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LOMA LINDA UNIVERSITY
School of Science and Technology
in conjunction with the
Faculty of Graduate Studies

Factors that Affect Performance on Executive Functioning after Coronary Artery Bypass Grafting

by

Sapna Mahesh Patel

A Thesis submitted in partial satisfaction of
the requirements for the degree of
Master of Arts in Experimental Psychology

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Each person whose signature appears below certifies that this thesis in his/her opinion is adequate, in scope and quality, as a thesis for the degree Master of Arts.

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CONTENTS

Chapter

TABLES

FIGURES

Figure Page

ABBREVIATIONS

CABG	Coronary Artery Bypass Grafting

ABSTRACT OF THE THESIS

Factors that Affect Performance on Executive Function Tests after Coronary Artery Bypass Grafting (CABG)

by

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Master of Arts, Graduate Program in Psychology
Loma Linda University, June 2008
Dr. Susan Anne Ropacki, Chairperson

Research suggests that individuals who undergo coronary artery bypass grafting (CABG) experience declines in neuropsychological functioning post-operatively. This decline has been observed in up to 80% of patients early after surgery, and in up to 30% of patients after six months. Many studies have examined the potential effects of CABG on neuropsychological functioning in general, and numerous studies have found that executive functions are impaired in particular. However, none have examined what factors contribute to observed executive dysfunction after CABG. This study investigated the role of memory functions on executive functions in a selected sample of patients undergoing CABG. This study also examined the role of selected individual variables and surgical variables on executive functioning after CABG. Archival data were used for this study. The sample consisted of 42 patients who had undergone elective, on-pump, normothermic CABG surgery. A battery of neuropsychological tests was administered 1-3 days before surgery and again approximately one week postoperatively, just before hospital discharge. It was hypothesized that there would be a significant decline on neuropsychological tests of executive functioning after CABG surgery. It was also hypothesized that impairment in executive functions would be impacted by performance on tests of long term memory as well as demographic and surgical factors including age, education, cardiopulmonary bypass time, anesthesia time and surgery time. Results revealed that there were significant declines in executive functions after CABG. Despite significant declines in long term memory functions after CABG, performance on long-term memory tests did not contribute significantly to performance on executive functioning tasks. Executive functioning was significantly impacted, however, by age, education, cardiopulmonary bypass time, anesthesia time and surgery time. Together, these results suggest that impairments in executive functioning after CABG may be due to demographic and perioperative factors and may exist independent of deficits in long term memory.

Introduction

Coronary heart disease (CHD) is the most common form of heart disease and is caused by the accumulation of fatty deposits in the arteries. The most recent update of the American Heart Association (2007) reveals that in 2004 over 15.8 million people (approximately 7.3% of the population) were affected by CHD. Of these people, Caucasian males have the highest prevalence of coronary heart disease (9.4%), followed by African American females (7.8%) and African American males (7.1%). Of all cardiovascular diseases, CHD has the highest mortality rate. In 2004, there were 452,300 deaths caused by CHD, representing the single leading cause of death in the U.S.

Studies have shown there is a decline in certain cognitive abilities in individuals diagnosed with heart disease. This decline is observed as the disease progresses (Muller, Grobbee, Aleman, Bots & van der Schouw, 2006; Ernest et al., 2006), as well as after certain interventions, such as coronary artery bypass grafting (CABG). Research suggests that a majority of individuals who undergo CABG experience declines in neuropsychological functioning post-operatively. This decline has been observed in up to 80% of patients early after surgery, and in up to 30% of patients after 6 months (Knipp et al., 2004). In particular, a decline is evident with verbal memory, word fluency and psychomotor speed (Mosley et al., 2005), visual memory, processing speed and executive functioning (Muller et al., 2006), as well as attention (Almeida & Flicker, 2001). Although studies have shown a general decline in neuropsychological functioning and specific declines on executive functions no studies to date have focused specifically on the factors that contribute to executive dysfunction after CABG. For example, research has demonstrated the interconnectedness and codependence of memory systems and executive functions (Heilman & Valenstein, 2003; Holthausen et al., 2003; Tremont et al., 2000; Fletcher & Henson 2001). Yet no studies have examined whether memory dysfunction may be a factor underlying observed executive dysfunction after CABG. Similarly, there is research to suggest that individual factors such as age and education or surgical variables such as cardiopulmonary bypass time, anesthesia time and surgery time affect neuropsychological functioning; however, very few studies have examined the relative contribution of such factors to observed executive dysfunction specifically after CABG.

Coronary Artery Bypass Grafting (CABG) – General Procedures

As mentioned previously, coronary heart disease is more common than other forms of cardiovascular disease. CABG is a surgical procedure used in the treatment of ischemic heart disease and to relieve angina (Symes, Maruff, Ajanie, & Currie, 2000). It has been found to be an effective treatment for patients with coronary heart disease, allowing sufficient blood flow so that oxygen and nutrients can be delivered to the heart. The purpose of CABG is to restore the blood flow to areas of the heart muscle that receive an insufficient amount of blood and oxygen due to the narrowing of the arteries. During CABG, the left internal thoracic artery and the right internal thoracic artery are used for the bypass. If additional bypasses are required, a portion of the saphenous vein from the patient's leg or the radial artery from the forearm can be used as well. This vein or artery is used as a graft by attaching it at one end to the aorta. The other end is sewn to an opening in the coronary artery, beyond the blockage. In this way, the graft creates a detour that allows the blood to go around the blockage, improving the blood supply to the heart. This entire process may be done with or without a heart-lung machine. The utilization of the heart-lung machine to perform cardiopulmonary bypass is referred to as "on-pump," and not utilizing the heart-lung machine to perform cardiopulmonary bypass is referred to as "off-pump." With the heart-lung machine, the heart is stopped. The oxygen-poor blood is diverted to the machine. The machine oxygenates the blood by removing the carbon dioxide and then the oxygenated blood is returned to the heart (Horowitz, 1988).

Neuropsychological Functions after CABG

Many studies have examined the potential effects of CABG on neuropsychological functioning in general. Most of these studies have examined cognitive domains such as memory, visual memory, visuo-spatial perception, psychomotor speed, attention, executive function and affect (McKhann et al, 2005; Knipp et al, 2004; Selnes, McKhann, Borowicz & Grega, 2006). Studies have reported significant early decline in memory, psychomotor speed, executive functions and visuo-spatial abilities. Motor functions and psychomotor speed continue to be affected by CABG five years later (Selnes et al, 2006). Interestingly, none of the studies have examined the contribution of memory functioning, individual variables or surgical variables on executive functioning.

CABG and the Frontal Lobes

Findings from several studies suggest that the frontal lobes, and thus executive functions, may be particularly vulnerable to damage subsequent to CABG. One study, for example, examined the effects of CABG (on pump and off pump) on cognitive functions and cerebral perfusion in 65 coronary artery disease patients. Single photon emission computed tomography (SPECT) and neuropsychological tests were performed one day before surgery, 10-14 days after surgery and six months after surgery. SPECT imaging captures regional cerebral blood flow images. Of these patients, 22 patients underwent on pump, normothermic CABG surgery (group 1), 21 patients underwent on pump normothermic CABG surgery and were administered the drug instenon ("Nycomed") (group 2), and 22 patients underwent off pump CABG surgery (group 3). Instenon is a drug that helps with cerebral perfusion and may prevent ischemic and hypoxic cerebral damage. Ninety six percent of those in group 1, 61% of those in group 2, and 54% of those in group 3 experienced neuropsychological deficits in the early period after CABG. These patients showed significant impairments in the Trail Making Test, Rey Auditory Verbal Learning Test and the Complex Figure Test, all of which are primarily executive functioning and memory tasks. After six months, the incidence of cognitive decline decreased to 55% in all of the cases combined. Results also revealed that in 68% of the patients there was a decrease in the regional cerebral blood flow in the right inferior frontal cortex in the early postoperative period which suggests that there may be brain tissue damage in this area. In the six-month follow-up, researchers found that brain perfusion was lower than the baseline in 55% of the patients (Chernov, Efimova, Efimova, Akhmedov & Lishmanov, 2006).

Another study examined neuron loss after CABG surgery. In this study, there were 15 patients undergoing CABG surgery. Neuropsychological testing was performed before, postoperatively at discharge and 3 months after surgery. SPECT imaging was performed before surgery and 3 months after surgery. SPECT was used in order to estimate the density of benzodiazepine receptors in the cerebral cortex. The patients were given iomazenil which has a binding affinity for benzodiazepine receptors.

