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University of Cape Town

# THE SHORT–TERM EFFECTS OF OFF-PUMP CARDIOPULMONARY BYPASS GRAFT SURGERY ON COGNITIVE PERFORMANCE

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A minor dissertation submitted in partial fulfillment of the requirements for the award of the degree of Master of Arts in Psychological Research

Faculty of the Humanities

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2008

DECLARATION

This work has not been previously submitted in whole, or in part, for the award of any degree. It is my own work. Each significant contribution to, and quotation in, this dissertation from the work, or works, of other people has been attributed, and has been cited and referenced.

Signature: Signed by candidate

Date: 14/02/08

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# ABSTRACT

Postoperative neurocognitive impairment has been associated with coronary artery bypass graft surgery (CABG). This study investigates the short-term effects of off-pump cardiopulmonary bypass graft surgery (OPCAB) on cognitive performance, as a possible safer alternative in the treatment of coronary artery disease. This research forms part of a larger study in which, in addition to the OPCAB procedure, the cognitive effects of CABG surgery and percutaneous transluminal coronary angioplasty with intra-coronary stenting are assessed. 36 participants undergoing OPCAB surgery were included in the study, with a further 36 participants included as an age- and education- matched non-surgical control group. A standardized battery of neuropsychological tests, designed to assess seven cognitive domains, was administered on two occasions, preoperatively at 1-2 days prior to surgery, and postoperatively at 1 month after surgery, with control participant assessments at the same intervals. Emotional state scales assessing depression and anxiety levels were administered at each assessment. Data analysis included a two-way mixed analysis of variance conducted on each measure of cognitive function, and on the indicators of emotional state. In addition, standard multiple regression was conducted to assess whether change in emotional state is able to predict change in any of the cognitive domains. Results indicated no evidence of short-term cognitive decline, and highlighted an improvement in cognitive performance in both surgical and control groups in the domain of language, psychomotor speed, executive function and visual memory, with the control group demonstrating a consistently superior performance. This counter-intuitive finding could not be attributed to practice effects.

# INTRODUCTION

## Coronary Artery Disease

Coronary artery disease (CAD), a prevalent form of cardiovascular disease, is the leading cause of death in the developed world, affecting 16 million adults in the United States alone (American Heart Association (AHA), 2008; Kaiser, Kron & Spray, 2007). Indeed, it is the most common cause of chronic heart failure accounting for 60-70% of all cases (Gheorghiade & Bonow, 1998; Sosin, Bhatia, Lip & Davies; 2006). It is a condition in which fatty deposits (atheromas) build up in the cells lining the walls of a coronary artery, thereby narrowing the artery and obstructing blood flow to the heart (Berkow, Beers, Bogin & Fletcher, 1997; Garden, Bradbury & Forsythe, 2002; Phibbs, 2007; Quinn, 2006). The heart muscle (myocardium) requires a continual and steady supply of oxygen-enriched blood in order to contract and pump blood normally. However, as the obstruction of the coronary artery worsens, ischaemia (inadequate blood supply) can develop, resulting in the heart muscle being unable to pump adequately and going into failure as myocardial oxygen demand exceeds supply. Myocardial infarction occurs when the blood supply to the heart is completely cut off, as a result of a blocked coronary artery, causing an area of the heart muscle to die (Phibbs, 2007; Steingart & Scheuer, 1990 in Hurst and Schlant, 1990; Quinn, 2006).

The aetiology of CAD is multifactorial, with a number of risk factors known to predispose to the condition. Some risk factors are of a fixed nature, such as age,

gender, race and family history, and are unable to be changed. Other risk factors include obesity, cigarette smoking, diabetes mellitus, hypertension, and hypercholesterolaemia (Timmis, Nathan & Sullivan, 1997; Kumar & Clark, 2002). Medical treatment comprises both acute and long-term management. Acute treatment involves symptomatic relief, such as nitrates and calcium channel blockers which cause cardiac smooth muscle relaxation, whilst long-term therapy involves preventative or disease modifying aspects, such as aspirin and lipid-lowering management in order to reduce the risk of further coronary events, such as myocardial infarct, and to prevent the progression of the disease (Kumar & Clark, 2002).

