. F., Rebok, G. W., & Ott, B. R. (2003). Results of a randomized placebo-controlled study of memory training for mildly impaired Alzheimer's disease patients. *Applied Neuropsychology*, 10(4), 215-223.
- Canet, J., Raeder, J., Rasmussen L. S., Enlund, M., Kuipers, H. M., Hanning, C. D., et al. (2003). Cognitive dysfunction after minor surgery in the elderly. *ACTA Anaesthesiologica Scandinavica*, 47, 1204-1210.
- Caprio-Prevette, M. D., & Fry, P. S. (1996). Memory enhancement program for community-based older adults: Development and evaluation. *Experimental Aging Research*, 22, 281-303.
- Carmichael, S. T. (2003). Plasticity of cortical projections after stroke. *Neuroscientist*, 3, 64-75.
- Carney, N., Chestnut, R. M., Maynard, H., Mann, N. C., Patterson, P., & Helfand, M. (1999). Effect of cognitive rehabilitation on outcomes for persons with traumatic brain injury: A systematic review. *The Journal of Head Trauma Rehabilitation*, 14(3), 277-307.

- Carter, L. T., Howard, B. E., & O'Neil, W. A. (1983). Effectiveness of cognitive skill remediation in acute stroke patients. *The American Journal of Occupational Therapy*, 37(5), 320-326.
- Carter, L. T., Oliveira, D. O., Duponte, J., & Lynch, S. V. (1988). The relationship of cognitive skills performance to activities of daily living in stroke patients. *The American Journal of Occupational Therapy*, 42(7), 449-455.
- Cavallini, E., Pagnin, A., & Vecchi, T. (2003). Aging and everyday memory: The beneficial effect of memory training. *Archives of Gerontology and Geriatrics*, 37(3), 241-257.
- Charlesworth, D. C., Likosky, D. S., Marrin, C. A., Maloney, C. T., Quinton, H. B., Morton, J. R., et al. (2003). Development and validation of a prediction model for strokes after coronary artery bypass grafting. *The Annals of Thoracic Surgery*, 76(2), 436-443.
- Chernow, B., Alexander, H. R., Smallridge, R. C., Thompson, W. R., Cook, D., Beardsley, D., et al. (1987). Hormonal responses to graded surgical stress. *Archives of Internal Medicine*, 147(7), 1273-1278.
- Cipriani, G., Bianchetti, A., & Trabucchi, M. (2006). Outcomes of a computer-based cognitive rehabilitation program on Alzheimer's disease patients compared with those on patients affected by mild cognitive impairment. *Archives of Gerontology and Geriatrics*, 43(3), 327-335.
- Collie, A., Darby, D. G., Falletti, M. G., Silbert, F. S., & Maruff, P. (2002). Determining the extent of cognitive change after coronary surgery: A review of statistical procedures. *The Annals of Thoracic Surgery*, 73, 2005-2011.

- Crook, T. H. III, Larrabee, G. J. (1990). A self-rating scale for evaluation memory in everyday life. *Psychology and Aging*, 5(1), 48-57.
- Crooks, V. C., Clark, L., Petitti, D. B., Chui, H., & Chiu, V. (2005). Validation of multi stage telephone-based identification of cognitive impairment and dementia. *BMC Neurology*, 5, 8-18.
- Crosby, G. & Culley, D. J. (2003). Anesthesia, the aging brain, and the surgical patient. *Canadian Journal of Anesthesia*, 50(6), R1-R5.
- Culley, D. J., Xie, Z., & Crosby, G. (2007). General anesthetic-induced neurotoxicity: an emerging problem for the young and old? *Current Opinion in Anaesthesiology*, 20, 408-413.
- Cusack, S. A., & Thompson, W. J. A. (1998). Mental fitness: Developing a vital aging society. Research and development of an Older Adult Education Program in the context of a seniors centre in Western Canada. *International Journal of Lifelong Learning*, 17(5), 307-317.
- Cusack, S. A., Thompson, W. J. A., & Rogers, M. E. (2003). Mental fitness for life: assessing the impact of an 8-week mental fitness program on health aging. *Educational Gerontology*, 29, 393-403.
- Das, J. P., Kirby, J. R., & Jarman, R. F. (1979). *Simultaneous and successive cognitive processes*. New York: Academic Press.
- Das, J. P., Naglieri, J. A., & Murphy, D. B. (1995). Individual differences in cognition processes of planning: A personality variable? *The Psychological Record*, 45, 355-371.

- Davis, R. N., Massman, P. J., & Doody, R. S. (2001). Cognitive intervention in Alzheimer disease: A randomized placebo-controlled study. *Alzheimer's Disease and Associated Disorders*, 15(1), 1-9.
- Dayan, P., & Abbot, L. F. (2005). *Theoretical neuroscience: Computational and Mathematical modeling of neural systems*. Cambridge, MA: MIT Press.
- De Beni, R., Mazzoin, G., & Pagotto, S. (1996). Memory self-efficacy and attributional style in elderly people: A comparison among different ages and different living places. *Ricerche di Psicologia*, 3, 62-93.
- De Jager, C. A., Budge, M. M., & Clarke, R. (2003). Utility of TICS-M for the assessment of cognitive function in older adults. *International Journal of Geriatric Psychiatry*, 18, 318-324.
- Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (2000). *California Verbal Learning Test-Second Edition (CVLT-II)*. San Antonio, TX: Psychological Corporation.
- Dijkerman, H. C., Letswaartm M., Johnston, M., & MacWalter, R. S. (2004). Does motor imagery training improve hand function in chronic stroke patients: A pilot study. *Clinical Rehabilitation*, 18, 538-549.
- Dijkstra, J. B., Houx, P. J., & Jolles, J. (1999). Cognition after major surgery in the elderly: Test performance and complaints. *British Journal of Anaesthesia*, 82(6), 867-874.
- Dodds, C., & Allison, J. (1998). Postoperative cognitive deficit in the elderly surgical patient. *British Journal of Anaesthesia*, 81, 449-462.

- Draganski, B., Gaser, L., Busch, V., Schuierer, G., Bogdahn, U., & May, A. (2004). Neuroplasticity: Changes in grey matter induced by training. *Nature*, 427, 311-12.
- Edwards, B., Waterhouse, J., & Reilly, T. (2007). The effects of circadian rhythmicity and time-awake on a simple motor task. *Chronobiology International*, 24(6), 1109-1124.
- Edwards, J. D., Wadley, V. G., Myers, R. S., Roenker, D. L., Cissell, G. M., & Ball, K. K. (2002). Transfer of speed of processing intervention to near and far cognitive functions. *Gerontology*, 48, 329-40.
- Edwards, J. D., Wadley, V. G., Vance, D. E., Wood, K., Roenker, D. L., & Ball, K. K. (2005). The impact of speed of processing training on cognitive and everyday performance. *Aging & Mental Health*, 9(3), 262-271.
- Erdfelder, E., Faul, F., & Buchner, A. (1996). A General power analysis program. *Behavioral Research Methods, Instrument, & Computers*, 28 1-11.
- Eriksen, H. R., Ihlebaek, C., & Ursin, H. (1999). A scoring system for subjective health complaints (SHC), *Scandinavian Journal of Public Health*, 27(1), 63-72.
- Farag, E., Chelune, G. J., Schubert, A., & Mascha, E. J. (2006). Is depth of anesthesia, as assessed by the Bispectral Index, related to postoperative cognitive dysfunction and recovery. *Anesthesia & Analgesia*, 103(3), 633-640.
- Flacker, J. M., & Lipsitz, L. A. (1999a). Serum anticholinergic activity changes with acute illness in elderly medical patients. *Journal of Gerontology: Series A, Biological Sciences and Medical Science*, 54(1), M12-16.

- Flacker, J. M., & Lipsitz, L. A. (1999b). Neural mechanisms of delirium: current hypotheses and evolving concepts. *Journal of Gerontology: Series A, Biological Sciences and Medical Science*, 54(6), B239-246.
- Folstein, M., Folstein, S., & McHugh, P. (1975). Mini-Mental State: a practical method for grading the mental state of patients for the clinician. *Journal of Psychiatric Research*, 12, 189-198.
- Franks, N. P., & Lieb, W. R. (1994). Molecular and cellular mechanisms of general anaesthesia. *Nature*, 367, 607-614.
- Gau, L., Taha, R., Gauvin, D., Othmen, L. B., Wang, Y., & Blaise, G. (2005). Post-operative cognitive dysfunction after cardiac surgery. *Chest*, 128(5), 3664-3670.
- Gauthier, L., Dehaut, F., & Joanette, Y. (1989). The Bells Test: A quantitative and qualitative test for visual neglect. *International Journal of Clinical Neuropsychology*, 11, 49-54.
- Giovagnoli, A. R., Del Pesce, M., Macheroni, S., & Capitani, E. (1996). Trail Making Test: normative values from 287 normal adult controls. *Italian Journal of Neurological Sciences*, 17, 305-309.
- Goodglass, H., & Kaplan, E. (2001). *The Boston Naming Test*. Philadelphia: Lippincott Williams & Wilkins.
- Grant, D. A., & Berg, E. A. (1948). A behavioral analysis of the degree of reinforcement and ease of shifting to new responses in a Weigl-type card sorting problem. *Journal of Experimental Psychology*, 38(4), 404-411.

- Gray, J. M., Robertson, I., Pentland, B., & Anderson, S. (1992). Microcomputer-based attentional retraining after brain damage: A randomized group controlled trial. *Neuropsychological Rehabilitation*, 2, 97-115.
- Greydanus, D. E., Pratt, H. D., & Patel, D. R. (2007). Attention deficit hyperactivity disorder across the lifespan: the child, adolescent, and adult. *Disease-a-Month*, 53(2), 70-131.
- Grimm, M., Zimpfer, D., Czerny, M., Kilo, J., Kasimire, M. T., Kramer, L. et al. (2003). Neurocognitive deficit following mitral valve surgery. *European Journal of Cardio-thoracic Surgery*, 23, 265-271.
- Gronwall, D. M. A. (1977). Paced Auditory Serial Addition Task: A measure of recovery from concussion. *Perceptual and Motor Skills* 44, 367-373.
- Gunther, V. K., Schafer, P., Holzner, B. J., & Klemmer, G. W. (2003). Long-term improvements in cognitive performance through computer-assisted training: A pilot study in a residential home for older people. *Aging & Mental Health*, 7(3), 200-206.
- Guyton, A. C., & Hall, J. E. (2006). *Textbook of Medical Physiology* (11th ed.). Philadelphia: Elsevier Saunders.
- Hazard Munro, B. (2005). *Statistical Methods for Health Care Research*, (5th ed.). Philadelphia: Lippincott Williams & Wilkins.
- Ho, P. M., Arciniegas, D.B., Grigsby, J., McCarthy, M., McDonald, G. O., Moritz, T. E., et al. (2004). Predictors of cognitive decline following coronary artery bypass graft surgery. *Annals of Thoracic Surgery*, 77, 597-603.