Benzodiazepine receptor density is a “measure of the number of GABAergic synapses in the cerebral cortex and is therefore assumed to indicate the intactness of cortical neurons” (pg. 1579). Cognitive dysfunction was found in 46.7% of patients at discharge from the hospital. Furthermore, there was a significant decrease in the density of neurons in the frontal cortex after CABG. However, the SPECT scan results did not correlate with neuropsychological test performance. This suggests that there may be other causes for the cognitive dysfunction (including executive dysfunction) and it may not be solely due to neuron loss, specifically benzodiazepine receptors (Rasmussen, Sperling, Abildstrom & Moller, 2002).

Various studies have also revealed that the frontal lobes are vulnerable to damage due to ischemia and hypoxia that occur during CABG. As mentioned previously, cerebral ischemia is a lack of blood supply to areas of the brain. The incidence of stroke in CABG patients is 0.8-5.2%. Studies have shown that emboli strokes are the most common type (Gotesman & Wityk, 2006). Postoperative cerebral ischemic injury can be assessed using magnetic resonance imaging (MRI). MRI studies have shown that there are new focal lesions after surgery in 21-45% of patients. One study examined the effects of CABG on new postoperative cerebral ischemic lesions. The sample consisted of 101 patients undergoing on-pump and off-pump CABG surgery. The results revealed that at the 3-month postoperative assessment, nine on-pump patients and four off-pump patients had one or more new lesions, with more lesions in the middle cerebral artery territory (Lund et al, 2005). Cerebral hypoxia is a lack of oxygen to the brain despite adequate blood flow (Kolb & Wishaw, 1996). One study examined the relationship between CABG and hypoxia. The sample consisted of 115 patients undergoing CABG. Using arterial blood gas measurements, they found that five days after CABG, there is a significant correlation between postoperative cognitive dysfunction and hypoxia (Browne, Halligan, Wade & Taggart, 2003).

Although recent studies have shown that hippocampal structures are directly impacted by hypoxia (Browne et al., 2003), intermittent hypoxia during development or in sleep disordered breathing have affected other areas of the brain as well. One particular study examined intermittent hypoxia in postnatal rats. At 4 months, the rats' working memory was assessed using a water maze. The results showed that male rats exposed to intermittent hypoxia had deficits in working memory. In addition, the researchers found that there was a decrease in dendritic branching in the prefrontal cortex, but not in the hippocampus of the male rats (Kheirandish, Gozal, Pequignot, Pequignot & Row, 2005). Since working memory is an executive task, it is reasonable to suggest that executive functions may be impacted by the hypoxia that may be occurring after CABG.

Executive Functions

The frontal lobes are theorized to play a role in what are commonly known as executive functions. Executive functions are higher order processes which include planning and organization of information (Busch et al., 2005). It includes the ability to attend to several components at the same time and change the focus of concentration, resist distractions and interferences, follow multi-step instructions and continue behaviors without perseverating (Stuss & Knight, 2002). Many studies have implicated the role of the frontal lobes in executive functioning. Research on the frontal lobes began in 1848 when an explosion at a railroad construction site caused an iron bar to pierce through the head of a 25 year-old man named Phineas Gage. The iron bar penetrated through a sizeable part of the frontal lobe. This injury led to a major change in his behavior and personality (Stuss & Knight, 2002).

The frontal lobes are made up of three distinct regions. The motor cortex is responsible for making movements, the premotor cortex selects the movements, and the prefrontal cortex controls the cognitive processes so that the correct movements are made at the appropriate time and place. The prefrontal cortex is divided into three regions: dorsolateral prefrontal cortex, inferior (or ventral) prefrontal cortex and medial frontal cortex (sometimes considered to be a part of the anterior cingulated region). A portion of the inferior prefrontal cortex may also be referred to as orbital frontal cortex (Kolb & Whishaw,1996). The dorsolateral prefrontal cortex is responsible for focused attention, initiative and decision making, making plans and executing them, working memory, and verbal fluency. Individuals with damage to the orbital frontal cortex are impulsive, distracted easily, irritable, have excessive energy and drive, tend to repeat things, and have a lack of moral restraint. Damage to the medial frontal cortex causes lack of initiation and performance in limb, eye and speech movements and apathy (Fuster, 1997). Damage to the dorsolateral prefrontal region may result in working memory deficits. The prefrontal cortex involvement in working memory was first studied in primates through delayed-response tasks. In these tasks, food is placed under one of two cups while the animal watches. An opaque screen covers the cups for an interval of seconds to minutes. The animal has to keep the information in working memory so that it may choose the correct cup. Monkeys and chimpanzees with dorsolateral prefrontal lesions demonstrated impairment on this working memory task (Stuss & Knight, 2002).

Factors Affecting Executive Functioning after CABG

Memory Functions

Research has shown that numerous neuropsychological functions are impacted by CABG. However, none have endeavored to show any causal relationship between functional domains. Given the anatomical relationship between the frontal and temporal regions of the brain, it is reasonable to presume that executive functions (primarily a frontal lobe function) may be directly impacted by memory functions (primarily a temporal lobe function). There are subcortical and cortical projections from the frontal lobe to the hippocampus and temporal cortex and projections from the hippocampus and temporal cortex to the frontal lobes. There are strong projections from the hippocampus in the temporal lobe to the orbital cortex in the frontal lobe suggesting that functioning of the temporal lobe could affect functions of the frontal lobe and vice versa. Some projections from the mesial and orbital aspects and from the inferior ventral dorsolateral aspect of the frontal lobe go to the rostral temporal cortex. There are projections that go indirectly from the frontal lobe to the temporal lobe via the limbic cortex of the cingulate and hippocampal gyri (Heilman & Valenstein, 2003). Thus, due to the collaborative connections, damage or dysfunction in one area of the brain may affect functioning in another area of the brain.

This relationship between memory and executive functions is illustrated in populations characterized by memory deficits. In Alzheimer's disease, for example, there is a storage deficit of episodic memory. In Huntington and Parkinson's disease, there is impairment in the initiation of retrieval strategies. In schizophrenia, there are impairments in explicit memory, both learning and retrieval processes. As mentioned previously, executive functions involve organization of information, which is a strategic process that plays a role in the encoding of new information. Recall for word lists is better when it can be organized in semantic categories. Therefore, an impairment in organization can impact memory functions (Holthausen et al., 2003). A study by Holthausen and colleagues (2003) examined the role of central executive functions and processing speed on memory functions in schizophrenia. The results revealed that there were deficits in verbal learning and retrieval in episodic and semantic memory. They also found that coordination, processing speed and organization of information were the best predictors of long-term memory deficits. Another study by Tremont and colleagues (2000), examined the relationship between executive functions and episodic memory. They found that those individuals who had severe impairment in executive functions had more difficulty with the unstructured memory tasks (non-routine, unfamiliar and complex) than the structured memory tasks.

The relationship between memory and executive functions, and thus the impact of memory functions on executive functions, has also been illustrated in studies of working memory. Working memory is conceptualized as an executive function, as it involves the holding and mental manipulation of information (Stuss & Knight, 2002). In order for information to be transferred from working memory to long term memory and retrieved again from long term memory, the involvement of the frontal lobes is required in which there is the holding and manipulating of information. Fletcher and Henson (2001) reviewed the research on imaging studies of the frontal lobes and memory. The review revealed that many imaging studies have implicated the dorsolateral, ventrolateral and anterior frontal cortex in different memory processes. The ventrolateral frontal cortex has been shown to be involved in the updating and maintaining the contents of working memory as well as selecting information from long term memory to working memory. The dorsolateral frontal cortex is involved in selecting, monitoring, and manipulating information that is active in working memory. The anterior frontal cortex controls the switching between these processes to make the most of task performance (Fletcher & Henson, 2001).

Although many studies have shown that the medial temporal lobe structures contribute to memory, research has also revealed that there are certain aspects of memory that are primarily functions of the frontal lobes. In one study, subjects were given a list of words to remember. A positron emission tomography scan was conducted while they were retrieving information about what words were in the list (item retrieval) and when these words occurred in the list (temporal order retrieval). Results showed that while item retrieval was correlated with an increase in neural activity in the medial temporal and basal forebrain regions, temporal order retrieval correlated with an increase in neural activity in the frontal and posterior regions of the brain (Cabeza et al., 1997). The role of the frontal lobes on memory functions is also illustrated in studies of cognitive functioning in amnesia patients. Several of these studies have found that patients with amnesia due to damage to the medial temporal lobe who show normal frontal activity during encoding fail to form new memories. Normal subjects who have an intact medial temporal lobe, but have an absence of frontal activity also fail to form new memories (Buckner, Kelley & Petersen, 1999; Buckner & Koutstaal, 1998; Gabrieli, Poldrack & Desmond, 1998).