In addition, various lifestyle changes are likely to assist in controlling the symptoms, and inhibiting the progression, of CAD in a portion of patients. Amongst others, the adoption of a regular exercise routine, cessation of smoking and ideal weight management through a balanced diet are all factors decreasing the risk of CAD. These changes aim to lower blood pressure and cholesterol levels, therefore enabling blood to flow more freely, and consequently slowing or reversing the progress of CAD (Berkow *et al.*, 1997).

**Surgical Procedures as Revascularization**

For a number of patients, a change in lifestyle and medication is insufficient in treating the symptoms of CAD, in which case, surgical intervention becomes a necessity. Patients diagnosed with ischaemia firstly undergo coronary angiography in which contrast medium is injected into the coronary circulation via a catheter inserted through the femoral artery. It is suggested that patients are referred for bypass

surgery when the stenoses exceed a 70% reduction in vessel diameter (Garden *et al.*, 2002; Phibbs, 2007). Although cardiac surgical procedures are currently still among the most invasive and expensive therapeutic techniques, they are nonetheless widely used as successful therapy for patients with coronary, valvular and myocardial disease (Baumgartner *et al.*, 2005). Three procedures currently employed in the treatment of CAD are Coronary Artery Bypass Graft Surgery (CABG); Off-pump Cardiopulmonary Bypass Graft Surgery (OPCAB); and Percutaneous Angioplasty with Intra-coronary Stenting (PTCA). This particular research is specifically concerned with the short-term cognitive effects of off-pump cardiopulmonary bypass graft surgery in patients with CAD. Indeed, it is suggested that coronary artery bypass graft surgery is highly effective in reducing angina and improving ventricular function, and quality of life for patients with ischaemic heart disease, and is currently one of the most commonly performed major operations in the industrialised world with more than one million procedures being performed worldwide per annum (Ahonen & Salmenpera, 2004; Haddock *et al.*, 2003; Taggart, 2002).

The off-pump CABG procedure, as in the on-pump procedure, involves the grafting of a saphenous vein from the leg or the internal mammary artery onto the narrowed coronary artery, in order for blood to be able to bypass the obstructed area (Berkow *et al.*, 1997). This procedure is effective due to the nature of the atherosclerotic process, which normally affects only a few segments in the artery whilst leaving the rest of the artery untouched, allowing a graft to be inserted so that the blocked area is able to be bypassed (Haddock, *et al.*, 2003). The important difference between the surgical procedures, however, lies in the fact that during the CABG on-pump procedure, the heart is stopped, referred to as cardioplegic arrest, and the role of circulating blood

around the body falls to a machine, a procedure known as cardiopulmonary bypass (CPB), whereas in the off-pump procedure, although still an open-heart surgical procedure, the grafting is carried out with the heart still beating, without the aid of a machine, once hypotension (low blood pressure) and bradycardia (slowed heart beat) have been induced (Keenan, Abu-Omar & Taggart, 2005; Pillai & Wright, 1999). The CPB procedure involves the extraction of venous blood via cannulae inserted into the right atrium or vena cavae and drained to a reservoir. This blood is then pumped through an oxygenator, which adds oxygen and removes carbon dioxide, and through a heat exchanger coil so that its temperature can be varied and is returned to the arterial circulation via a cannula in the ascending aorta (Garden, *et al.*, 2002).

The OPCAB procedure, although hailed as a relatively new technique, was indeed the original approach used prior to the advent of CPB techniques in the 1960's, although without the innovative techniques and instruments used today, in that the construction of an anastomosis between a donor artery or vein and the coronary artery were performed without the use of extracorporeal circulation and cardiac arrest (de Jaegere & Suyker, 2002; Mack, 2000). However, it soon became clear that the success of these procedures was largely unpredictable and that in order to create the delicate and precise hand sewn anastomoses, the surgeon required a still and bloodless field with full exposure of the target area. As a result, the subsequent introduction of CPB enabled cardiac surgeons to bypass multiple coronary arteries with greater control and precision, resulting in more favourable clinical outcomes, an increase in bypass operations and the clinical status of "gold standard" (de Jaegere & Suyker, 2002, Verma *et al.*, 2004).