- Houk, J. C., Davis, J. L., & Beiser, D. G. (1998). *Models of Information Processing in the Basal Ganglia*. Cambridge, MA; The MIT Press.
- Hudetz, J. A., Iqbal, Z., Gandhi, S. D., Patterson, K. M., Hyde, T. F., Reddy, D. M., et al. (2007). Postoperative cognitive dysfunction in older patients with a history of alcohol abuse. *Anesthesiology*, 106(3), 423-430.
- Huppert, F. A., Brayne, C., Gill, C., Paykel, E. S., & Beardsall, L. (1995). CAMCOG-a concise neuropsychological test to assist dementia diagnosis: socio-demographic determinants in a elderly population sample. *The British Journal of Clinical Psychology*, 34, 529-541.
- Inouye, S. K. (2006). Delirium in older persons. *New England Journal of Medicine*, 354(11), 1157-1165.
- Inouye, S. K., Foreman, M. D., Mion, L. C., Katz, K. H., & Cooney, L. M. (2001). Nurses' recognition of delirium and its symptoms: Comparison of nurse and researcher ratings. *Archives of Internal Medicine*, 161(20), 2467-2473.
- Iohom, G., Szarvas, S., Larney, V., O'Brien, J., Buckley, E., Butler, M., et al. (2004). Perioperative plasma concentrations of stable nitric oxide products are predictive of cognitive dysfunction after laparoscopic cholecystectomy. *Anesthesia & Analgesia*, 99, 1245-1252.
- Ivanov, J., Weisel, R. D., David, T. E., & Naylor, C. D. (1998). Fifteen-year trends in risk severity and operative mortality in elderly patients undergoing coronary artery bypass graft surgery. *Circulation*, 97, 673-680.
- Jensen, A. R., & Rohwer, W. D. (1966). The Stroop Color-Word Test: A review. *Acta Psychologica*, 25, 36-93.

- Jette, A.M., Davies, A.R., Cleary, P.D., Calkins, D.R., Rubenstein, L.V., Fink, A. et al. (1986). The functional status question: Reliability and validity when used in primary care. *Journal of General Internal Medicine*, 1(3), 143-149.
- Jobe, J. B., Smith, D. M., Ball, K., Tennstedt, S. L., Marsiske, M., Willis, S. L., et al. (2001). ACTIVE: A cognitive intervention trial to promote independence in older adults. *Controlled Clinical Trials*, 22, 453-479.
- Kadoi, Y. & Goto, F. (2006). Factors associated with postoperative cognitive dysfunction in patients undergoing cardiac surgery. *Surgery Today*, 36(12), 1053-1057.
- Kaplan, E. F., Goodglass, H., & Weintraub, S. (1983). *The Boston Naming Test* (2nd ed.). Philadelphia: Lea & Febiger.
- Kaschel, R., Della Sala, S., Cantagallo, A., Fahlbock, A., Laaksonen, R., & Miguel, K. (2002). Imagery mnemonics for the rehabilitation of memory: A randomized group controlled trial. *Neuropsychological Rehabilitation*, 12(2), 127-153.
- Keith, J. R., Puente, A. E., Malcolmson, K. L., Tartt, S., Coleman, A. E., & Marks, H. F. (2002). Assessing postoperative cognitive change after cardiopulmonary bypass surgery. *Neuropsychology*, 16, 411-421.
- Klove, H. (1963). Clinical neuropsychology. In F.M. Forster (Ed.), *The Medical Clinics of North America*. New York: Saunders.

- Knipp, S. C., Matatko, N., Wilhelm, H., Schlamann, M., Massoudy, P., Forsting, M., et al. (2004). Evaluation of brain injury after coronary artery bypass grafting. A prospective study using neuropsychological assessment and diffusion-weighted magnetic resonance imaging. *European Journal of Cardio-thoracic Surgery*, 25, 791-800.
- Kojima, Y., & Narita, M. (2005). Postoperative outcome among elderly patients after general anesthesia. *Acta Anaesthesiologica Scandinavica* 50(1), 19-25.
- Koltai, D. C., Welsh-Bohmer, K. A., & Schmechel, D. E. (2001). Influence of anosognosia on treatment outcome among dementia patients. *Neuropsychological Rehabilitation*, 11, 455-475.
- Kramer, A. F., Erickson, K. I., & Colcombe, S. J. (2006). Exercise, cognition, and the aging brain. *Journal of Applied Physiology*, 101, 1237-1242.
- Leshner, E. L., & Whelihan, W. M. (1986). Reliability of mental status instruments administered to nursing home residents. *Journal of Consulting and Clinical Psychology*, 54, 726-727.
- Lewis, M. S., Maruff, P. T., & Silbert, B. S. (2004). Examination of the use of cognitive domains in postoperative cognitive dysfunction after coronary artery bypass graft surgery. *Annals of Thoracic Surgery*, 80, 910-917.
- Lewis, M. S., Maruff, P., Silbert, B. S., Evered, L. A., & Scott, D. A. (2007). The influence of different error estimates in the detection of postoperative cognitive dysfunction using reliable change indices with correction for practice effects. *Archives of Clinical Neuropsychology*, 22, 249-257.

- Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological Assessment* (4th ed.). New York: Oxford University Press.
- Likert, R. (1932). *A Technique for the Measurement of Attitudes*. New York: Archives of Psychology.
- Likosky, D.S., Caplan, L.R., Weintraub, R.M., Hartman, G.S., Malenka, D.J., Ross, C. S. et al. (2004a). Intraoperative and postoperative variables associated with strokes following cardiac surgery. *Heart Surgery Forum*, 7(4), E271-276.
- Likosky, D. S., Leavitt, B. J., Marrin, A.S., Malenka, D. J., Reeves, A. G., Weintraum, R. M., et al. (2003). Intra- and postoperative predictors of stroke after coronary artery bypass grafting. *Annals of Thoracic Surgery*, 76, 428-435.
- Likosky, D. S., Roth, R. M., Saykin, A.J., Eskey, C. J., Ross, C. S., & O'Connor, G. T. (2004b). Neurologic injury associated with CABG surgery: Outcomes, mechanisms, and opportunities for improvement. *Heart Surgery Forum*, 7(6), E650-662.
- Lines, C. R., McCarroll, K. A., Lipton, R. B., & Block, G. A. (2003). Telephone screening for amnesic mild cognitive impairment. *Neurology*, 60, 261-266.
- Linstedt, U., Meyer, O., Kropp, P., Berkau, A., Tapp, E., & Zenz, M. (2002). Serum concentration of S-100 protein in assessment of cognitive dysfunction after general anesthesia in different types of surgery. *Acta Anaesthesiologica Scandinavica*, 46, 384-389.
- Loewenstein, D. A., Acevedo, A., Czaja, S. J., & Duara, R. (2004). Cognitive rehabilitation of mildly impaired Alzheimer's disease patients on cholinesterase inhibitors. *The American Journal of Geriatric Psychiatry*, 12, 395-402.

- Luria, A. R. (1970). The functional organization of the brain. *Scientific America*, 222, 66-78.
- Luria, A. R. (1973). *The working brain: An introduction to neuropsychology*. New York: Basic Books.
- Luria, A. R. (1980). *Higher cortical functions in man* (2nd ed.). New York: Basic Books.
- Mahanna, E. P., Blumenthal, J. A., White, W. D., Croughwell, N. D., Clancy, C. P., Smith, L. R., et al. (1996). Defining neuropsychological dysfunction after coronary artery bypass grafting. *Annals of Thoracic Surgery*, 61, 1342-1347.
- Mahncke, H. W., Connor, B. B., Appelman, J., Ahsanuddin, O. N., Hardy, J. L., Wood, R. A. et al. (2006). Memory enhancement in healthy older adults using a brain plasticity-based training program: A randomized, controlled study. *Proceedings of the National Academy of Sciences*, 103(33), 12523-12528.
- Mahoney, F. I., & Barthel, S. W. (1965). Functional evaluation: The Barthel Index. *Maryland State Medical Journal*, 44, 61-65.
- Martens, P., Raabe, A., & Johnsson, P. (1998). Serum S-100 and neuron-specific enolase for prediction of regaining consciousness after global cerebral ischemia. *Stroke*, 29(11), 2363-2366.
- Mathew, J. P., Grocott, H. P., Phillips-Bute, B., Stafford-Smith, M., Laskowitz, D. T., Rossignol, D., et al. (2003). Lower endotoxin immunity predicts increased cognitive dysfunction in elderly patients after cardiac surgery. *Stroke*, 34, 508-513.
- Maxwell, S. E., & Delaney, H. D. (2004). *Designing experiments and analyzing data: A model comparison perspective* (2nd ed.). Mahwah, NJ: Lawrence Erlbaum Associates, Publishers.

- McDougall, G.J. (1999). Cognitive interventions among older adults. *Review of Nursing Research*, 17, 219-240.
- Mesulam, M. M. (2000). *Principles of Behavioral and Cognitive Neurology* (2nd ed.). New York: Oxford University Press Inc.
- Mohs, R. C., Ashman, T. A., Jantzen, K., Albert, M., Brandt, J., Gordon, B., et al. (1998). A study of the efficacy of a comprehensive memory enhancement program in healthy elderly persons. *Psychiatry Research*, 77, 183-195.
- Moller, J. T. (1997). Cerebral dysfunction after anaesthesia. *Acta Anaesthesiologica Scandinavica*, 110, 13-16.
- Moller, J. T., Cluitmans, P., Rasmussen, L. S., Houx, P., Rasmussen, H., Canet, J., et al. (1998). Long-term postoperative cognitive dysfunction in the elderly: ISPOCD1 study. *Lancet*, 351, 857-861.
- Moller, J. T., Sennild, I., Johannessen, N. W., Jensen, P. F., Espersen, K., Gravenstein, M. D., et al. (1993). Perioperative monitoring with pulse oximetry and late postoperative cognitive dysfunction. *British Journal of Anaesthesia*, 71, 340-347.
- Monk, T. G., Saini, B., Weldon, B. C., & Sigl, J. C. (2005). Anesthetic management and one-year mortality after noncardiac surgery. *Anesthesia and Analgesia* 100, 4-10.
- Monk, T. G., Weldon, B. C., Garvan, C. W., Dede, D. E., van der As, M. T., Heilman, K. M., et al. (2008). Predictors of cognitive dysfunction after major noncardiac surgery. *Anesthesiology* 108(1), 18-30.
- Morris, J. N., Fries, B. E., Steel, K., Ikegami, N., Bernabei, R., Carpenter, G. I., et al. (1997). Comprehensive clinical assessment in community setting: Applicability of the MDS-HC. *Journal of the American Geriatrics Society*, 45(8), 1017-1024.