Surgical Variables

Results have been mixed about the etiology of neuropsychological impairment after CABG, but it has been hypothesized that the use of the heart-lung machine to conduct the cardiopulmonary bypass is a cause of cerebral injury (Roach et al., 1996). With the use of a heart-lung machine, cardiopulmonary bypass diverts blood flow to an extracorporeal circuit that maintains sufficient circulation and respiration. It basically replaces the heart and lungs in order to assist with the heart surgery (Casthely & Bregman, 1991). To avoid the morbidity associated with the on-pump technique, some surgeons are performing the off-pump technique. In this technique a stabilizing device is used on the "beating" heart allowing the surgeon to work on the heart without the machine (Mitka, 2004).

One study demonstrated that there is a higher embolic load in those undergoing on-pump surgery than those undergoing off-pump surgery (Stroobant, Van Nooten, Belleghen & Vingerhoets, 2005). Embolic load refers to the number of cerebral emboli which travel through the blood stream, and potentially lodge in and block a blood vessel. Embolic load is calculated by counting and measuring the diameter, length and volume of the emboli (Brown, Moody, Challa, Stump & Hammon, 2000). An emboli can be a blood clot, fat, oil, bubble of air, or a mass of cells which is brought through the blood from a large vessel. The emboli is pushed into a smaller vessel where it blocks circulation. This may cause cerebral ischemia in which there is an insufficient supply of blood to the brain. This may lead to stroke or there may be a gradual decrease in blood flow causing brain damage or death (Kolb & Wishaw, 1996).

There is also evidence of less neuropsychological impairment in those patients undergoing off-pump surgery (Diegeler et al.,2000; Zamvar et al., 2002). Although most studies have examined the immediate postoperative cognitive outcome and have found hopeful results of the off-pump technique, significant differences between off-pump and on-pump surgery in longitudinal cognitive outcomes have not been observed (Lund et al., 2005; Van Dijk et al., 2002).

There has also been considerable variability in surgical procedures within on-pump surgery such as cross-clamping technique, degree of hypothermia, and rate of rewarming (Selnes & McKhann, 2005). Many studies have examined the differences in neuropsychological functioning in normothermic versus hypothermic cardiopulmonary bypass. The normothermic technique involves keeping the blood temperature at approximately 37°C as it passes through the extracorporeal circuit. The mild hypothermic technique involves keeping the blood temperature approximately between 32-34°C (Grimm et al., 2000). The hypothermic technique has been used in order to reduce oxygen and glucose consumption during cardiopulmonary bypass thereby protecting the cells from hypoxic ischemia (Casthely & Bregman, 1991). Some investigators have reported that they were unable to reveal an effect of systemic temperature on neuropsychological functioning (Grigore et al., 2001). One study found that cognitive impairment was more prominent in patients undergoing mild hypothermia cardiopulmonary bypass (Grimm et al., 2000). Other investigators found that mild hypothermia has neuroprotective effects and there is less cognitive impairment compared to normothermic cardiopulmonary bypass (Kadoi, Saito,Takahashi, Fujita & Goto, 2004; Nathan, Wells, Munson & Wozny, 2001).

Certain perioperative events, such as cardiopulmonary bypass time, have been associated with cognitive impairment after CABG. In one study it was found that there was a relationship between cardiopulmonary bypass time and undesirable postoperative events. The greater the cardiopulmonary bypass time, the more likely patients were to have undesirable postoperative events such as neurologic complications, mortality, circulatory failure, respiratory failure, renal failure, infection and other events (Wesselink, de Boer, Morshuis & Leusink, 1997). In another study, the researchers found that there was an inverse relationship between cardiopulmonary bypass time and cognitive decline (Ho et al., 2004). One study compared those with open-heart surgery and those with coronary artery bypass grafting. They were specifically examining the asymmetry of cerebral embolic load and how it effects cognitive functioning. The researchers revealed that CABG patients had a decline in verbal memory which was associated with cardiopulmonary bypass time, but not with embolic load (Bokeriia et al., 2007). It is important to note that no studies have examined the effects of cardiopulmonary bypass time on executive functions after CABG.

Other perioperative factors such as anesthesia time and surgery time have been noted to have an association with cognitive decline. Studies have shown a postoperative cognitive decline in older adults after receiving general anesthesia during cardiac and non-cardiac surgery (Anwer, Swelem, el-Sheshai & Moustafa, 2006; Rasmussen et al., 2003), particularly in the area of memory (Williams-Russo, Sharrock, Mattis, Szatrowski & Charlson, 1995). One study examined elderly patients undergoing non-cardiac surgery under general anesthesia and their cognitive functioning after surgery. They found that the duration of anesthesia did not predict short-term or long-term change in cognitive functioning (Dijkstra, Houx & Jolles, 1999). However, in another study, it was found that the duration of anesthesia was a risk factor for early postoperative cognitive dysfunction (Moller et al., 1998).

A study by Ille and colleagues (2007) examined patient-related and surgery-related risk factors on cognitive performance. The study included patients that were undergoing cardiac surgery, including coronary artery bypass grafting. Results revealed that for elderly patients, older age, preexisting medical risk factors, and surgery duration were the most important factors influencing their cognitive performance.

Individual Differences

Age and education are individual factors that have been examined in CABG studies. Many of the studies have shown that age, specifically increasing age, is associated with postoperative cognitive dysfunction (Tuman, McCarthy, Najafi & Ivankovich, 1992; Newman et al., 1994). Moller and colleagues (1998) found that age may be a risk factor for late postoperative cognitive dysfunction. Their results showed age to be associated with executive functioning and memory tasks. A study done by Newman and colleagues (1994) examined whether age-related cognitive declines are associated with dysfunction of cerebral blood flow autoregulation during CPB. They found that increasing age was associated with impairments in immediate verbal memory, delayed verbal memory, visual memory, psychomotor speed, short-term memory, focused attention and cognitive flexibility. Age has been found to be a significant mediating variable when examining postoperative decline, but there are no studies of age as a factor specifically with a broad array of executive tests.

Years of education of CABG patients has also been examined in many studies and has been found to be associated with cognitive decline (Moller et al., 1998; Newman et al., 2004). A study by Ho and colleagues (2004) examined various predictors of cognitive decline after CABG. They found many that many medical variables as well as education were associated with cognitive decline. Specifically, the more years of education the patients had, the less cognitive decline they had. Another study by Dupuis and colleagues (2006) examined the cognitive performance of patients before and after CABG, while controlling for certain variables. Results revealed that patients with less than a high school education had greater cognitive declines on tasks of attention/concentration, verbal fluency, and logical/verbal memory. However, there was one study by Selnes and colleagues (1999) which found that education was not a predictor of cognitive change. Ultimately, education has not been examined as a factor affecting executive functions specifically.

Research shows that the frontal lobes are vulnerable in CABG and this is manifested as executive dysfunction. While numerous studies have examined what factors affect cognitive functioning after CABG in general, none have examined the specific role of these factors on executive functions. There is theoretical reason to suggest that memory functions may impact performance on executive tasks. There is evidence to suggest that age, education, cardiopulmonary bypass time, anesthesia time and surgery time are also factors that may impact performance on executive tasks.

Aims and Hypotheses

Aim 1

To examine the effects of CABG on executive functions. This will be examined by analyzing changes in scores on executive function tasks from before to after CABG surgery.

Hypothesis. There will be significant declines on neuropsychological tests of executive functioning after CABG.

Aim 2

To examine whether impairment in long-term memory contributes to impairment in executive functioning. This aim will be examined by covarying changes in scores on memory tasks out of analyses of change on executive functions tests.

Hypothesis. Performance on memory tasks will contribute significantly to performance on executive function tasks.

Aim 3

To examine whether perioperative factors (i.e., cardiopulmonary bypass time, anesthesia time and surgery time) or demographic factors (i.e., age and education) moderate executive functioning after CABG. This aim will be examined by covarying these individual variables and surgical variables out of analyses of change on executive functions tests.

Hypothesis. Greater age, less education, longer cardiopulmonary bypass time, longer anesthesia time, and longer surgery time will contribute to greater impairment in executive functioning.