Despite the technological advances in cardiac surgery, however, it became clear that this essential extracorporeal circulation appeared to impose widespread organ dysfunction, including in the brain (Taylor, 1998). With the recent drive for less invasive procedures, interest in the OPCAB procedure, or 'beating-heart' surgery has been renewed (Raja & Dreyfus, 2004). Since the late 1990's, the number of OPCAB surgical procedures conducted has continued to grow, and it is suggested that 20-25% of coronary revascularization procedures are now being performed off-pump (Ascione & Angelini, 2003; Keenan, *et al.*, 2005; Mack, 2003).

**Cardiopulmonary Bypass (CPB)**

The OPCAB procedure became of interest as a result of increasing concern over the cardiopulmonary bypass procedure (CPB) involved in CABG surgery. Of utmost importance to this particular research are the claims that the effects of CPB include neurocognitive changes and stroke (Diegeler, 2000; Raja & Dreyfus, 2004). CPB has been associated with numerous adverse effects, such as postoperative myocardial, renal dysfunction, coagulopathies, respiratory failure and multiple organ dysfunction, in addition to neurological dysfunction. The effects of CPB are largely related to a systemic inflammatory response caused by the circulation of blood coming into contact with the extracorporeal circuit of the CPB machine (Keenan *et al.*, 2005; Verma *et* al., 2004). In addition, CPB requires the cannulation of the heart and the ascending aorta which may induce atherosclerotic microemboli. It has been shown that the highest embolic load of the brain occurs during the aortic manipulation in preparation of CPB and that the magnitude of the embolic load is associated with the

duration of CPB (de Jaegere & Suyker, 2002). It is suggested that increased time on CPB is strongly correlated with adverse neurological outcome, with patients undergoing longer pump times experiencing a greater severity of postoperative neurological events (Eagle & Guyton *et al.*, 1999). In addition, the literature suggests complications associated with the CPB procedure include a potentially inadequate perfusion pressure, nonpulsatile flow, possible cerebral edema induced by inflammatory reactions, microscopic air bubbles in the pump whilst running, anemia and post-operative extra-cellular brain water (Baumgartner *et al.*, 2005; Bowles *et al.*, 2001; De Jaegere & Suyker, 2002; Lee *et al.*, 2003; Taylor, 1998; Wan & Yim, 2001).

**Neurocognitive Injury**

Much of the available literature focuses on a comparison of the CABG and OPCAB procedures, with the result that information regarding cognitive decline after the OPCAB procedure is inextricably linked to that of the CABG procedure. Numerous studies have focused on the cognitive deficits following the CABG procedure finding that, in a proportion of patients, neuropsychological dysfunction and cognitive decline is evident and is considered to be the most significant and disabling complication of CABG surgery (Alhgren, Lundqvist, Nordlund, Aren & Rutberg, 2003; Keenan *et al.*, 2005; Andrew, Baker, Kneebone & Knight, 2000; McKhann *et al.*, 1997; Newman *et al.*, 2001; Royter, Bornstein and Russell, 2004; Selnes *et al.*, 1999; Selnes *et al.*, 2003; Van Dijk *et al.*, 2000; Währborg *et al*, 2004).