- Mrak, R. E., Griffin, S. J., & Graham, D. I. (1997). Aging associated changes in human brain. *Journal of Neuropathology and Experimental Neurology*, 56(12), 1269-1275.
- Muravchick, S. (2006). Anesthesia for the geriatric patient. In: P.G. Barash, B. F. Cullen, & R.K. Stoelting (Eds.), *Clinical Anesthesia* (5th ed.) (pp. 1219-1228). Philadelphia: Lippincott Williams & Wilkins.
- Murkin, J. M., Newman, S. P., Stump, D. A., & Blumenthal, J. A. (1995). Statement of consensus on assessment of neurobehavioral outcomes after cardiac surgery. *Annals of Thoracic Surgery*, 59, 1289-1295.
- Murkin, J. M., Stump, D. A., Blumenthal, J. A., & McKhann, G. (1997) Defining dysfunction: Group means versus incidence analysis – a statement of consensus. *Annals of Thoracic Surgery*, 64(3), 904-905.
- Newman, M. F., Kirchner, J. L., Phillips-Bute, B., Gaver, B., Grocott, H., Jones, R. H., et al. (2001). Longitudinal assessment of neurocognitive function after coronary artery bypass surgery. *NEJM*, 344(6), 395-402.
- Newman, S.P. (1995). Analysis and interpretation of neuropsychologic tests in cardiac surgery. *Annals of Thoracic Surgery*, 59, 1351-1355.
- Newman, S., Stygall, J., Hirani, S., Shaewfi, S., & Maze, M. (2007). Postoperative cognitive dysfunction after noncardiac surgery: A systematic review. *Anesthesiology*, 106(3), 572-590.
- Niemann, H., Ruff, R. M., & Baser, C. A. (1992). Computer assisted attention retraining in head injured individuals: A controlled efficacy study of an out-patient program. *Journal of Consulting and Clinical Psychology*, 58, 811-817.

- Novack, T. A., Caldwell, S. G., Duke, L. W., & Berquist, T. (1996). Focused versus unstructured intervention for attention deficits after traumatic brain injury. *Journal of Head Trauma and Rehabilitation, 11*(3), 52-60.
- Novelli, G., Laiacona, M., Papagno, C., Vallar, G., Capitani, E., & Cappa, S. F. (1986). Tre test clinici di ricerca e produzione lessicale. Taratura su soggetti normali. *Archives of Neurological, Psychological, and Psychiatric, 47*, 477-506 (In Italian).
- Nudo, R. J. (2006). Plasticity. *The Journal of the American Society for Experimental NeuroTherapeutics, 3*(4), 420-427.
- Olson, A. K., Eadie, B. D., Ernst, C., & Christie, B. R. (2006). Environmental enrichment and voluntary exercise massively increase neurogenesis in the adult hippocampus via dissociable pathways. *Hippocampus, 16*, 250-260.
- Page, S. J., Levine, P., & Leonard, A. C. (2005). Effects of mental practice on affected limb use and function in chronic stroke. *Archives of Physical Medicine and Rehabilitation, 86*, 399-402.
- Page, S. J., Levine, P., Sisto, S., & Johnston, M. V. (2001). A randomized efficacy and feasibility study of imagery in acute stroke. *Clinical Rehabilitation, 15*, 233-240.
- Practico, C., Quattrone, D., Lucanto, T., Amato, A., Penna, O., Roscitano, C., et al. (2005). Drugs of anesthesia acting on central cholinergic system may cause post-operative cognitive dysfunction and delirium. *Medical Hypotheses, 65*, 972-982.
- Prigatano, G. P. (1997). Learning from our successes and failures: Reflections and comments on "Cognitive rehabilitation: How it is and how it might be". *Journal of the International Neuropsychological Society, 3*(5), 497-499.

- Quattara, A., Amour, J., & Bouzguenda, H. (2009). Cognitive impairment after cardiac surgery. *Presse Med*, 38(11), 1607-1612.
- Radloff, L. S. (1977). The Center for Epidemiologic Studies Depression Scale: A self report depression scale for research in the general population. *Applied Psychological Measurement* 1(3), 385-401.
- Randolph, C. (1998). *RBANS manual: Repeatable Battery for the Assessment of Neuropsychological Status*. San Antonio, TX: The Psychological Corporation.
- Randt, C. T. & Brown, E. R. (1986). *Randt Memory Test*. Bayport, NY: Life Science Associates.
- Rapp, S., Brenes, G., & Marsh, A. P. (2002). Memory enhancement training for older adults with mild cognitive impairment: a preliminary study. *Aging & Mental Health*, 6(1), 5-11.
- Rasmussen, L. S., Christiansen, M., Eliassen, K., Sander-Jensen, K., & Moller, J. T. (2002a). Biochemical markers for brain damage after cardiac surgery – Time profile and correlation with cognitive dysfunction. *Acta Anaesthesiologica Scandinavica*, 46, 547-551.
- Rasmussen, L. S., Larsen, K., Houx, P., Skovgaard, L. T., Hanning, C. D., & Moller, J.T. (2001). The assessment of postoperative cognitive function. *ACTA Anaesthesiologica Scandinavica*, 45, 275-289.
- Rasmussen, L. S. & Moller, J. T. (2000). Central nervous system dysfunction after anesthesia in the geriatric patient. *Anesthesiology Clinics of North America*, 18, 59-70.

- Rasmussen, L. S., O'Brien, J. T., Silverstein, J. H., Johnson, T.W., & Siersma, V. D. (2005). Is perioperative cortisol secretion related to postoperative cognitive dysfunction. *Acta Anaesthesiologica Scandinavica*, 49, 1225-1231.
- Rasmussen, L. S., Sperling, B., Abildstrom, H. H., & Moller, J. T. (2002b). Neuron loss after coronary artery bypass detected by SPECT estimation of benzodiazepine receptors. *Annals of Thoracic Surgery*, 74, 1576-1580.
- Rasmussen, L. S., Steentoft, A., Rasmussen, H., Dristensen, P. A., & Moller, J. T. (1999). Benzodiazepines and postoperative cognitive dysfunction in the elderly. *British Journal of Anaesthesia*, 83(4), 585-589.
- Rasmusson, D. X., Rebok, G. W., Bylsma, F. W., & Brandt, J. (1999). Effects of three types of memory training in normal elderly. *Aging Neuropsychology and Cognition*, 6, 56-66.
- Reitan, R. M. (1955). The relation of the Trail Making Test to organic brain damage. *Journal of Consulting Psychology*, 19, 393-394.
- Reitan, R. M. & Wolfson, H. J. (1988). Verbal processing by the brain. *Journal of Clinical and Experimental Neuropsychology*, 10(4), 400-408.
- Requena, C., Lopez Ibor, M. I., Maestu, F., Campo, P., Lopez Ibor, J. J., & Ortiz, T. (2004). Effects of cholinergic drugs and cognitive training on dementia. *Dementia and Geriatric Cognitive Disorders*, 18(1), 50-54.
- Reuben, D. B., Laliberte, L., & Hiris, J. (1990). A hierarchical exercise scale to measure function at the advanced activities of daily living (AADL) level. *Journal of the American Geriatrics Society*, 38, 855-861.

- Rey, A. (1964). *L'examen clinique en psychologie*. Paris: Presses Universitaires de France.
- Rosen, H., Rosengren, L., Herlitz, J., & Blomstrand, C. (1998). Increased serum levels of the S-100 protein are associated with hypoxic brain damage after cardiac arrest. *Stroke*, 29(2), 473-477.
- Rosenburg, J., & Kehlet, H. (1993). Postoperative mental confusion: Association with postoperative hypoxemia. *Surgery*, 114, 76-81.
- Roy, C. (1984). *Introduction to nursing: An adaptation model* (2nd ed.). Englewood Cliffs, NJ: Prentice-Hall.
- Roy, C. (1999). Domain primacy: Use of a theoretical framework to guide the selection of subject matter for theory development and methods of inquiry. *Symposium on Knowledge Development and Synthesis*. University of Rhode Island.
- Roy, C. (2001). Alterations in cognitive processing. In C. Stewart-Amidei, & J.A. Kunkel (Eds.), *AANN's Neuroscience Nursing: Human Responses to Neurologic Dysfunction* (2nd ed.) (pp.275-323). Philadelphia, PA: W.B. Saunders Co.
- Roy, C., & Anderson, H. (1999). *The Roy Adaptation Model* (2nd ed.). Stamford, CT: Appleton & Lange.
- Rubens, F. D., Boodhwani, M., Mesana, T., Wozny, D., Wells, G., & Nathan, H. J. (2007). The Cardiotomy Trial: A randomized, double-blind study to assess the effect of processing of shed blood during cardiopulmonary bypass on transfusion and neurocognitive function. *Circulation*, 116(Suppl. I), I-89-I-97.

- Saghaei, M. (2004). *Random Allocation Software: (Version 1.0)* [Computer software].
Isfahan: Iran <http://mahmoodsaghaei.tripod.com/Softwares/randalloc.html>
- Salazar, A. M., Warden, D. L., Schwab, K., Spector, J., Braverman, S., Walter, J., et al. (2000). Cognitive rehabilitation for traumatic brain injury. *JAMA*, 283(23), 3075-3081.
- Salthouse, T. A., & Ferrer-Caja, E. (2003). What needs to be explained to account for age-related effects on multiple cognitive variables? *Psychology and aging*, 18, 91-110.
- Santacroce, S. J., Maccarelli, L. M., & Grey, M. (2004). Intervention fidelity. *Nursing Research*, 53(1), 63-66.
- Sarajuuri, J. M., Kaipio, M. L., Koskinen, S. K., Niemela, M. R., Servo, A. R., & Vilkki, J. (2005). Outcome of a comprehensive neurorehabilitation program for patients with traumatic brain injury. *Archives of Physical Medicine and Rehabilitation*, 86, 2296-2302.
- Satz, P. (1993). Brain reserve capacity on symptom onset after brain injury: A formulation and review of evidence for threshold theory. *Neuropsychology*, 7(3), 273-295.
- Schmidt, M. (1996). *Rey Auditory and Verbal Learning Test. A Handbook*. Los Angeles: Western Psychological Services.
- Schwartz, J. M., & Begley, S. (2002). *The Mind and the brain: Neuroplasticity and the power of mental force*. New York: Harper Collins.
- Selkoe, D. J. (1992). Aging brain, aging mind. *Scientific America*, 267(3), 134-142.