Materials and Methods

Participants

Archival data were utilized for this study. Forty-two elective CABG patients from the Rhode Island Hospital participated in the study. Patients that were recruited were treated by one surgeon who only performed normothermic cardiopulmonary bypass in order to control for differences in surgical techniques and cardiopulmonary bypass temperature. Participants who had a history of head injury, neurodegenerative disease, history of drug or alcohol abuse, psychiatric disorder, renal disease, active liver disease, previous cardiac surgery or left ventricular ejection fraction of less than 20% were not included in the study.

Materials

In the original study (Ropacki, Bert, Ropacki, Rogers & Stern, 2007), neuropsychological tests were selected particularly to measure a wide range of cognitive abilities. For the purposes of this study, specific tests were chosen to assess for impairment in executive and memory functions. The battery of tests included the Digit Span Backward subtest (from the Wechsler Adult Intelligence Scale-III), Letter-Number Sequencing subtest (from the Wechsler Adult Intelligence Scale-III), Trail Making Test Part B, short story subtest of the Randt Memory Test and the revised Hopkins Verbal Learning Test (HVLT-R). Alternate forms of these tests were used, when available, to avoid potential practice effects.

Various neuropsychological tests have been found to be reliable measures of executive functioning. The Digit Span Backward and Letter-Number Sequencing subtests (of the Wechsler Intelligence Scale-III) are measures of verbal working memory. A study conducted in 1973 examined functional images and found that there is hemodynamic activation in the lateral frontal lobe during the digit span task (Risberg & Ingvar, 1973). In contrast, performance on the Digit Span Backward subtest has not been shown to be impaired in those with temporal lobe lesions. Such studies have revealed that individuals who had temporal lobectomy did not perform significantly different on the Digit Span Backward subtest than the control group (Lezak, 1995).

Attention is considered to be an executive function (Stuss & Knight, 2002) and refers to how an individual becomes open to stimuli and begins to process the information (Lezak, 1995). Attention is divided into two main areas: deployment and encoding. Deployment is how well an individual can guide and focus attentional resources. It also includes arousal, focused and sustained attention. Encoding is how well an individual can retain information and then process it despite distractions. The Trail Making Test (TMT; Reitan, 1958) is a reliable measure of focused attention. Focused attention requires that the individual discard irrelevant information while they focus on relevant information. Parts A and B of the TMT measure different functions. The differences between parts A and B may indicate problems in the ability to execute and adjust a plan of action or to sustain two trains of thought at the same time. This may be possibly connected to frontal lobe damage (Spreen & Strauss, 1998). One study compared frontal lobe damage and nonfrontal lobe damaged patients to controls on the TMT. The results revealed that the frontal group showed more slowing and all patients who made more than one error had frontal lesions. The most impairment was seen in patients with dorsolateral frontal lesions (Stuss et al., 2001).

Various neuropsychological tests have been found to be reliable measures of memory functioning. One of these measures is the Hopkins Verbal Learning Test which was “designed as a relatively brief test of verbal learning and memory to be used when more comprehensive memory assessment is not feasible” (Lacritz & Cullum, 1998). This test has been used in various neurologic populations such as Alzheimer’s Disease, Huntington’s Disease (Lacritz & Cullum, 1998) and dementia (Frank & Byrne, 2000). Another memory measure is the Randt Memory Test, which is designed for longitudinal assessment of mild to moderate memory deficits. One study examined the reliability of the test and found that it has a high internal consistency and stability when it is used in a repeated measures model (Fioravanti, Thorel, Ramelli & Napoleoni, 1985).

Procedure

Patients undergoing elective CABG surgery at the Rhode Island Hospital were approached during their pre-surgery medical examination or in the surgeon’s office to be potential participants in the study. They were assessed at two different times: before the CABG surgery and before discharge from the hospital. For inpatients, the first testing was 1-3 days before surgery and for outpatients, the first testing took place 1-7 days before surgery. The second testing was 1-2 days before discharge from the hospital (typically, this was approximately 6-7 days after surgery). Patients were considered appropriate for postoperative testing when determined by the consulting neurosurgeon to be alert and medically/ pharmaceutically stable. By conducting baseline preoperative assessment and comparing it to the participants’ postoperative assessment, each participant served as their own control.

Statistical Analyses

Analyses were carried out using the SPSS (version 14.0) statistical software package (SPSS, Inc., Chicago, IL). An confirmatory factor analysis was conducted to choose the neuropsychological tests from the larger original battery of tests that would be used to measure executive and memory functions. Specifically, a principal components factor analysis with varimax rotation and the Kaiser normalization method was conducted using raw test scores obtained at baseline testing. A two factor solution was requested given the objectives of this study. The raw scores were converted into standardized scores for all the tests selected from factor analysis. The standardized scores were multiplied by the factor loadings (weights) of each test and summed to construct the two domain scores (executive and memory) at baseline and comparable domain scores at post test. The factors scores in one domain were summed to create an executive functions composite score for each subject at each testing point and the factors scores in the other domain were summed to create a memory composite score for each subject at each testing point. A repeated measures analysis of variance (ANOVA) was conducted to examine the differences between the composite executive functions score at baseline and the composite executive functions score after surgery. A repeated measures analysis of variance (ANOVA) was also conducted to examine the differences between the composite memory score at baseline and the composite memory score post-surgery. In order to examine whether or not memory functions affect executive functioning, a memory functions change score was created by subtracting the pre- and post-surgery composite scores and was added as a covariate into an ANCOVA. Other covariates such as age, education, cardiopulmonary bypass time, anesthesia time, and surgery time were also added as covariates in the ANCOVA.

Operational Definitions:

Independent Variable:

Time: Neuropsychological tests were conducted on each participant before surgery and after surgery.

Dependent Variables: Tests of Executive Functions

Digit Span Backward of the Wechsler Adult Intelligence Scale (WAIS-III; Wechsler, 1997). measures verbal working memory. In this test, digits are read to individuals and the individual is asked to say them back in an exact reverse order. Two trials are presented for each string length. Digit string length is increased by one digit with each successful trial. The score is based on the number of digit strings correctly said backwards.

Trail Making Test Part B (Reitan, 1958). measures focused attention and cognitive flexibility. On a piece of paper, there are 25 encircled numbers and letters in alternating order. Individuals are asked to connect the circles in ascending order alternating between numbers and letters. The score is based on the time in seconds to correctly connect all of the numbers and letters.

Letter Number Sequencing of the Wechsler Adult Intelligence Scale (WAIS-III; Wechsler, 1997). measures attention and working memory. The individual is asked to order numbers and letters that are presented in an unordered sequence. The score is based on the number of letter and number strings correctly repeated and ordered.

Dependent Variables: Tests of Memory Functioning

Hopkins Verbal Learning Test – Revised (HVLT-R; Benedict, Schretlen, Groninger & Brandt, 1998). assesses verbal learning and memory. It is a list-learning task that consists of three immediate recall trials, a 20 minute delayed recall trial and a recognition trial consisting of 12 words. There is a learning score which is the highest score of the three trials, a delayed memory score which is the total number of words recalled after the delay, and a recognition score which is the total number of words recalled in a list of target words and distractors. A retention score representing the percentage of information retained was also created using the following formula: {[(learning score – delayed recall score) / learning score] x 100} – 100. The retention score was the only score used in factor analysis.

Modified Randt Memory Test Short Story subtest (Randt & Brown, 1983). assesses verbal learning and memory. The task requires individuals to recall the details of a short story immediately after presented and again after a 30-minute delay. There are four scores - immediate verbatim recall/learning, immediate gist recall, delayed verbatim recall, and delayed gist recall. The delayed recall verbatim was the only score used in factor analysis.

Results

Demographics

The sample consisted of primarily Caucasian (95%) males (77%) with a mean age of approximately 63 years and a mean education of 12.86 years. There was a high percentage of individuals with a history of hypertension (81%), high cholesterol (76%), and smoking history (71%). The mean time for surgery, cardiopulomary bypass, cross-clamp and anesthesia were 220.39 minutes, 81.21 minutes, 67.50 minutes, and 277.37 minutes, respectively (see Table 1).