In the American College of Cardiology / American Heart Association guidelines for CABG surgery (Eagle & Guyton *et al.*, 1999) it is suggested that postoperative

neurological deficits are divided into two types: "type 1 deficits are those associated with major, focal neurological deficits, stupor, and coma; type 2 deficits are characterized by deterioration in intellectual function or memory." In the first type, the most overt manifestation of brain damage is stroke, which occurs infrequently (in roughly 3% of patients). Perhaps more importantly for this research, however, is the second form of injury, which reflects a more diffuse and subtle injury, involving the impairment of higher cognitive function. This type of injury is far more common with some studies showing a degree of impairment in as many as 60% - 80% of patients at discharge. Subtle impairment may take the form of a loss of memory, impaired concentration and attention, confusion, disorientation and vague complaints of "just not being the same" (Alston, 2005; Eagle & Guyton *et al.*, 1999; Keenan *et al.*, 2005; Taggart, 2002; Taylor, 1998; Ward & Kelly, 2004). The reported prevalence of postoperative deficits, however, varies greatly, with some studies reporting no decline and others reporting a decline in up to 80% of patients in 6 month to one year follow up periods (See Dupuis *et al.*, 2006). However, it has also been reported that dysfunction is mild and transient in many patients (Selnes *et* al. 2003; Taggart, 2002). This is set in contrast to type 1 injuries, such as stroke, and rather reflects a global or diffuse injury with a sense of disorientation and a usually reversible intellectual decline of variable duration (Eagle & Guyton *et al.*, 1999; Keenan *et al.*, 2005).

**Off-pump Cardiopulmonary Bypass Graft Surgery (OPCAB)**

It has therefore been suggested that the off-pump procedure, through avoidance of CPB and cardioplegic arrest, reduces surgical complications and is a safe and

effective alternative to traditional on-pump surgery (Bowles *et al.*, 2001; Chamberlain *et al.*, 2002; Raja & Dreyfus, 2004). It is claimed that OPCAB, although expected to produce superior results, should at the very least yield results comparable to conventional surgery in terms of mortality and long-term clinical outcomes (Ascione & Angelini, 2003). In addition, studies have shown the OPCAB procedure to be safe and well-tolerated by most patients, suggesting that up to 90% of patients referred for CABG are able to successfully undergo OPCAB surgery and that, in addition, high-risk patients (such as diabetics, re-operative CABG, and elderly patients) may gain the most benefit from this particular surgery (Keenan *et al.*, 2005; Verma *et al.*, 2004). However, whether OPCAB is indeed superior to the original "gold standard" CABG procedure has remained a fiercely debated topic in cardiac surgery. In a scientific statement by the American Heart Association Council, Sellke *et al.* (2005) suggest that it "remains uncertain whether OPCAB is associated with a distinct advantage or whether the outcome with OPCAB is similar or identical to that achieved by CABG with CPB."

In terms of neurocognitive impairment, the question of whether or not OPCAB does indeed result in a better outcome has caused an abundance of conflicting evidence. Logically, as a result of the avoidance of both aortic cannulation and CPB, one would expect a reduction in neurological deficits (Eagle & Guyton *et al.*, 2004). However, Wan and Yim (2001) claim that causes for neuropsychological impairment after CABG procedures are indeed multifactorial in nature and, hence, the precise role of CPB in cognitive decline is controversial. It is important to note that surgical risk may well be influenced by numerous patient related factors and the presence of comorbid conditions such as diabetes, renal insufficiency, obesity and so forth, in

addition to the numerous procedure related factors (de Jaegere & Suyker, 2002). It has been suggested that predictors for neurological injury following cardiac surgery include advanced age (particularly over 70 years), female sex, and a history, or presence of, significant hypertension. The predictors for type 1 injury specifically include the presence of aortic atherosclerosis, a history of neurological disease, diabetes, and a history of unstable angina, whereas predictors for type 2 injury include a history of alcohol consumption, dysrhythmia (including atrial fibrillation), and prior CABG, peripheral vascular disease or congestive heart failure (Eagle & Guyton *et al.*, 1999; Van Dijk *et al.*, 2004). Age is referred to as the most consistent and least controversial factor predictive of neurocognitive decline as it is associated with an increased incidence of atherosclerosis and an increased vulnerability to injury, with patients tending to have a higher risk of cerebral embolization, a greater frequency of stroke and associated cognitive deficits. The rate of stroke in patients younger than 64 years is less than 1%, whereas it increases to 5% in patients 65 years or more, and 7-9% in patients aged 75 years or more (Ahonen & Salmenpera, 2004; Dupuis *et al.*, 2006; Sendelbach, 2006).