- Selnes, O. A., Goldsborough, M. A., Borowitz, L. M., & McKhann, G. M. (1999). Neurobehavioral sequelae of cardiopulmonary bypass. *Lancet*, 353, 1601-1606.
- Selnes, O. A., Grega, M. A., Borowicz, L. M., Barry, S., Zeger, S., Baumgartner, W. A., et al. (2005). Cognitive outcomes three years after coronary artery bypass surgery: A comparison of on-pump coronary artery bypass graft surgery and nonsurgical controls. *Annals of Thoracic Surgery*, 79, 1201-1209.
- Selnes, O. A., Grega, M. A., Borowicz, L. M., Royall, R. M., McKhann, G. M., & Baumgartner, W. A. (2003). Cognitive changes with coronary artery disease: A prospective study of coronary artery bypass graft patients and nonsurgical controls. *Annals of Thoracic Surgery*, 75, 1377-1386.
- Selnes, O. A., Royall, R. M., Grega, M. A., Borowicz, L. M., Quaskey, S., & McKhann, G. M. (2001). Cognitive changes 5 years after coronary artery bypass grafting: Is there evidence of late decline? *Archives of Neurology*, 58(4), 598-604.
- Shann, K. G., Likosky, D. S., Murkin, J. M., Baker, R. A., Baribeau, Y. R., DeFoe, G., et al. (2006). An evidence-based review of cardiopulmonary bypass in adults: A focus on neurologic injury, glycemic control, hemodilution, and the inflammatory response. *Journal of Thoracic and Cardiovascular Surgery*, 132, 283-290.
- Sharrock, N. E., Fischer, G., Goss, S., Flynn, E., Go, G., Sculco, T., et al. (2005). The early recovery of cognitive function after total hip replacement under hypotensive epidural anesthesia. *Regional Anesthesia and Pain Medicine*, 30(2), 123-127.

- Shaw, P. J., Bates, D., Cartlidge, N. E., French, J. M., Heaviside, D., Julian, D. G., et al. (1987). Neurologic and neuropsychological morbidity following major surgery: comparison of coronary artery bypass and peripheral vascular surgery. *Stroke*, 18, 700-707.
- Shumaker, S. A., Legault, C., & Coker, L. H. (2006). Behavior-based interventions to enhance cognitive functioning and independence in older adults. *JAMA*, 296(23), 2852-2854.
- Silbert, B. S., Scott, D. A., Evered, L. A., Lewis, M. S., Kalpokas, M., Maruff, P., et al. (2006). A comparison of the effect of high- and low-dose Fentanyl on the incidence of postoperative cognitive dysfunction after coronary artery bypass surgery in the elderly. *Anesthesiology*, 104(6), 1137-1145.
- Silverstein, J. H., Steinmetz, J., Reichenberg, A., Harvey, P. D., & Rasmussen, L. S. (2007). Postoperative cognitive dysfunction in patients with preoperative cognitive decline. *Anesthesiology*, 106(3), 431-435.
- Singer, T., Lindenberger, U., & Baltes, P. B. (2003). Plasticity of memory for new learning in very old age: A story of major loss? *Psychology and Aging*, 18(2), 306-317.
- Sivan, A. B. (1992). *Benton Visual Retention Test* (5th ed.). San Antonio, TX: The Psychological Corporation.
- Spinner, H., & Tognoni, G. (1987). Standardizzazione e taratura Italiana di test neuropsicologici. *Italian Journal of neurological Sciences*. 6(Suppl. 8). (in Italian).

- Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society*, 8, 448-460.
- Stern, Y. (2003). The concept of cognitive reserve: A catalyst for research. *Journal of Clinical and Experimental Neuropsychology*, 25(5), 589-593.
- Strauss, E., Sherman, E. M. S., & Spreen, O. (2006). *A Compendium of Neuropsychological Tests* (3rd ed.). New York: Oxford University Press.
- Stroobant, N., Van Nooten, G., Van Belleghem, Y., & Vingerhoets, G. (2005). Relation between neurocognitive impairment, embolic load, and cerebrovascular reactivity following on- and off-pump coronary artery bypass grafting. *Chest*, 127(6), 1967-1976.
- Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology*, 18, 643-662.
- Stump, D., Rogers, A., Hammon, J., & Newman, S. (1996). Cerebral emboli and cognitive outcome after cardiac surgery. *Journal of Cardiothoracic and Vascular Anesthesia*, 10(1), 113-119.
- Symes, E., Marruf, P., & Ajani, A. (2000). Issues associated with the identification of cognitive change following coronary artery bypass grafting. *Australian and New Zealand Journal of Psychiatry*, 34, 770-784.
- Tabachnick, B. G., & Fidell, L. S. (2007). *Using Multivariate Statistics*, (5th ed.). Boston: Pearson Educational, Inc.

- Taub, E., Uswatte, G., King, D. K., Morris, D., Crago, J. E., & Chatterjee, A. (2006). A placebo controlled trial of constraint-induced movement therapy for upper extremity after stroke. *Stroke*, 37, 1045-1049.
- Thompson, G. (2005). Cognitive-training programs for older adults: What are they and can they enhance mental fitness? *Educational Gerontology*, 31, 603-626.
- Thornton, E. W., Groom, C., Fabri, B. M., Fox, M. A., Hallas, C., & Jackson, M. (2005). Quality of life outcomes after coronary artery bypass graft surgery: Relationship to neuropsychologic deficit. *Journal of Thoracic and Cardiovascular Surgery*, 130(4), 1022- 1027.
- Tondat-Ruggeri, L., Languirand, M., & Caruso, J. L. (2000). *The Thinking Skills Workbook: A Cognitive Skills Remediation Manual for Adults*, (3rd ed.). Springfield, IL: Charles C Thomas Publisher LTD.
- Triola, M. F. (2008). *Elementary Statistics*, (10th ed.). New York, NY: Pearson Publisher Inc.
- Troyer, A. K. (2001). Improving memory knowledge, satisfaction and functioning via an education and intervention program for older adults. *Aging, Neuropsychology, and Cognition* 8(4), 256-268.
- Troyer, A. K., Murphy, K. J., Anderson, N. D., Moscovitch, M., & Craik, F. I. (2008). Changing everyday memory behavior in amnesic mild cognitive impairment: A randomized controlled trial. *Neuropsychological Rehabilitation*, 18(1), 65-88.
- Tune, L. E. (2001). Anticholinergic effects of medication in elderly patients. *Journal of Clinical Psychiatry*, 62(Suppl. 21), 11-14.

- Vandelandotte, C., & De Bourdeaudhuij, I. (2003). Acceptability and feasibility of a computer-tailored physical activity intervention using stages of change: Project FAITH. *Health Education Research*, 18(3), 304-317.
- Van Dijk, D., Spoor, M., Hijman, R., Nathoe, H. M., Borst, C., Jansen, E. W., et al. (2007). Cognitive and cardiac outcomes 5 years after off-pump vs on-pump coronary artery bypass graft surgery. *JAMA*, 297(7), 701-708.
- Van Zant, G., & Liang, Y. (2003). The role of stem cells in aging. *Experimental Hematology*, 31(8), 659-672.
- Verhaeghen, P., Marcoen, A., & Goossens, L. (1992). Improving memory performance in the aged through mnemonic training: A meta-analytic study. *Psychology and Aging*, 7(2), 242-251.
- Wadley, V. G., Benz, R. L., Ball, K. K., Roenker, D. L., Edwards, J. D., & Vance, D. (2006). Development and evaluation of home-based speed-of-processing training for older adults. *Archives of Physical Medicine and Rehabilitation*, 87, 757-763.
- Wan, H., Sengupta, M., Velkoff, V. A., & DeBarros, K. A. (2005). U.S. Census Bureau, Current Population Reports. *65+ in the United States: 2005*, U.S. Government Printing Office, Washington, DC.
- Wang, V., Sands, L. P., Vaurio, L., Mullen, E. A., & Leung, J. M. (2007). The effects of postoperative pain and its management on postoperative cognitive dysfunction. *The American Journal of Geriatric Psychology*, 15(1), 50-59.
- Ware, J. E., Kosinski, M., & Keller, S. D. (1996). A 12-item Short Form Health Survey: Construction of scales and preliminary tests of reliability and validity. *Medical Care*, 34, 220-223.

- Wechsler, D. (1945). A standard memory scale for clinical use. *Journal of Psychology*, 19, 87-95.
- Wechsler, D. (1981). *WAIS-R manual*. New York: The Psychological Corporation.
- Wechsler, D. (1997). *Wechsler Memory Scale* (3rd ed.). San Antonio, TX: The Psychological Corporation.
- Westaby, S., Saatvedt, K., White, S., Katsumata, T., van Oeveren, W., & Halligan, P. W. (2001). Is there a relationship between cognitive dysfunction and systemic inflammatory response after cardiopulmonary bypass? *Annals of Thoracic Surgery*, 71, 667-672.
- Westerberg, H., Jacobaeus, H., Hirvikoski, T., Clevberger, P., Ostensson, M. L., Bartfai, A., et al. (2006). Computerized working memory training after stroke – A pilot study. *Brain Injury*, 21(1), 21-29.
- Weuve, J., Kang, J. H., Manson, J. E., Breteler, M. M.B., Ware, J. H., & Grodstein, F. (2004). Physical activity, including walking, and cognitive function in older women. *JAMA*, 292(12), 1454-1461.
- Willis, S. L. (1996). Everyday cognitive competence in elderly persons: Conceptual issues and empirical findings. *Gerontologist*, 36, 595-601.
- Willis, S. L., Jay, G. M., Diehl, M., & Marsiske, M. (1992). Longitudinal change and prediction of everyday task performance in the elderly. *Research on Aging*, 14, 68-91.
- Willis, S. L., Tennstedt, S. L., Marsiske, M., Ball, K., Elias, J., Koepke, K. M., et al. (2006). Long-term effect of cognitive training on everyday functional outcomes in older adults. *JAMA*, 296(23), 2805-2814.