Table 1
Demographics – Means and Percentages

	Mean (s.d.)	%
Age (yrs)	63.67 (8.17)	
Education (yrs)	12.86 (2.66)	
Surgery time (minutes)	220.39 (50.80)	
Cardiopulmonary Bypass Time	81.21 (22.53)	
Cross Clamp Time	67.50 (19.91)	
Anesthesia Time	277.37 (55.58)	
Gender (%)		
Male		77.0
Female		23.0
Ethncity (%)		
African American		2.4
Hispanic		0.0
Other		2.4
Caucasian		95.2
Occupation (%)		
Student		0.0
Homemaker		4.8
Unskilled/semi-skilled		19.0
Skilled trade or craft		19.0
Clerical/office worker		14.3
Manager business/government		23.8
Professional/technical		19.0
Diabetes		31.0
Hx of high cholesterol		76.2
Hx of hypertension		81.0
Hx of smoking		71.4

Descriptives

There were decreases in the means of Letter-Number Sequencing (pre-surgery: 8.57, post-surgery: 8.26), Digit Span Backward (pre-surgery: 6.05, post-surgery: 5.38), HVLT-Retention (pre-surgery: 0.90, post-surgery: 0.80), and Randt Delayed Recall (pre-surgery: 6.39, post-surgery: 6.07). However, with Trail Making Test Part B, there was an increase in the mean time due to patients taking longer to complete the task suggesting they did worse after surgery (pre-surgery: 103.67, post-surgery: 121.55) (see Table 2).

Table 2

Paired T-Tests of Executive and Memory Functions Before and After Surgery

	Pre-surgery scores		Post-surgery scores			
	Mean	Sd	Mean	Sd	t	p
Letter-Number Sequencing	8.57	3.05	8.26	3.18	0.77	0.45
Trail Making Test Part B	103.67	49.18	121.55	51.81	-2.20	0.03
Digit Span Backward	6.05	2.23	5.38	2.00	2.93	0.006
HVLT Retention	0.90	0.21	0.80	0.20	2.19	0.04
Randt Delayed Recall	6.39	3.04	6.07	2.95	0.62	0.54

Factor Analysis

Digit Span Backward (total score), Trail Making Test Part B (total time), Letter-Number Sequencing (total score), Hopkins Verbal Learning Test (retention score) and Randt – Delayed Recall (total score) were included in a factor analysis. Factor analysis yielded a theoretically meaningful solution with two components/factors. Only those measures that loaded highly (i.e., +/- 0.30) on each component and did not cross load were included. On the basis of scale content, the two factors were given the following labels: (1) executive functions and (2) memory functions. The executive functions factor was comprised of the raw score on the Letter-Number Sequencing subtest, total time to completion on the Trail Making Test (part B) and total raw score on the Digit Span Backward subtest. The memory functions factor was comprised of the total words on the RANDT Delayed Recall and retention on the Hopkins Verbal Learning Test (see Table 3).

Table 3

Factor Loadings for Confirmatory Factor Model of Executive and Memory Functions

	Component	
	1	2
Letter Number Sequencing	.876	
Trail Making Part B	-.810	
Digit Span Backward	.776	
HVLT Retention		.858
Randt - Delayed Recall		.680

ANOVA

A repeated-measures analysis of variance (ANOVA) was conducted using the pre- and post-surgery composite executive functions score to examine differences in executive functioning before and after surgery. ANOVA results showed there was a significant decline in executive functions, F(1,41) = 6.69, p= 0.01 (see Table 4). An additional ANOVA analysis was conducted using the pre and post surgery composite memory scores to examine differences in memory functioning before and after surgery. It was found that there was a significant decline in memory functions, F(1,41) = 4.92, p = 0 .04 (see Table 5).

Table 4

Analysis of Variance for Executive Functioning Before and After CABG

Source	SS	df	MS	F	p	Partial Eta Squared
Executive Functions	7.95	1	7.95	6.69	0.01	0.14
Error	48.70	41	1.19			

Table 5

Analysis of Variance for Memory Functions Before and After CABG

Source	SS	df	MS	F	p	Partial Eta Squared
Memory Functions	4.82	1	4.82	4.92	0.03	0.11
Error	40.16	41	0.98			

ANCOVA

A repeated measures analysis of covariance (ANCOVA) was conducted to examine the differences between the composite executive functioning scores at baseline and after surgery while controlling for the change in memory functioning. With change in memory function scores as the covariate, the ANCOVA model continued to be significant, F(1,40) = 4.80, p = 0.03 (see Table 6). This suggests that the significant changes in memory functioning do not contribute to the observed significant decline in executive functioning. Figure 1 shows a scatterplot of the association between executive and memory functions.

Table 6

Analysis of Covariance for Executive Functions Before and After CABG with Memory Functions Change Covariate

Source	SS	df	MS	F	p	Partial Eta Squared
Executive Functions	5.77	1	5.77	4.80	0.03	0.11
Executive * Change in Memory	0.64	1	0.64	0.54	0.47	0.01
Error	48.06	40	1.20			

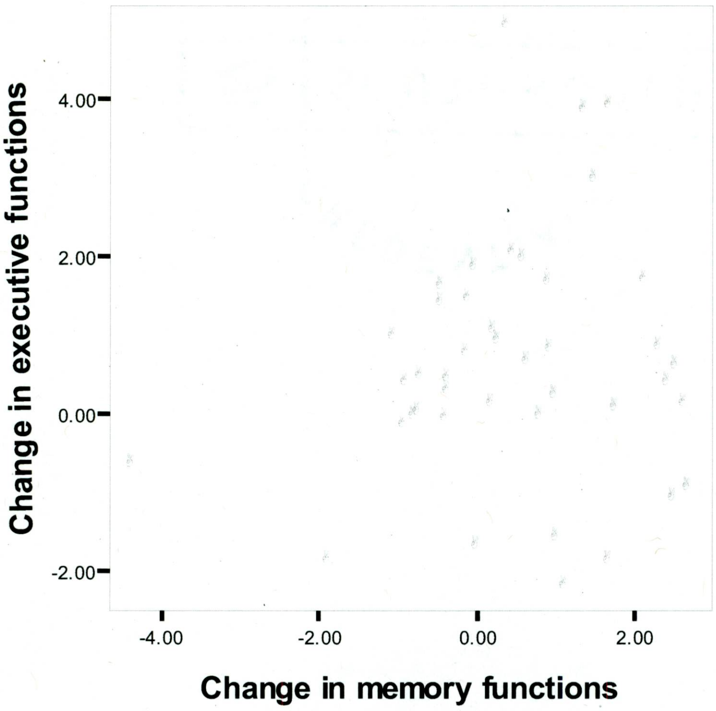

Figure 1. Scatterplot of the association between executive and memory functions.

An ANCOVA was also conducted using the executive functions score pre- and post- surgery with age, education, cardiopulmonary bypass time, anesthesia time and surgery time as covariates. Results revealed that when these variables were added as covariates, the model was no longer significant, F(1,35) = 1.56, p = 0.22, indicating that age, education, cardiopulmonary bypass time, anesthesia time and surgery time significantly impact changes in executive functioning (see Table 7). Basically, the change in executive functioning differs across levels of age, education, cardiopulmonary bypass time, anesthesia time and surgery time.

Table 7

Analysis of Covariance for Executive Functions Before and After Surgery with Covariates (Age, Education, Cardiopulmonary Bypass Time, Anesthesia Time and Surgery Time)

Source	SS	df	MS	F	p	Partial Eta Squared
Executive Functions	1.99	1	1.99	1.56	0.22	0.04
Executive * Age	1.40	1	1.40	1.09	0.30	0.03
Executive * Education (yrs)	0.04	1	0.04	0.03	0.87	0.00
Executive * CPB time	0.03	1	0.03	0.02	0.88	0.00
Executive * Anesthesia time	0.25	1	0.25	0.20	0.66	0.01
Executive * Surgery time	0.00	1	0.00	0.00	0.96	0.00
Error	44.43	35	1.28			

Post Hoc Analyses

Paired samples t-tests were conducted on each individual test to highlight more clearly the nature of deficits after CABG. For the tests of executive functioning, there were significant declines on the Digit Span Backward Test, $t(42) = 2.93$, $p < 0.01$ (see Figure 2) and Trail Making Test Part B, $t(42) = -2.20$, $p = 0.03$ (see Figure 3), but there was no significant decline on Letter Number Sequencing, $t(42) = 0.77$, $p = 0.45$ (see Figure 4). For tests of memory functioning, there was a significant decline on HVLT-R retention, $t(42) = 2.19$, $p =0.04$ (see Figure 5), but no significant decline on the Randt Delayed Recall, $t(42) = 0.62$, $p = 0.54$ (see Figure 6) (see Table 2).