Cognitive decline has been reported to be most common in the domains of visuoconstruction, language, memory and psychomotor speed, with a decline in executive function and attention also fairly common (Mckhann *et al.*, 1997; Selnes *et al.*, 1999; Borowicz *et al.*, 1996). There have been numerous studies suggesting that OPCAB surgery does in fact result in a lower incidence of neurocognitive impairment as opposed to the conventional CABG procedure (Zamvar *et al.*, 2002; Zangrillo, Crescenzi & Landoni, 2005) and indeed that the use of CPB in the CABG procedure, although successful in revascularization, nearly triples the risk of postoperative

neurologic difficulties (Zangrillo *et al.*, 2005). In a recent study by Al-Ruzzeh *et al.* (2006) it was reported that the OPCAB group had better preservation of neurocognitive function at both six weeks and six months, with subjects performing significantly better in three memory subtests at six weeks and in two memory subtests at six months. Importantly, this difference occurred in the absence of any accompanying change in emotional state which may perhaps have contributed to a deterioration in performance. In addition, it has been shown that patients undergoing OPCAB surgery had few cerebral microemboli, as opposed to the CABG surgical group, and preserved early brain perfusion, as opposed to evidence highlighting a reduced early perfusion to the left temporal lobe and posterior brain in the CABG group (Lee, 2003). This particular study also highlighted the improved performance of the OPCAB group on the Rey-Auditory Verbal Learning Test at both two weeks and one year, suggesting that OPCAB may perhaps result in less injury to the brain (Lee, 2003). A study by Keenan *et al.* (2005) reports a substantial reduction in the total number of intraoperative microemboli as well as a reduction in proportion of solid microemboli in the OPCAB group. Despite this, however, it is interesting to note the study failed to demonstrate any significant reduction in cognitive decline with the OPCAB procedure. Indeed, a number of studies have reported the safety and efficacy of OPCAB, with randomized trials demonstrating that OPCAB surgery yields results at least comparable to on-pump surgery in the early and midterm postoperative periods, and that OPCAB has advantages in a number of areas (See Verma, 2004). In addition, it has been suggested that the OPCAB procedure is associated with a shorter stay in hospital, a shorter duration of mechanical ventilation in the intensive therapy unit, and fewer blood transfusions (Al-Ruzzeh *et al.*, 2006).

Despite these studies, however, the notion that OPCAB results in inferior long-term results is a matter that has been raised on numerous occasion in the literature. Concerns regarding the quality and adequacy of revascularization in the OPCAB procedure have been voiced, specifically regarding suboptimal anastomoses and hence, poor long-term results (Keenan *et al.*, 2005). In a study by Khan *et al.* (2004) it was reported that OPCAB caused less myocardial damage and was as safe as conventional CABG, but that it resulted in lower graft-patency rates after 3 months, which may have an effect on long-term outcomes. Another important issue revolves around the integration of OPCAB into surgical practice and the training required. The reason for this is that the adoption of OPCAB by new surgeons has been associated with a steep "learning curve." Indeed, the decision as to which procedure to use has often been left to individual surgeons, many of whom remain reluctant to adopt OPCAB as it is a more technically demanding procedure and is being offered in the place of an already successful procedure (Keenan *et al.*, 2005; Verma, 2004). In addition, it has been claimed that OPCAB entails a number of potential problems such as the risk of incomplete revascularization, the technically demanding nature of the procedure, the risk of perioperative myocardial infarction, myocardial stunning and arrhythmias as a result of the temporary occlusion of the target artery (Cooley, 2000; Jegaden & Mikaeloff, 2001).