- Wilson, B. A., Cockburn, J., & Baddeley, A. D. (1985). *The Rivermead Behavioural Memory Test Manual*. Valley Test Co., Reading: Thames.
- Wilson, R. S., Mendes de Leon, C. F., Barnes, L. L., Schneider, J. A., Bienias, J. L., Evans, D. A., et al. (2002). Participation in cognitively stimulating activities and risk of incident Alzheimer disease. *JAMA*, 287(6), 742-748.
- Wolkowitz, O. M., Lupien, S. J., & Bigler, E. D. (2007). The “steroid dementia syndrome”: A possible model of human glucocorticoid neurotoxicity. *Neurocase*, 13(3), 189-200.
- Woolfe, N. J. (2006). Acetylcholine, cognition, and consciousness. *Journal of Molecular Neuroscience*, 30, 219-222.
- Wu, C. L., Hsu, W., Richman, J. M., & Raja, S. N. (2004). Postoperative cognitive function as an outcome of regional anesthesia and analgesia. *Regional Anesthesia and Pain Medicine*, 29(3), 257-268.
- Yin, Y., Luo, A., Guo, X., Li, L., & Huang, Y. (2007). Postoperative neuropsychological change and its underlying mechanism in patients undergoing coronary artery bypass grafting. *Chinese Medical Journal*, 120(22), 1951-1957.
- Yu, F., Kolanowski, A. M., Strumpf, N. E., & Eslinger, P. J. (2006). Improving cognition and function through exercise intervention in Alzheimer’s disease. *Journal of Nursing Scholarship*, 38(4), 358-365.
- Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, 67(6), 361-370.
- Zimpfer, D., Czerny, M., Kilo, J., Kasimir, M. T., & Madl, C. (2002). Cognitive deficit after aortic valve replacement. *Annals of Thoracic Surgery*, 74, 407-412.

Zimpfer, D., Czerny, M., Schuch, P., Fakin, R., & Madl, C. (2006). Long-term neurocognitive function after mechanical aortic valve replacement. *Annals of Thoracic Surgery*, 81, 29-33.

Zimpfer, D., Czerny, M., Vogt, F., Schuch, P., Kramer, L., Wolner, E., et al. (2004). Neurocognitive deficit following coronary artery bypass grafting: A prospective study of surgical patients and nonsurgical controls. *Annals of Thoracic Surgery*, 78, 513-519.

APPENDIX A

Institutional Review Board Approval

Boston College

Catholic Medical Center



BOSTON COLLEGE
Institutional Review Board
 Office for Research Protections
 Waul House, 3rd Floor
 Phone: (617) 552-4778, fax: (617) 552-0948

IRB Protocol Number: 08.265.01

DATE: April 23, 2008

TO: Calvin, Connie

FROM: Institutional Review Board – Office for Research Protections

RE: Feasibility, Acceptability, And Effectiveness Of A Cognitive Training Intervention For Post-Operative Cardiac Surgical Patients

Notice of IRB Review and Approval
Expedited Review as per Title 45 CFR Part 46.110, FR 60366, FR, # 5&7

The project identified above has been reviewed by the Boston College Institutional Review Board (IRB) for the Protection of Human Subjects in Research using an expedited review procedure. This is a minimal risk study. This approval is based on the assumption that the materials, including changes/clarifications that you submitted to the IRB contain a complete and accurate description of all the ways in which human subjects are involved in your research.

This approval is given with the following standard conditions:

1. You are approved to conduct this research only during the period of approval cited below;
2. You will conduct the research according to the plans and protocol submitted (approved copy enclosed);
3. You will immediately inform the Office for Research Protections (ORP) of any injuries or adverse research events involving subjects;
4. You will immediately request approval from the IRB of any proposed changes in your research, and you will not initiate any changes until they have been reviewed and approved by the IRB;
5. You will only use the informed consent documents that have the IRB approval dates stamped on them (approved copies enclosed).
6. You will give each research subject a copy of the informed consent document;
7. You may enroll up to 60 participants.

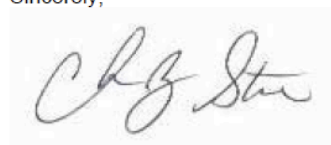
8. If your research is anticipated to continue beyond the IRB approval dates, you must submit a Continuing Review Request to the IRB approximately 60 days prior to the IRB approval expiration date. Without continuing approval the Protocol will automatically expire on April 23, 2009.

Additional Conditions: Any research personnel that have not completed CITI education certificates should be removed from the project until they have completed the training. When they have completed the training, you must submit a Protocol Revision and Amendment Form to add their names to the protocol, along with a copy of their CITI education certificate.

Approval Period: **April 23, 2008- April 22, 2009**

Boston College and the Office for Research Protections appreciate your efforts to conduct research in compliance with Boston College Policy and the federal regulations that have been established to ensure the protection of human subjects in research. Thank you for your cooperation and patience with the IRB process.

Sincerely,



Christina Booth Steele, MS, CIPP
IRB Designee
Director of Research Protections
coc

Boston College IRB
Approved

APR 23 2008

Thru: April 22, 09



BOSTON COLLEGE
Institutional Review Board
 Office for Research Protections
 Waul House, 3rd Floor
 Phone: (617) 552-4778, fax: (617) 552-0498

IRB Protocol Number: 08.265.01A

DATE: August 26, 2008

TO: Connie Calvin

CC: Barbara Wolfe

FROM: Institutional Review Board – Office for Research Protections

RE: Acceptability, Feasibility, And Effectiveness Of A Cognitive Training Intervention For Postoperative Cardiac Surgical Patients

Notice of IRB Review and Approval-Amendment
Expedited Review as per Title 45 CFR Part 46.110, FR 60366, FR, # 5&7

The amendment dated August 5, 2008 for the project identified above has been reviewed and approved by the Boston College Institutional Review Board (IRB) for the Protection of Human Subjects in Research using an expedited review procedure. This is a minimal risk study. This approval is based on the assumption that the materials, including changes/clarifications that you submitted to the IRB contain a complete and accurate description of all the ways in which human subjects are involved in your research.

Amendment:

- Increasing the participant compensation from \$20.00 to \$50.00
- Include a new educational manual for the participants

This approval is given with the following standard conditions:

1. You are approved to conduct this research only during the period of approval cited below;
2. You will conduct the research according to the plans and protocol submitted (approved copy enclosed);
3. You will immediately inform the Office for Research Protections (ORP) of any injuries or adverse research events involving subjects;

4. You will immediately request approval from the IRB of any proposed changes in your research, and you will not initiate any changes until they have been reviewed and approved by the IRB;
5. You will only use the informed consent documents that have the IRB approval dates stamped on them (approved copies enclosed);
6. You will give each research subject a copy of the informed consent document;
7. **If your research is anticipated to continue beyond the IRB approval dates, you must submit a Continuing Review Request to the IRB approximately 60 days prior to the IRB approval expiration date. Without continuing approval the Protocol will automatically expire on April 22, 2009.**

Additional Conditions: Any research personnel that have not completed CITI education certificates should be removed from the project until they have completed the training. When they have completed the training, you must submit a Protocol Revision and Amendment Form to add their names to the protocol, along with a copy of their CITI education certificate.

Approval Period: August 26, 2008- April 21, 2009

Boston College and the Office for Research Protections appreciate your efforts to conduct research in compliance with Boston College Policy and the federal regulations that have been established to ensure the protection of human subjects in research. Thank you for your cooperation and patience with the IRB process.

Sincerely,



Stephen Erickson
Interim Director
Office for Research Protections
COC



BOSTON COLLEGE
Institutional Review Board
 Office for Research Protections
 Waul House, 3rd Floor
 Phone: (617) 552-4778, fax: (617) 552-0498

IRB Protocol Number: 08.265.02A

DATE: June 15, 2009

TO: Connie Calvin

CC: Barbara Wolfe

FROM: Office of Research Protections

RE: Acceptability, Feasibility, and Effectiveness of a Cognitive Training Intervention for Postoperative Cardiac Surgical Patients

Notice of IRB Review and Approval-Continuing Review
Expedited Review as per Title 45 CFR Part 46.110, FR 60366, FR, # 5 & 7

The project identified above has been reviewed by the Boston College Institutional Review Board (IRB) for the Protection of Human Subjects in Research using an expedited review procedure. This is a minimal risk study. This approval is based on the assumption that the materials, including changes/clarifications that you submitted to the IRB contain a complete and accurate description of all the ways in which human subjects are involved in your research.

This approval is given with the following standard conditions:

1. You are approved to conduct this research only during the period of approval cited below;
2. You will conduct the research according to the plans and protocol submitted (approved copy enclosed);
3. You will immediately inform the Office for Research Protections (ORP) of any injuries or adverse research events involving subjects;
4. You will immediately request approval from the IRB of any proposed changes in your research, and you will not initiate any changes until they have been reviewed and approved by the IRB;
5. You will only use the informed consent documents that have the IRB approval dates stamped on them (approved copies enclosed);
6. You will give each research subject a copy of the informed consent document;

7. **If your research is anticipated to continue beyond the IRB approval dates, you must submit a Continuing Review Request to the IRB approximately 60 days prior to the IRB approval expiration date. Without continuing approval the Protocol will automatically expire on April 21, 2010**

Additional Conditions: *Any research personnel that have not completed an acceptable education/training program should be removed from the project until they have completed the training. When they have completed the training, you must submit a Protocol Revision and Amendment Form to add their names to the protocol, along with a copy of their education/training certificate.*

Approval Period: **April 22, 2009 - April 21, 2010**

Boston College and the Office for Research Protections appreciate your efforts to conduct research in compliance with Boston College Policy and the federal regulations that have been established to ensure the protection of human subjects in research. Thank you for your cooperation and patience with the IRB process.

Sincerely,



Stephen Erickson
Interim Director
Office for Research Protections

coc

CATHOLIC
Medical
CENTER

March 10, 2008

Yvon Baribeau, M.D. and Connie Calvin, ARNP
New England Heart Institute
Catholic Medical Center
100 McGregor Street
Manchester, NH 03102

IRB Action: Approval pending application revision
IRB Approval Expires: March 04, 2009

Re: Initial Review of Substudy

Principal Investigators: Yvon Baribeau, M.D. **Co Investigator:** Connie Calvin, ARNP
Sponsor: Northern New England Cardiovascular Disease Study Group
Study Number: CARD2006-1B (**PLEASE INCLUDE THIS NUMBER ON ALL CORRESPONDENCE**)
Title: Redesigning Cardiac Surgery to Reduce Neurologic Injury: Sub-study 1: Feasibility, Acceptability, and Effectiveness of a Cognitive Training Intervention for Postoperative Cognitive Dysfunction in Cardiac Surgical Patients

Dear Dr. Baribeau:

The Institutional Review Board at Catholic Medical Center reviewed the above human subject research study at the March 05, 2008 IRB meeting. The protocol, consent documents and other material as described below were approved pending minor changes to the IRB application.