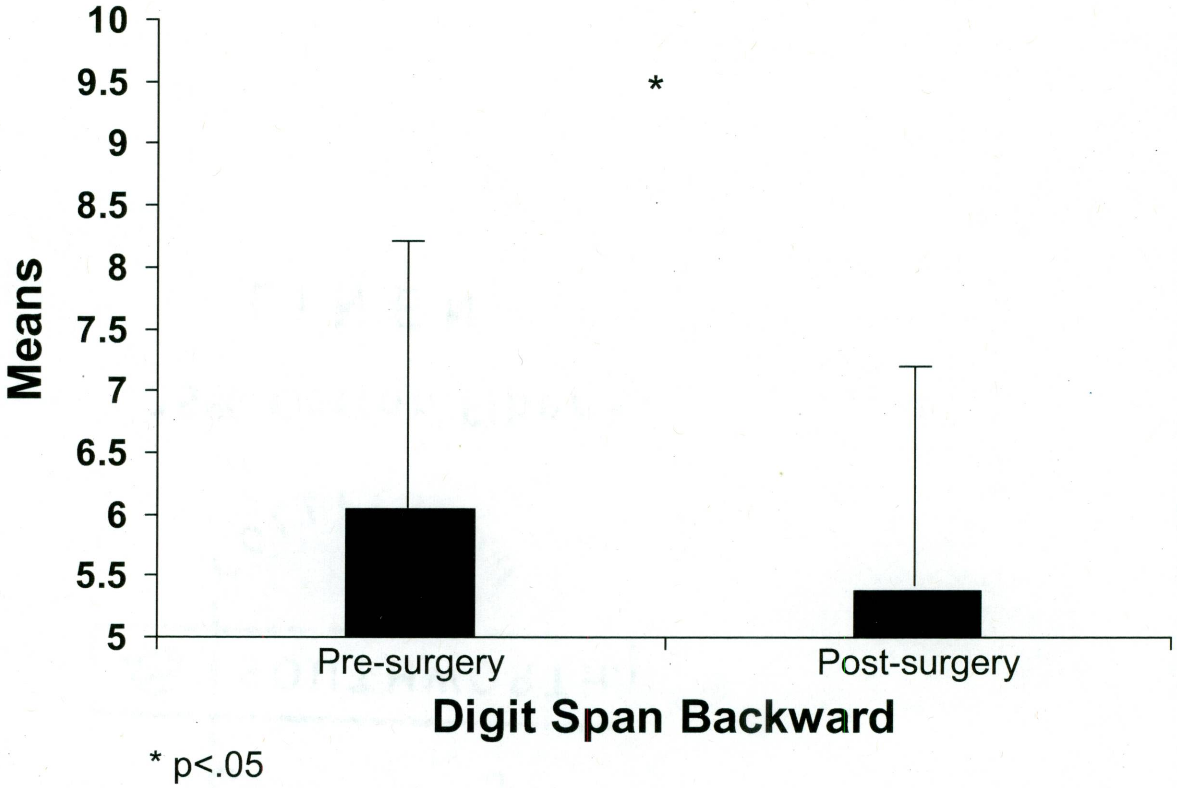

Figure 2. Pre- and Post-Surgery Performance on Digit Span Backward.

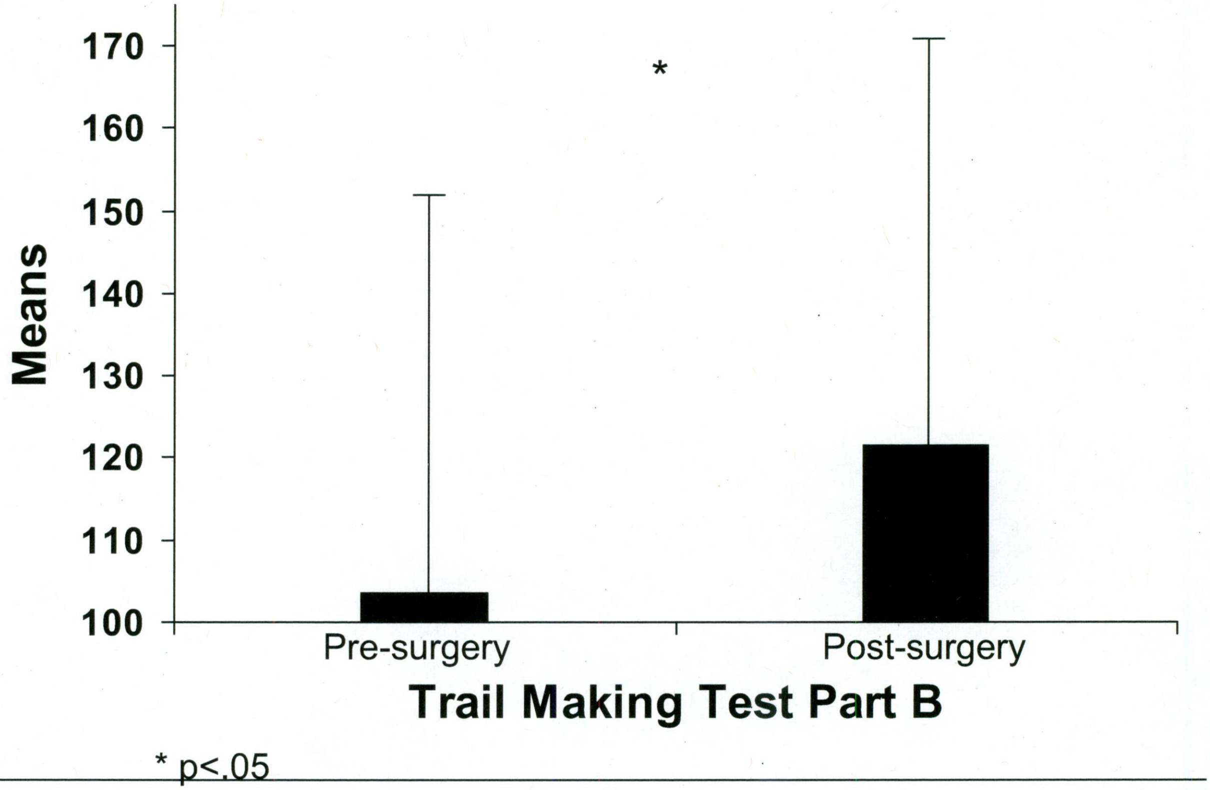

Figure 3. Pre- and Post-Surgery Performance on Trail Making Test Part B.

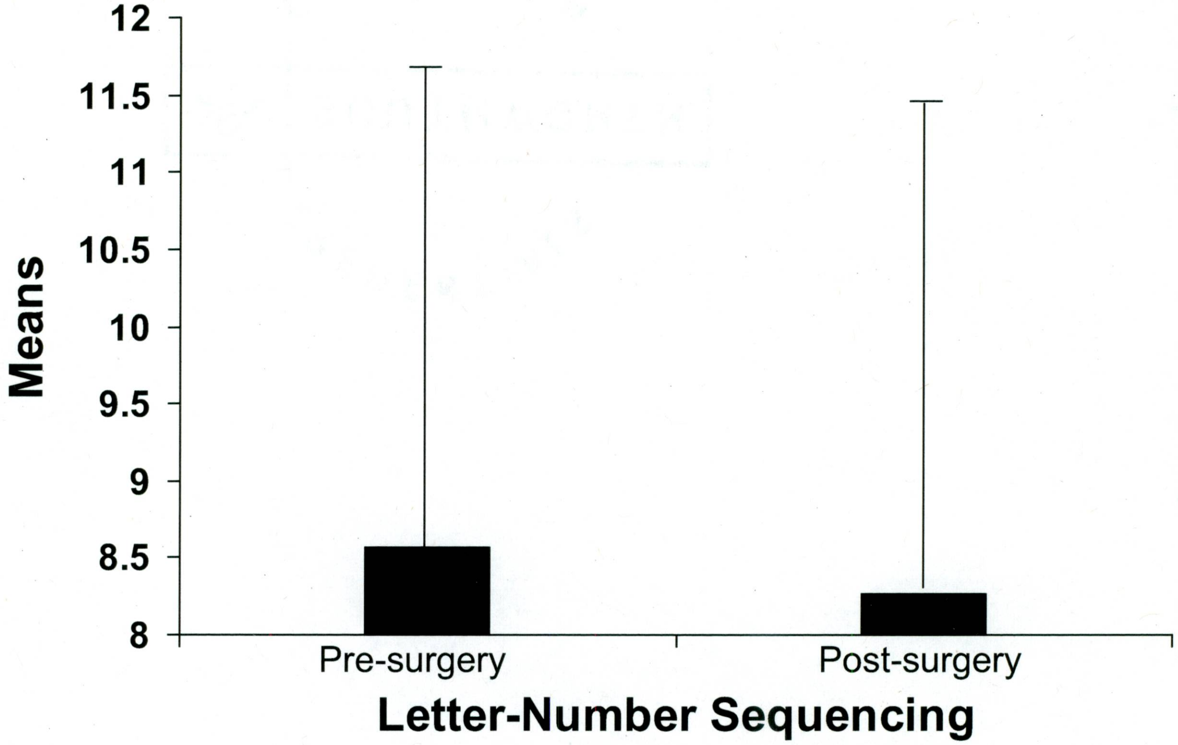

Figure 4. Pre- and Post-Surgery Performance on Letter-Number Sequencing.