Other studies have shown, however, that rates of graft patency after OPCAB surgery are similar, and at least as effective, as those after conventional CABG (Al-Ruzzeh *et al.*, 2006; Angelini, Taylor, Reeves & Ascione, 2002) and have found no significant postoperative difference in terms of neurocognitive function between the OPCAB and CABG procedures (Van Dijk, Jansen & Hijman, 2002). Taggart (2002) has reported

that neurocognitive impairment appears to be similar in patients undergoing either surgery, and that early deterioration is not exclusive to the use of CPB. In an earlier study conducted by Taggart *et al.* (1999) it is suggested that perhaps anaesthetic and non-specific general operation effects may be responsible for producing a postoperative pattern of cognitive dysfunction. This notion is supported by a recent study in which Hernandez *et al.* (2007) suggest that the effect of CPB on cognitive decline may not be as significant as has been previously claimed, and that other factors associated with major surgical procedures may play a role.

In terms of short-term and long-term differences in outcome following OPCAB and CABG surgery, the literature appears contradictory. Reports have claimed that OPCAB patients have better cognitive outcomes 3 months after surgery than CABG patients, but that by one year this difference becomes negligible (Van Dijk *et al.*, 2002). Indeed, Zamvar *et al.* (2002) found that patients undergoing the OPCAB procedures had less neurocognitive impairment at 1 and 10 weeks than the CABG procedure. However, others claim no short-term difference between the groups, but a more favourable long-term result for OPCAB group (Stroobant, Van Nooten, Van Belleghem & Vingerhoets, 2002). Other reports also claim that short–term neurocognitive outcomes between the two groups are not significantly different, and that no significant effect of CPB was found on early cognitive outcome (Hernandez *et al.*, 2007; Van Dijk *et al.*, 2004). Van Dijk *et al.* (2007) extended this study in order to assess long-term neurocognitive outcomes, resulting in the same conclusion that CPB displays no significant effect on cognitive outcome. Nevertheless, it has been suggested that short-term decline may be due to the bypass procedure, while any long-term decline may be caused by factors such as age-related changes, or poor control of

cerebrovascular risk factors such as hypertension and hypercholesterolaemia (Selnes & McKhann, 2005).

Bearing the above studies in mind, it is yet uncertain whether OPCAB surgery does indeed lead to improved cognitive outcome when compared with the CABG procedure, in either the early post-operative or long-term cognitive functioning, as a result of discrepancies and insufficient evidence in the literature (Baumgartner *et al.*, 2005; Van Dijk & Kalkman, 2003). It is suggested that many studies have demonstrated methodological limitations such as small patient cohorts, differing definitions and patient selection, inadequate assessment of cognitive functioning and depression, an absence of both pre- and post-operative assessment, significant patient attrition from the research, and no comparison intervention group (Eagle & Guyton *et al.*, 2004; Haddock *et al.*, 2003). Many authors believe that the main potential advantage of OPCAB lies in the sphere of neurocognitive injury and as yet, although OPCAB has been proven as a safe alternative, no clear advantage has been shown over the conventional CABG procedure, which at present remains the procedure most commonly used (Hernandez *et al.*, 2007). Indeed, Baumgartner *et al.* (2005) suggest that an abundance of conflicting information has lead to a haphazard adoption of OPCAB, poorly serving the patient population. Clearly, in order to gain definitive answers, carefully controlled studies need to be conducted, bearing the limitations of previous studies in mind.

# AIM

As this research forms part of a larger study, the specific aim is to assess the short-term cognitive effects of off-pump cardiopulmonary bypass graft surgery (OPCAB) in patients undergoing the surgery as a result of coronary artery disease, whilst attempting to overcome some of the methodological limitations in this field by including a comparison non-surgical control group, ensuring that a recommended test battery be employed to assess a wide range of cognitive domains, assessing emotional state indicators and by matching the samples in terms of age, education and baseline functioning.