The required changes are:

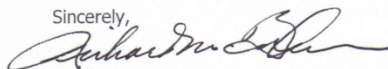
- Page 2 of 15, signature missing,
- page 11 of 15 question not answered,
- Section 4, indicates that patients are not chronically ill. The board feels that the subjects are chronically ill. If you disagree, please defend your answer.

Material submitted in support of this review:

- Initial Review Application
- Research protocol, undated
- Elements of informed consent
- Appendix A, Informed consent document
- Study schema
- Appendix B, telephone interview for cognitive status (TICS) tool
- Appendix C, timing of measurements
- Appendix D, Demographic questionnaire
- Appendix E, Thinking Skills Workbook tool
- Appendix F, Feasibility and Acceptability Questionnaire tool
- PhD proposal defense form and PhD proposal
- CV for Connie Calvin, MS, CRNA, ARNP
- Ethics education certificate for Connie Calvin, Boston College transcript listing completed ethics course at the graduate level

This study requires Continuing Review by the CMC IRB on an annual basis. IRB approval for this study expires March 04, 2009. Application for renewal is required 3 weeks before the IRB meeting. If you have any questions, please contact Bonnie Frisard at BFRisard@CMC-NH.org or at 603.663.6726.

Sincerely,



Richard M. Bunker, Chairman
Institutional Review Board

100 McGregor Street Manchester, New Hampshire 03102-3770
phone 603.668.3545 fax 603.668.5348



September 08, 2008

Yvon Baribeau, M.D. and Connie Calvin, ARNP
 New England Heart Institute
 Catholic Medical Center
 100 McGregor Street
 Manchester, NH 03102

IRB Action: Approval granted September 03, 2008
 IRB Approval Expires: July 01, 2009

Re: Amendment Review of Substudy B

Principal Investigators: Yvon Baribeau, M.D. **Sub Investigator:** Connie Calvin, ARNP
Sponsor: Northern New England Cardiovascular Disease Study Group
Study Number: CARD2006-1B (**PLEASE INCLUDE THIS NUMBER ON ALL CORRESPONDENCE**)
Title: Redesigning Cardiac Surgery to Reduce Neurologic Injury: Sub-study 1: Feasibility, Acceptability, and Effectiveness of a Cognitive Training Intervention for Postoperative Cognitive Dysfunction in Cardiac Surgical Patients

Dear Dr. Baribeau and Ms. Calvin:

The Institutional Review Board at Catholic Medical Center reviewed the above human subject research study at the September 03, 2008 IRB meeting. Your request to increase subject compensation was approved. The material described below was reviewed and approved as submitted.

Material submitted in support of this review:

- Progress Report
- Amendment #1
- Consent document, site version date August 07, 2008
- Educational booklet

A copy of the IRB approved consent document is enclosed with this letter. The approved consent document will also be sent to the research coordinator as a PDF file.

This study requires Continuing Review by the CMC IRB on an annual basis. IRB approval for this study expires July 01, 2009 which coincides with the IRB expiration date for the primary study. Application for renewal is required 3 weeks before the IRB meeting.

The CMC IRB must approve, prior to initiation, any revision to the protocol or the consent form. All SERIOUS and UNEXPECTED adverse events must be reported to the SNHMC IRB. All FDA and sponsor reporting requirements must also be followed. Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to the CMC IRB office.

If you have any questions, please contact Bonnie Frisard at BFrisard@CMC-NH.org or at 603.663.6726.

Sincerely,

A handwritten signature in cursive script, appearing to read "Richard M. Bunker".

Richard M. Bunker, Chairman
 Institutional Review Board

100 McGregor Street Manchester, New Hampshire 03102-3770
 phone 603.668.3545 fax 603.668.5348



July 16, 2009

Yvon Baribeau, M.D. and Connie Calvin, ARNP
 New England Heart Institute
 Catholic Medical Center
 100 McGregor Street
 Manchester, NH 03102

IRB Action: Approval granted July 01, 2009
 IRB Approval Expires: June 30, 2010

Re: Continuing Review of Substudy B

Principal Investigators: Yvon Baribeau, M.D. **Sub Investigator:** Connie Calvin, ARNP
Sponsor: Northern New England Cardiovascular Disease Study Group
Study Number: CARD2006-1B (**PLEASE INCLUDE THIS NUMBER ON ALL CORRESPONDENCE**)
Title: Redesigning Cardiac Surgery to Reduce Neurologic Injury: Sub-study 1: Feasibility, Acceptability, and Effectiveness of a Cognitive Training Intervention for Postoperative Cognitive Dysfunction in Cardiac Surgical Patients

Dear Dr. Baribeau and Ms. Calvin:

The Institutional Review Board at Catholic Medical Center reviewed the above human subject research study at the July 01, 2009 IRB meeting. Your request to continue this study was approved. The material described below was reviewed and approved as submitted.

Material submitted in support of this review:

- Progress Report
- Consent document, site version date 8-7-2008

A copy of the IRB approved consent document is enclosed with this letter. The approved consent document will also be sent to the research coordinator as a PDF file.

This study requires Continuing Review by the CMC IRB on an annual basis. IRB approval for this study expires June 30, 2010 which coincides with the IRB expiration date for the primary study. Application for renewal is required 3 weeks before the IRB meeting.

The CMC IRB must approve, prior to initiation, any revision to the protocol or the consent form. All SERIOUS and UNEXPECTED adverse events must be reported to the IRB. All FDA and sponsor reporting requirements must also be followed. Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to the CMC IRB office.

If you have any questions, please contact Bonnie Frisard at BFrisard@CMC-NH.org or at 603.663.6726.

Sincerely,

A handwritten signature in black ink, appearing to read "Richard M. Bunker".

Richard M. Bunker, Chairman
 Institutional Review Board

APPENDIX B

Permissions



Boston College
William F. Connell School of Nursing

April 11, 2010

Connie Calvin, CRNA, ARNP
PhD Candidate
Connell School of Nursing
Boston College
Chestnut Hill, MA 02467

Dear Ms. Calvin:

This letter is written to extend permission to use the following:

The Roy Adaptation Model of Nursing Cognitive Processing from Roy, C. (2001). Alterations in Cognitive Processing in C. Stewart-Amidei & J.A. Kunkel (Eds.), *AANN's Neuroscience Nursing: Human Responses to Neurologic Dysfunction*, (2nd Edition), W.B. Saunders Company, Philadelphia, PA. 275-323.
The Roy Adaptation model from Roy, C. (2009). *The Roy Adaptation Model*, 3rd ed. Upper Saddle River, NJ: Prentice Hall Health.

This permission extends to the educational use, reports, and extending the investigator's current work. It excludes proprietary use of a given research tool or figure developed by Dr. Roy.

Best wishes with your dissertation and your continued contributions to nursing.

Sincerely,

A handwritten signature in black ink that reads "Callista Roy". The signature is fluid and cursive.

Sr. Callista Roy, PhD, RN, FAAN
Professor and Nurse Theorist

Charles C Thomas

PUBLISHER • LTD.

2600 S. First Street
Springfield, Illinois 62704

Tel: (217) 789-8980
Toll Free: (800) 258-8980
Fax: (217) 789-9130
E-mail: books@ccthomas.com

INVOICE

Date: March 11, 2008

Invoice #: PR 955

name Doctor Connie Calvin company _____
address Northeastern University city Boston state MA zip 02115-5000
phone 617-373-3115 fax _____ e-mail c.calvin@neu.edu

CREDIT CARD
(Please check one)

☐ Visa

☐ MasterCard

Card #: _____ Exp. date: _____ / _____
(MM/YY)

Signature (Required) _____

Amount: \$ _____

Name as it appears on card (Please print)

CONTENT AND USES:

For book: **THE THINKING SKILLS WORKBOOK: A Cognitive Skills Remediation Manual for Adults**

AUTHOR	DATE	DESCRIPTION	CHARGES
TONDAT-RUGGERI, Lynn, Mary Languirand, and John Caruso	3-11-08	pp. 58, 88, 160, & 161	\$40.00

_____ nonexclusive world rights in all languages
_____ nonexclusive distribution rights throughout the world in English
_____ nonexclusive distribution rights in the U.S.A. and its possessions and Canada in English

WE ARE GLAD to grant you permission to reprint the materials listed in your attached letter or form, provided:

That these materials you wish to reproduce have appeared in our publications without any credit or acknowledgement given to any other source which might have a responsibility for granting the permissions to you,

and

That there be a suitable acknowledgement to the original source, preferably in the following form: "From (name of author or editor), (Book Title), (Edition), (Publication Date). Courtesy of Charles C Thomas Publisher, Ltd., Springfield, Illinois." When you are reproducing illustrations with our permission, we ask that this acknowledgement be in the legend below the illustration. With tables, this should appear below the tables. We are willing to accept the standard editorial forms and practices of other publishers as long as these essential items, above, are included in the acknowledgement.

CHARGES

Permission: \$40.00

Tax: \$

Grand Total: \$40.00

SEND PAYMENT & INVOICE TO:

Charles C Thomas Publisher, Ltd.
2600 S. First Street
Springfield, Illinois 62704

Remittance must be made in U.S. dollars payable through a U.S. bank or paid by an INTERNATIONAL POSTAL MONEY ORDER or it will be returned.

PLEASE RETURN A COPY OF THIS FORM WITH YOUR PAYMENT

PAR
Psychological
Assessment
Resources

INCORPORATED

16204 N. FLORIDA AVENUE

LUTZ, FLORIDA 33549

Tel.: (813) 958-3003

Fax: (813) 958-2598

www.parinc.com

Sent via email: c.calvin@neu.edu

January 23, 2008

Connie Lorette Calvin, CRNA, APRN, MS, PhD(c)
 Boston College
 6 Mountain Farm Rd
 Bow, NH 03304

Dear Ms. Calvin:

In response to your recent request, permission is hereby granted to you to include Table 1: Suggested Qualitative Interpretive Ranges for TICS Total Score from page 9 of the Telephone Interview for Cognitive Status (TICS) Professional Manual in the appendix of your dissertation titled, *Feasibility, Acceptability, and Effectiveness of a Cognitive Training Intervention in Patients with Postoperative Cognitive Dysfunction Following Cardiac Surgery*.