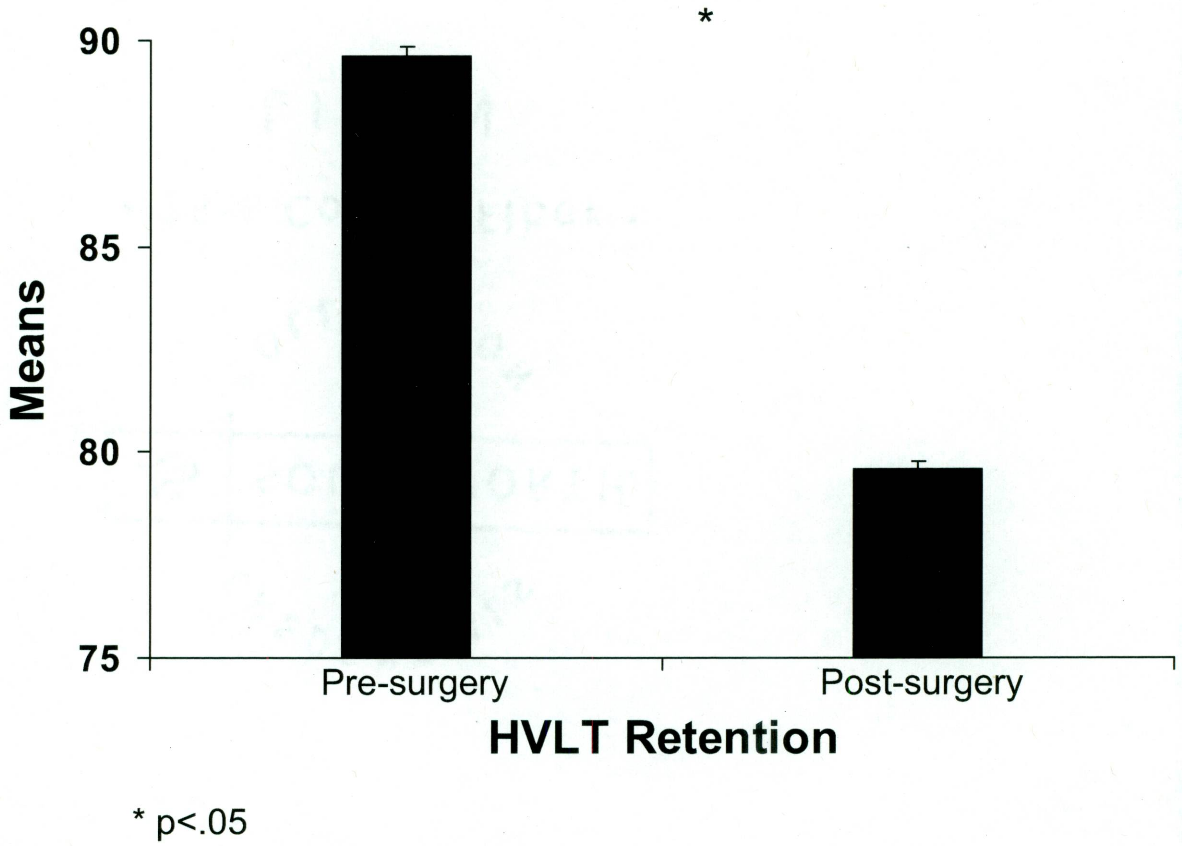

Figure 5. Pre- and Post-Surgery Performance on the Hopkins Verbal Learning Test-Retention.

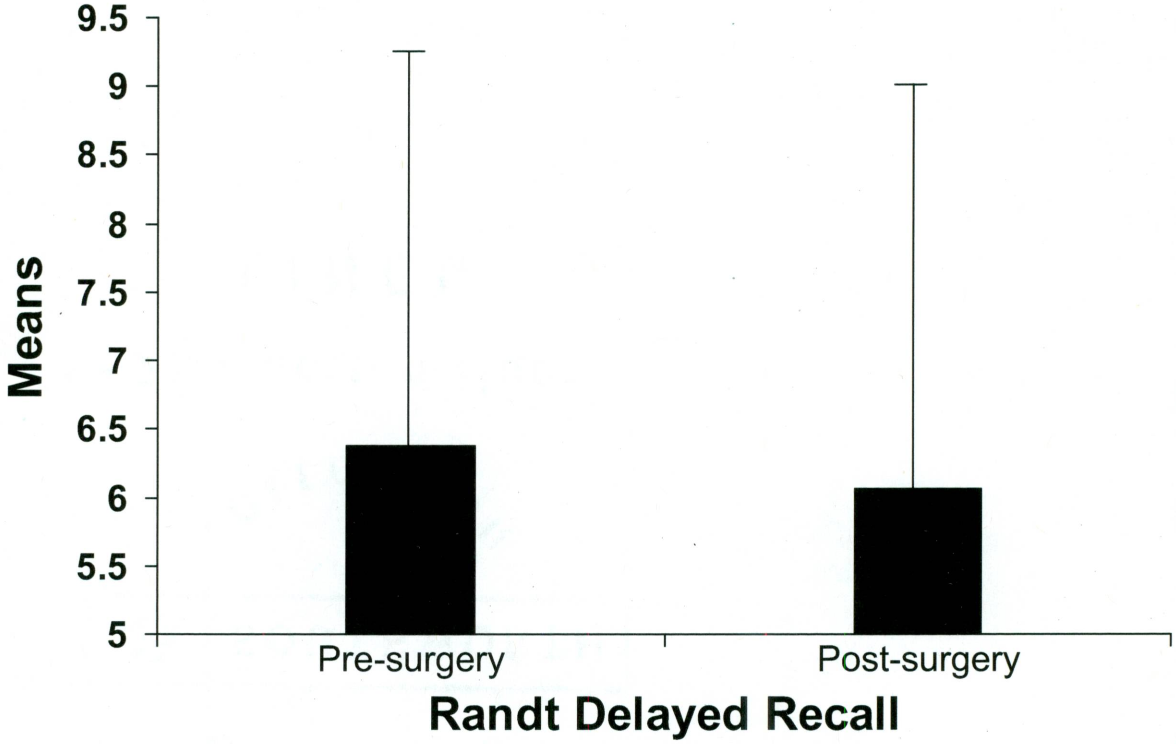

Figure 6. Pre- and Post-Surgery Performance on the Randt Delayed Recall.

In order to quantify the incidence of impairment on executive and memory functions, the mean change score and standard deviation was calculated for the entire sample for the executive functions composite and the memory functions composite. Similarly, a change score for the executive functions composite and the memory functions composite was calculated for each individual. "Impairment" was operationally defined as a decline of one or more standard deviations in the individual's change score. This method of defining impairment has been utilized in previous research (Kneebone, Andrew, Baker & Knight, 1998). Overall, there were 4 individuals (9.5% of the sample) who were identified as impaired on executive functions and 7 individuals (16.7% of the sample) identified as impaired on memory functions (see Table 8).

Table 8

Frequency and Means of Significant Declines (1 standard deviation from the mean) on Overall Executive and Memory Functions and Individual Tests

Variables	Frequency	Hyper-tension	High Cholesterol	Diabetes Mellitus	Smoking History	CPB time	Education
Executive Functions	4	4	3	1	3	74.00	14.0
Memory Functions	7	4	5	0	3	71.14	13.29
Letter Number Sequencing	5	5	5	1	4	74.00	12.80
Trail Making Test Part B	6	5	4	1	6	73.83	13.08
Digit Span Backward	5	3	3	3	2	85.60	14.00
HVLT Retention	6	3	5	1	4	74.17	14.00
Randt Delayed Recall	7	6	5	1	3	59.43	11.79

Discussion

There have been many studies that have examined the overall cognitive functioning of patients after CABG, but none have focused on executive functions specifically and the factors that impact executive functions after CABG. Long term memory functioning was examined as one potential factor affecting scores on executive functions tasks because of the identified anatomical link between frontal and temporal lobes and findings from previous research showing that executive functions impact memory functioning. Other variables such as age, education, cardiopulmonary bypass time, anesthesia time and surgery time were controlled for as well given previous research showing that these factors affect the physiology of the brain and its cognitive functioning in general.