# 2. METHOD

## Sample

The research sample originally consisted of 88 participants, divided into two groups, an OPCAB surgical group and a matched control group. Of the surgical group, two participants were excluded as a result of an incomplete post-operative assessment, a further two participants were excluded as a result of post-operative stroke (although important to note that this type 1 injury occurred), three participants were excluded owing to death and one participant was excluded as a result of a further, unrelated oncological diagnosis. The control group was modified to match the surgical group attrition by excluding eight participants, and the final sample consisted of 72 participants, with demographics shown in Table 1. The OPCAB group consisted of

patients currently undergoing treatment, namely off-pump cardiopulmonary bypass graft surgery, for CAD at Groote Schuur Hospital, Gatesville Medical Centre, N1 City Hospital and Kuilsriver Hospital in Cape Town. Access was secured through two cardiothoracic surgeons, and the cardiothoracic wards at the various treatment centres.

Patients considered suitable for the OPCAB surgical group were those with no prior history of coronary artery procedures or stroke, no major non-cardiac impairment which may have an effect on post-operative recovery, were English or Afrikaans speaking and able to sit up-right in order to complete the assessment. In addition, the study required patients to be available for pre- and post operative cognitive assessments and able to give informed consent.

Table 1

*Demographic Variables*

| Variable | | Surgical Participants (n = 36) | Control Participants (n = 36) |
|---|---|---|---|
| **Age (years)** | | | |
| | Mean | 61.6 | 60.2 |
| | SD | 10.3 | 10.4 |
| | Range | 35 - 81 | 36 - 78 |
| **Education (years)** | | | |
| | Mean | 10.7 | 10.7 |
| | SD | 2.26 | 2.08 |
| | Range | 6 - 13 | 6 – 13 |

| Variable | | Surgical Participants (n = 36) | Control Participants (n = 36) |
|---|---|---|---|
| **Gender** | | | |
| | Males | 29 | 18 |
| | Females | 7 | 18 |

The literature suggests that it is vital to include a non-surgical control group in the design in order to account for random fluctuations in cognitive performance over time (Murkin *et* al., 1995; Van Dijk & Kalkman, 2003). The control group in this research comprised willing participants without symptomatic heart disease or a history of coronary artery procedures, with no medical conditions that could directly or indirectly affect cognitive functioning, English or Afrikaans speaking, available for assessments at the same intervals as surgical group patients and able to give informed consent.

These participants were closely matched in demographic factors to surgical participants in terms of age and education level. It has been suggested that both these variables significantly affect performance on many neuropsychological tests (Borowicz, Goldsborough, Selnes & McKhann, 1996) and that an age- and education-matched sample is necessary in gaining an accurate picture of post-operative neurocognitive decline (Hogue, Selnes & McKhann, 2007; Moller, Cluitmans & Rasmussen, 1998). Additionally, it was planned to match the groups in terms of gender, however this was not possible as a result of difficulties in the sourcing and recruitment of willing participants closely matching the surgical group in terms of gender, in addition to that of age and education. In light of the literature mentioned

above, it was decided that a match in terms of age and education should be prioritised in the sourcing of control participants, particularly as it has been shown that there is no significant difference between men and women in terms of neurological outcomes following OPCAB surgery (Newman *et al.*, Patel, Smith & Engel, 2006).

Hogue *et al.* (2007) also suggest that groups should ideally be demographically similar in terms of premorbid IQ. In this research, participants were administered the Information Subtest of the Weichsler Adult Intelligence Scale (WAIS III) as an estimate of baseline functioning, resulting in a mean for the surgical group of 14.03 (scores ranging from 4 to 24) and 16.72 (scores ranging from 5 to 28) for the control group, highlighting that the groups were well matched.

**Neuropsychological Assessment**

This particular research forms part of a larger study in which, in addition to the OPCAB procedure, the cognitive effects of two alternative surgical procedures are assessed, that of conventional coronary artery bypass graft surgery (CABG) and percutaneous transluminal coronary angioplasty with intra-coronary stenting (PTCA). Cognitive performance was assessed through the administration of a battery of standardised neuropsychological tests on two separate occasions, namely a baseline assessment administered at one to two days prior to surgery, and a follow-up assessment administered at one month post-surgery. The control group was assessed at the same intervals as the surgical group. The participants were assessed in various clinical settings typically utilised by the hospitals involved.