This Agreement is subject to the following restrictions:

- (1) The following credit line will be placed at the bottom of the verso title or similar front page on any and all material used:

"Reproduced by special permission of the Publisher, Psychological Assessment Resources, Inc., 16204 North Florida Avenue, Lutz, Florida 33549 from the Telephone Interview for Cognitive Status by Jason Brandt, Ph.D. and Marshal F. Folstein, M.D., Copyright 1987, 2003. Further reproduction is prohibited without permission of the Publisher."

- (2) None of the material may be sold, given away, or used for purposes other than those described above.
- (3) Payment of a permission fee will be waived.

"The Best Customer Service in the Test Publishing Industry!"

- (4) One copy of any of the material reproduced will be sent to the Publisher to indicate that the proper credit line has been used.

TWO COPIES of this Permission Agreement should be signed and returned to me to indicate your agreement with the above restrictions. I will return a fully executed copy of the Agreement to you for your records.

Sincerely,

Vicki M. Mark
Permissions Specialist
vmark@parinc.com
1-800-331-8378 (phone)
1-800-727-9329 (fax)

ACCEPTED AND AGREED:

BY: *Connie Lorette Calvin*
CONNIE LORETTE CALVIN

ACCEPTED AND AGREED:

BY: *V. Mark*
VICKI MARK

DATE: *2/4/08*

DATE: *Feb. 11, 2008*

APPENDIX C

Demographic Data Instrument

Demographic Questionnaire

Please circle or check the number that corresponds to your response:

1) What is your age?

☐ 40-49

☐ 50-59

☐ 60-69

☐ 70-79

☐ 80-89

2) What is your gender?

☐ Male

☐ Female

3) What is your race?

☐ White

☐ Black/African-American

☐ Hispanic/Latino

☐ Asian/Pacific Islander

☐ Native American

☐ Other

4) What is your current Marital Status?

☐ Single, Never Married

☐ Married/Living with Partner

☐ Separated/Divorced

☐ Widowed

5) Who are the other members of your household?

☐ Spouse/Partner

☐ Parents

☐ Children

☐ Friends

☐ Other

☐ Live Alone

6) Which best describes your level of education?

- ☐ Less than high school
- ☐ Some high school
- ☐ High school graduate
- ☐ Trade School
- ☐ Some College
- ☐ College graduate
- ☐ Graduate degree

7) What is your current employment status?

- ☐ Employed full time
- ☐ Employed part time
- ☐ Student
- ☐ Homemaker
- ☐ Unemployed
- ☐ Retired

8) What is your approximate yearly income?

- ☐ Less than 10,000
- ☐ 10,000 - 20,000
- ☐ 21,000 - 35,000
- ☐ 36,000 - 50,000
- ☐ 51,000 - 65,000
- ☐ Over 65,000
- ☐ Decline to respond

APPENDIX D

Institutional Review Board Approved Study Materials

Feasibility and Acceptability Questionnaire

Please read each of the following statements carefully. Then indicate the extent to which you agree or disagree with each by circling the appropriate response.

1. This program has been helpful to me.

1	2	3	4	5
Strongly	Disagree	Neutral	Agree	Strongly
Disagree		Not Sure		Agree

2. I was satisfied with the information provided

1	2	3	4	5
Strongly	Disagree	Neutral	Agree	Strongly
Disagree		Not Sure		Agree

3. I think the workbooks had clear instructions.

1	2	3	4	5
Strongly	Disagree	Neutral	Agree	Strongly
Disagree		Not Sure		Agree

4. I think the workbooks are logical.

1	2	3	4	5
Strongly	Disagree	Neutral	Agree	Strongly
Disagree		Not Sure		Agree

5. I think the workbooks are user friendly.

1	2	3	4	5
Strongly	Disagree	Neutral	Agree	Strongly
Disagree		Not Sure		Agree

6. I think the workbooks are easy to read.

1	2	3	4	5
Strongly	Disagree	Neutral	Agree	Strongly
Disagree		Not Sure		Agree

7. I think the workbooks are easy to complete.

1	2	3	4	5
Strongly	Disagree	Neutral	Agree	Strongly
Disagree		Not Sure		Agree

8. I think the workbooks are interesting.

1	2	3	4	5
Strongly Disagree	Disagree	Neutral Not Sure	Agree	Strongly Agree

9. I think there were too many exercises.

1	2	3	4	5
Strongly Disagree	Disagree	Neutral Not Sure	Agree	Strongly Agree

10. I think the time requirements to complete the workbooks are reasonable.

1	2	3	4	5
Strongly Disagree	Disagree	Neutral Not Sure	Agree	Strongly Agree

11. I think the workbooks are personally relevant.

1	2	3	4	5
Strongly Disagree	Disagree	Neutral Not Sure	Agree	Strongly Agree

12. I would recommend this program to a friend.

1	2	3	4	5
Strongly Disagree	Disagree	Neutral Not Sure	Agree	Strongly Agree

13. I would be interested in continuing a program like this one.

1	2	3	4	5
Strongly Disagree	Disagree	Neutral Not Sure	Agree	Strongly Agree

14. I am satisfied that I took part in the program.

1	2	3	4	5
Strongly Disagree	Disagree	Neutral Not Sure	Agree	Strongly Agree

15. Overall how would you rate the CTI program.

1	2	3	4	5
Very Low	Low	Neutral Not Sure	High	Very High

Example of Attention Exercises

Directions: While reading each line from left to right, please cross out the following letter

N

C U W O M P

X R H N E L

N S W K Z N

U T F N D R

Y N X P H T

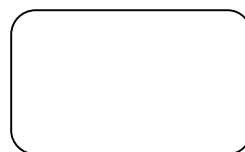
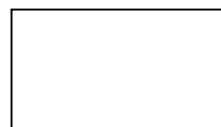
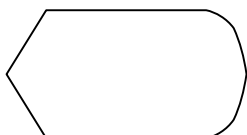
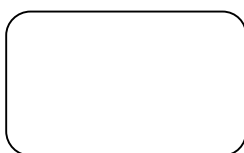
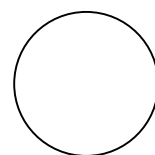
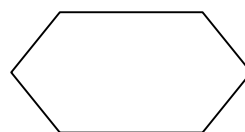
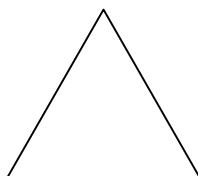
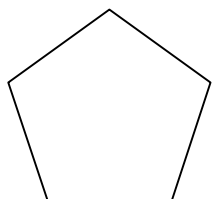
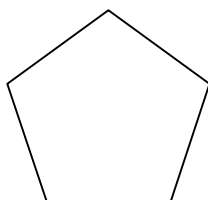
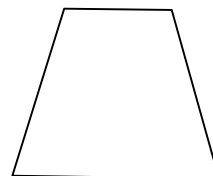
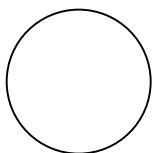
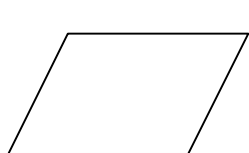
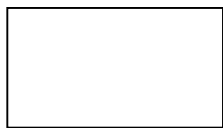
R B W R O E

N L D N M G

Score_____Correct

Example of Concentration Exercises

**FOR EACH SET FIND THE ONE OBJECT THAT
MATCHES THE OBJECT AT TOP**



Example of Memory Exercises

SET YOUR TIMER FOR “**01:00**” MINUTE. START THE TIMER AND STUDY THE LIST OF WORDS UNTIL YOU HEAR THE TIMER ALARM.

FORK

SPOON

KNIFE

PLATE

NAPKIN

TABLE

AFTER YOU HEAR THE TIMER SOUND, STOP STUDYING AND PROCEED TO THE NEXT PAGE.

SET YOUR TIMER AGAIN FOR “01:00” MINUTE

START THE TIMER
CIRCLE THE WORDS THAT APPEARED ON THE PRECEDING PAGE
DO NOT LOOK BACK AT THE LIST OF WORDS

FORK
SOUP
SPOON
PEN
KNIFE
PLATE
WOOD
CHAIR
TABLE
NAPKIN

STOP WHEN THE TIMER ALARMS.

ID#_____

Workbook#_____

Date_____

Please complete all the exercises in this workbook. Do not skip any of the exercises and try to answer all questions. If you forget how to do a certain exercise please refer to your INSTRUCTOR MANUAL. If you have any questions or concerns please call (603) 568-7901.

Your signature below affirms that you completed the exercises in this workbook without any assistance

Your Initials

Please write today's date and the time below:

Date_____

Time_____circle one: am pm

Patient and Family Education Booklet:

Postoperative Cognitive Dysfunction after Cardiac Surgery

Created by: Amanda Gilman, RN, BSN
Consultants: Connie Loretta Calvin, CRNA, ARNP, MS, PhD(c)

How common is cardiac surgery?

- Cardiac Surgery is one of the most commonly performed surgical procedures worldwide.
- The American population is getting older, right now there are more than 35 million Americans age 65 and older, many of whom will need cardiac surgery (U.S. Census Bureau, 2001).



What happens to our brains during anesthesia and cardiac surgery?

- Cardiac Surgery and anesthesia expose our bodies and our brains to many factors that can all affect our thinking abilities including:
 - Pain and discomfort
 - Fatigue
 - Stress
 - Depression
 - New medications



It is not unusual for patients to report that they don't feel "quite the same," and other vague feelings of being "just different" after cardiac surgery

- Patients and their families may notice:
 - Forgetfulness
 - Decreased ability to concentrate
 - Decreased attention span
 - Slowed processing of information
 - Decreased reaction time
 - Melancholies or Depression



- We call this Postoperative Cognitive Dysfunction or POCD

How long does POCD last?



- If POCD occurs there is no way to predict how long it will last.
- Studies suggest that POCD typically lasts a few weeks to a few months after surgery
- Yet, 2 Studies have reported that POCD was still present after 3-5 years in some patients

What can be done to help our brains process information better after cardiac surgery?

- Adequate sleep and rest
- Good nutrition and hydration
- Regular physical exercises
- Thinking exercises



Purpose of the study



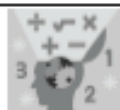
- Evaluate the effectiveness of thinking exercises designed to stimulate the brain's ability for attention, concentration, and memory
- Evaluate the ease of use of thinking exercises during the rehabilitation phase following cardiac surgery

What are thinking exercises and how will they help my recovery?