The results of this study were consistent with previous research in that there were significant declines on executive functioning tests after CABG. Results of this study were also consistent with prior research showing that long term memory functions are also affected by CABG. This study revealed that declines in executive functions were not accounted for by those declines in memory, but that they may be due to certain individual differences and perioperative factors. Specifically, age, education, cardiopulmonary bypass time, anesthesia time and surgery time significantly impacted executive functioning in this sample of CABG patients. While past studies have shown these variables to be associated with cognitive decline, no studies have examined or found that these variables are associated with executive functioning. Moreover, this study provided a unique contribution to the understanding of executive dysfunction after CABG by examining a composite of executive functions. That is, although many CABG studies have used tests of memory and executive functioning and controlled for the most of the covariates mentioned above, none of the studies examined executive functions as a composite of several tests. A composite score may be considered a more comprehensive measure of functioning in the executive domain because it represents the individuals' performances across several tests rather than on simply one test.

When executive functioning pre- and post-surgery was examined with a memory functioning change score as a covariate, results revealed that memory functioning was not significantly impacting executive functioning. This suggests that executive dysfunction exists independent of memory dysfunction and in spite of the neural connections and communication pathways between the temporal lobes and frontal lobes. Overall, it may therefore be reasonable to speculate that executive dysfunction occurs after CABG because primary damage is incurred to some aspect of the frontal lobe.

As a further exploration of this possibility, and to demonstrate the independence of temporal lobe (memory) functioning and frontal lobe (executive) functioning in this sample, a post hoc analysis (ANCOVA) was conducted on pre- and post-surgery memory functions with executive functions as a covariate. The executive score was not a significant covariate in the observed significant decline in memory which suggests that memory functions are not impaired due to executive dysfunction. However, education, cardiopulmonary bypass time and surgery time did significantly impact memory functioning. This suggests that executive functions and memory functions may be differentially impacted by the measured individual differences and perioperative factors in this sample of patients with CHD and CABG. It was especially interesting that age impacted the change in executive functioning, but did not impact the change in memory functioning. One area of the brain that is vulnerable to aging is the frontal cortex. The rates of cortical decline appear to be greater in the frontal lobes than the entire brain, hippocampal complex, amygdala, and other areas. There is also evidence that patterns of β-amyloid deposition suggest that the frontal lobes are compromised early in aging (Tapp et al., 2004).

Executive functioning and memory functioning were operationally defined in this study as composites of several test scores. In order to examine more closely the performance on each individual test comprising those composites, changes in scores on each test from pre- to post-surgery were examined. Paired samples t-tests revealed that patients declined significantly on the Digit Span Backward subtest and Trail Making Test Part B, but did not decline significantly in their performance on the Letter-Number Sequencing subtest. Although both Digit Span Backward and Letter-Number Sequencing involves holding the information in working memory and manipulating it, the difference in significance may be due to one task having letters as well as numbers while one task only has numbers. There may be subtle differences within the tasks that may lead individuals to do better on some tasks than others. According to Lezak (1995), normal letter span is identical with digit span except beyond age 60 when there is some loss in letter span. It has even been suggested that letter span may be slightly less than digit span because letters are not as susceptible to strategies such as "chunking into higher-order units". There is also the possibility that Letter-Number Sequencing and Digit Span backward may be tapping into two different executive skills.

In order to determine whether the amount of decline experienced by these patients is of clinical importance, the incidence of impairment was examined. There was a limited amount of individuals within the sample that had impairment (more than one standard deviation below the mean) in executive and memory functions. The small percentage of the sample that experienced clinical levels of decline in executive and memory functions suggests that although there are problems with executive and memory functioning post-surgery, it may not be at a significant level, clinically. The incidence of cognitive decline appears lower than in most studies. However, most of the studies may be using different indices to measure impairment. In addition, some studies may be examining whether there is a significant decline, but they may not be examining whether it is a significant clinical decline.

There are a couple of questions that arise when examining the results. Are the individuals' scores declining because they started out high and statistically speaking, can be expected to regress to the mean or do their scores decline because they are actually experiencing true declines in performance due to CABG related deficits? In order to address these questions, the group means on individual tests were compared with the norms for those tests. Results revealed that the group scored in the average range on each test (less than 1 standard deviation above and below the mean) before surgery. Post-surgery results revealed that they experienced declines, but not significant declines. However, there was one exception on the Hopkins Verbal Learning Test where the individuals experienced significant declines (more than 1 standard deviation below the mean). Therefore, the results could not be explained by regression to the mean.

Limitations

There were a few limitations to this study that should be considered. First, the composite scores used in this study were created from a limited number of tests, which may have compromised the reliability of the composites. Additionally, data for this study were archival, which limited tests available for selection. Perhaps a more comprehensive array of tests as well as tests shown to more definitively measure the intended cognitive functions (e.g., Wisconsin Card Sorting Test or Stroop Test for executive functions tests), would have yielded stronger results. Also, in order to increase the power of the study, it would have been beneficial to perform a correlational analysis on executive functions, memory functions, cardiopulmonary bypass time, surgery time, anesthesia time, education and age. Using fewer variables that correlated could have been used in the would have increased the power (see Table 9).

Table 9

Correlations between executive functions, memory functions, cardiopulmonary bypass time, anesthesia time, surgery times, age and education

	1	2	3	4	5	6	7
Change in memory functions	1	0.12	-0.24	-0.37**	-0.15	-0.32*	0.13
Change in executive functions		1	-0.07	-0.14	-0.10	-0.14	0.04
Cardiopulmonary bypass time			1	0.46**	0.81**	0.16	0.08
Anesthesia time				1	0.55**	0.12	-0.05
Surgery time					1	0.04	0.08
Age						1	-0.29
Education							1

Sample size and heterogeneity were additional limitations. In a factor analysis, the ideal sample size should be at least 100 or more. The sample size in this study was less than 100 so the reliability of the factors may have been compromised. Furthermore, the sample was rather homogeneous along several variables that have been shown to affect cognitive functions such as hypertension, high cholesterol and smoking history. Thus, examination of the impact of these variables on executive functioning was not statistically possible. The small sample size and homogeneity of the group meant small effect sizes and low power to detect meaningful differences.

Future Research and Treatment

Although there are several limitations to the study, it provides direction for future research and treatment. Results of this study suggest that executive functions are significantly impacted by CABG and that particular demographic and perioperative factors moderate executive dysfunction. Future research should turn the focus onto locating where the most damage is occurring in the brain after CABG. Not many studies have used brain imaging before and after CABG, although a few have. Specifically, no imaging studies have examined the frontal lobes pre- and post surgery. Given the results of the study, it seems reasonable that the frontal lobes should be an area of specific focus in imaging studies. The results of the imaging can then be correlated with various cognitive tests which should assess for the various aspects of executive functioning . Future research should also examine the various perioperative factors, as well as various individual differences that this study did not examine. For example, hypertenstion, high cholesterol, and smoking history have been shown in research to be associated with cognitive decline (Kuo et al., 2004;Ott et al., 2004; Richards, Jarvis, Thompson & Wadsworth, 2003; Stampfer, 2006) and therefore, it would be beneficial to look at how these medical factors may contribute to the declines. Studies can also examine the performance on executive function tasks between CABG and non-CABG patients with and without such conditions.

Results of this and related studies of the factors impacting cognitive functioning after CABG may help direct modifications in surgical procedures and techniques. There are also implications for neuropsychologists in that there should be a more detailed screening before surgery to identify factors in the patients' personal and medical history which may put them at greater risk for cognitive decline in general, and executive decline specifically. Another implication for individuals, in general, is to increase engagement in health behaviors, such as exercise and eating healthy, in order to limit the number of factors (e.g., hypertension, high cholesterol and smoking) which put them at greater risk for heart disease necessitating CABG and the subsequent cognitive decline that commonly occurs after CABG.

There are also several treatment implications if regions more vulnerable to damage are identified. If these areas or structures are located, then treatment may be directed appropriately. Knowing the areas of the brain that are the most vulnerable will also help us direct our attention to figuring out why this area is more vulnerable (i.e. perioperative factors, premorbid functioning). Ultimately, continued research conducted in a similar vein would lead to better interventions and treatments that improve the outcome of CABG and the cognitive well-being of the multitude of men and women who undergo this surgery.

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