- The brain is not unlike the many muscles in your body. After surgery our brain needs rest and then stretching and strengthening. The brain can actually relearn pathways for processing and using information. With "thinking exercises" these pathways may actually get stronger and faster, much like a muscle does with exercise!



What are thinking exercises?



- Thinking exercises are simple tasks that help the brain reorganize pathways and strengthen thought processes.
- Thinking exercises have been used to stimulate cognitive recovery with great success in areas such as Brain Injury, Alzheimer's and to help maintain mental sharpness and acuity as people age.

When will I perform the thinking exercises?

- We will meet with you before you go home to practice the exercises
- Each daily exercise should take between 5 and 10 minutes
- The exercises will be done over a 6 week period



Time of day to practice includes the normal body rhythms with alertness being better between 9:00 AM and 12 Noon or between 3:00 PM and 6 PM

Who do I contact if I have any questions?



Connie Calvin, CRNA, PhD(c)
(603) 225-8369

We will schedule times for Connie to contact you during the week to see if you have any questions

APPENDIX E

Patient Consent to Study

Catholic Medical Center

Informed consent for Participation as a Subject in: Feasibility, Acceptability, and Effectiveness of a Cognitive Training Intervention for Postoperative Cardiac Surgical Patients.

Investigator: Connie Lorette Calvin, APRN, CRNA, MS, PhD(c)

CONSENT TO PARTICIPATE IN RESEARCH

Introduction:

- You are being invited to participate in a research study titled “Feasibility, Acceptability, and Effectiveness of a Cognitive Training Intervention for Postoperative Cardiac Surgical Patients”.
- You were selected as a possible participant in this research study because you are having cardiac surgery.
- We ask that you read this form carefully and ask any questions that you may have before agreeing to be in the study.

Purpose of the Study:

- The purpose of this research study is to evaluate the effectiveness of a “thinking skills workbook” designed to stimulate the brain’s ability for attention, concentration, and memory. The study will also determine the ease and usefulness of a “thinking skills workbook” during the rehabilitation phase following cardiac surgery.
- It is our intention to recruit approximately 60 patients having cardiac surgery at Catholic Medical Center. Patients will be chosen based on eligibility for the study and availability of staff.
- The expected duration of your involvement would end at your first follow-up appointment with your surgeon, approximately 12 weeks after discharge from the hospital.

Description of the Study Procedures:

- If you agree to be in this study, we would ask you to do the following things:
 - All participants will be asked to complete a short (~5 minute) survey that describes your characteristics (such as age and gender). This confidential information will only be used for research purposes. This will be completed prior to surgery.
 - After surgery, you will be randomly assigned to the treatment group or usual care. You have a 50% chance of being assigned to either group.
 - The treatment group will receive the daily thinking skills workbooks, which are designed to help improve attention, concentration, and memory.
 - You will be asked to complete one workbook each day, which should take approximately 10 minutes, for a total of 6 weeks.

Subject Initials: _____

Page 1 of 5

Site version date: 8-07-2008

PROTOCOL : CARD2006-1B

CMC IRB APPROVAL EXPIRES: June 30, 2010

- At the end of each week, you will mail the workbooks to the investigator in the self-addressed stamped envelopes provided.
- All participants will be asked to take a short (~10 minute) survey to assess any changes in your ability to answer questions and complete tasks asked of you. This confidential information will only be used for research purposes. This survey may be completed by telephone. We will identify a time that is convenient to complete this survey at the following intervals.
 - In-hospital: Before and after surgery
 - After leaving the hospital: At six weeks and 3 months.
- All participants in the treatment group will be asked to complete a short (~10 minute) survey to evaluate your thoughts about the study. This survey will be given at the end of the study (3 months after surgery).

Risks/Discomforts of Being in the Study:

- There are no foreseeable or expected risks from this study as the intervention is an educational one.
- Some patients may feel tired or anxious while answering questions asked of you during the surveys or while using the thinking skills workbook. You may refuse to answer any questions. There are no anticipated risks of any questions asked of you.

Benefits of Being in the Study:

- There are no known direct benefits to you should you decide to participate in this study. Your contribution will help us learn more about the effects of thinking exercises following cardiac surgery.

Payments:

- All participants who are eligible for the research study, having signed the consent form, and having completed the study will be compensated with a **\$50.00** gift card for your time and travel expenses.

Costs:

- There is no cost to you to participate in this research study.
- Costs not related to the research will be charged to you or your insurance carrier just as though you were not a part of this study.

Confidentiality:

- The records of this study will be kept private. In any sort of report we may publish, we will not include any information that will make it possible to identify a participant. Research records will be kept in a locked file.
- Data from this study will be shared with Dartmouth College (Hanover, New Hampshire) for analysis and processing purposes. However, your identity will not be included. Data will be maintained in a locked office, on a password-protected computer at the Data Center at Dartmouth College.

Subject Initials: _____

Page 2 of 5

Site version date: 8-07-2008

PROTOCOL : CARD2006-1B

CMC IRB APPROVAL EXPIRES: June 30, 2010

- Access to the records will be limited to researchers; however, please note that regulatory agencies (The Office of Human Research Protection, and the Food and Drug Administration), Catholic Medical Center's Institutional Review Board, and the Institutional Review Board and internal Boston College auditors may review the research records.

Voluntary Participation/Withdrawal:

- Your participation is voluntary. If you choose not to participate, it will not affect your current or future relations with Catholic Medical Center.
- You are free to withdraw at any time, for any reason.
- There is no penalty or loss of benefits to which the Participant is otherwise entitled for not taking part or for stopping your participation.
- You may be provided with any significant new findings that develop during the course of the research that may make you decide that you want to stop participating.

Alternatives:

- The alternative to participating in this research study is not to participate.

Dismissal From the Study:

- If you do not follow the instructions you are given you will be dismissed from the study. OR if the study sponsor decides to stop or cancel the study you will be dismissed from the study.

Financial Disclosure/Compensation for Injury:

- The sponsor for the primary study (The Hitchcock Foundation) is the fiscal agent. CardioThoracic Systems, Inc. at 3200 Lakeside Drive, Santa Clara, California 95054, provides money to support the primary study. This money provides the salary support for the research study coordinators.
- If you experience an emergency medical problem or injury as a direct result of your participation in this research, you will receive care from Catholic Medical Center. The Sponsor will pay the reasonable costs of medical treatments. These costs may include hospitalizations to the extent not covered by your medical or hospital insurance or third party or government program providing coverage. Decisions regarding care and compensation for any other research related injury would be made on a case-by-case basis.

Contacts and Questions:

- The researchers conducting this study are Connie Calvin, CRNA, and Dr. Yvon Baribeau. For questions or more information concerning this research you may contact Connie Calvin at (603) 568-7901 or Dr. Baribeau at (603) 663-6340.
- If you have complaints about the research or a research staff member, or if you believe you may have suffered a research related injury, contact Connie Calvin at (603) 568-7901 who will give you further instructions.
- If you have any questions about your rights as a research subject, you may contact the Catholic Medical Center Institutional Review Board Administrator at (603) 663-6069 or

Subject Initials: _____

Page 3 of 5

Site version date: 8-07-2008

PROTOCOL : CARD2006-1B

CMC IRB APPROVAL EXPIRES: June 30, 2010

the Director, Office for Human Research Participation Protection, Boston College at (617) 552-4778, or irb@bc.edu.

Permission to Use or Release Identifiable Health Information for Research Purposes

1. Why am I being asked to release this information?

- As part of the above research study, you are being asked to allow Connie Calvin, CRNA, ARNP, MS, PhD(c), the sub-investigator, to release health information about yourself to investigators at the Data Center at Dartmouth College (Hanover, New Hampshire).
- As a part of the above research study, you are being asked to release your telephone number to Connie Calvin, CRNA, ARNP, MS, PhD(c), the sub-investigator, and Derek Evans, RN, BSN, research assistant, so that they may call you at the scheduled times during the study.
- This information will be collected and entered into a database with the health information from others taking part in this study.

2. What am I being asked to release?

- We will be collecting information about you which will include:
 - Your telephone number
 - Your address
 - This information will only be used for this and only this study.

3. Who will see this information?

- The members and staff of the Catholic Medical Center Institutional Review Board may see parts of your medical records related to this study. In this case, they will see your name and other personally identifiable information about you.
- The research information collected as part of this study is the property of Yvon Baribeau, M.D., principle investigator, and Connie Calvin, CRNA, ARNP, MS, PhD(c), sub investigator, and you will not be able to get it back.
- In the event of any publication of this study, your identity will not be disclosed.

4. Will the information you collect as part of this study be destroyed when it is no longer needed?

- It is difficult for the investigators to know how long your information will be kept. Your information will be kept as least until the study is completed.
- This information will be kept in a database at Catholic Medical Center and Dartmouth Medical School for an indefinite length of time.
- We do not know when your information will no longer be used, and there is not an expiration date after which it will be discarded.

5. Can I stop my information from being used?

Subject Initials: _____

Page 4 of 5
Site version date: 8-07-2008

PROTOCOL : CARD2006-1B
CMC IRB APPROVAL EXPIRES: June 30, 2010

- Yes, you can withdraw this authorization at any time, but you must do so in writing to:

Connie Calvin, CRNA, ARNP, MS, PhD(c)
Catholic Medical Center, 100 McGregor Street, Manchester, NH 03102

- Once you cancel your authorization, we will stop collecting data. However, any information that was collected before you revoked your authorization will continue to be used and be seen as described above. You can call us and we will honor your request to stop collecting information, but you must also do so in writing.

6. What if I do not authorize you to collect and release my health information?

- If you decide not to authorize release of your health information as part of this study, your decision will in no way affect your medical care.
- This decision will not cause you to lose any benefits to which you are entitled.
- However, you cannot be in this research study if you do not release your health information.

Copy of Consent Form:

- You will be given a copy of this form to keep for your records and future reference.

Statement of Consent:

- For Adult Consent Form combined Consent/Assent (full form): I have read (or have had read to me) the contents of this consent form and have been encouraged to ask questions. I have received answers to my questions. I give consent to participate in this study. I have received (or will receive) a copy of this form.

Signatures/Dates

Study Participant		Date	Time
Print name			
Signature of Witness		Date	Time
Print name of Witness			
Investigator Signature		Date	Time
Investigator's Name (Print)			
Subject Initials: _____			