Neuropsychological assessment is widely used in evaluating cognitive change after cardiac surgery and is able to reveal pathological changes where scanning and biochemical markers are insufficient or impractical (Ahonen & Salmenpera, 2004). Indeed, it is suggested that "the sensitivity and precision of neuropsychologic measures make them well suited for identification, assessment, and investigation of cognitive complications" and that they are able to provide reliable indications of cognitive change and how rapidly that change occurs (Borowicz *et al.*, 1996).

Neuropsychological testing typically includes measures of numerous cognitive domains, such as attention, memory, visuoconstructional ability, language and psychomotor speed. It is vital that tests selected to assess cognitive functioning do indeed assess all major cognitive domains, as cognitive changes occurring post cardiac surgery are highly varied in nature and domain for different patients (McKhann *et al.*, 1997; Murkin, Newman, Stump & Blumenthal, 1995; Selnes *et al.* 2003). In addition, the test battery should be chosen to avoid practice effects inherent in repeated testing, and any cultural bias (Ahonen & Salmenpera, 2004). It would, no doubt, be advantageous to administer an absolutely comprehensive battery of neuropsychological tests assessing a wide spectrum of function with each patient, however, this notion is unrealistic once in the practical setting (Ahonen & Salmenpera, 2004). Indeed, one must take the frail condition of the surgical patients into account as they are generally weaker, and find it difficult to concentrate for long periods of time, in addition to the practical difficulties and time pressure of administering a wide spectrum of tests. The tests selected for this particular research are known to be reliable in their ability to detect cognitive change, and to have high test-retest reliability, small or non-existent practice effects, short administration times,

and are relatively portable (Mahanna *et al.*, 1996; Silbert *et al.*, 2004). Each assessment was conducted in a time period of approximately 60-90 minutes, depending on the speed of the participant, and tests were administered in the same order on each assessment, according to standardized procedures (Murkin *et al.*, 1995). All assessments were conducted in English, although it was ensured that subjects with Afrikaans as a first language understood all instructions and test procedures prior to the commencement of each test.

The neuropsychological battery employed in assessing cognitive performance included the following measures:

- *Visuoconstruction*

  Rey-Osterrieth Complex Figure – Copy administration. The subject is given a complex visual figure and required to copy the design onto a separate sheet of paper. An alternate form, the Taylor Complex Figure, was administered at the second assessment.

- *Visual Memory*

  Rey-Osterrieth Complex Figure – Immediate and delayed recall administrations. A task requiring the participant to recall the complex design formerly copied. The immediate recall task is administered directly following the copy task, while the delayed recall task is administered at approximately 30-45 minutes later in the assessment, depending on the speed of the participant. Participants performed the immediate and delayed recall measures using the Taylor Complex Figure at the follow-up assessment.

- *Verbal Memory*

Rey Auditory-Verbal Learning Test (RAVLT) (Weichsler Memory Scale - WMS-R). This test requires the participant to recall items from a verbally presented word list containing 15 words. This is repeated over five trials. Following this, the participant is administered an additional interference list of 15 words. Once completed, the participant is once again required to recall items from the initial word list that had been administered in the first five trials. A delayed recall of the initial list is assessed at approximately 30-45 minutes later in the assessment process. A second word list was administered at the second assessment.

- *Psychomotor Speed*

Digit Symbol (WAIS III). The participant is required to reproduce a series of geometric symbols below randomly generated digits in a grid according to a coding system in which each digit is paired with a specific symbol. The measure is timed.

- *Executive Function*

a) Similarities Subtest (WAIS III). The participant is required to provide and explain aspects that are similar between pairs of words. The words become increasingly more abstract as one moves through the test.

b) Stroop Test (Delis Kaplan Executive Function System - DK EFS). Designed to investigate ventromesial functioning, and in particular, inhibition, this timed task involves the presentation of words describing particular colours (blue, red, green) that are printed in a different ink colour to that which the word reads (i.e. the word, blue, printed in green ink). The participant is required to name the colour of the ink in which the word is printed, and to avoid reading the word

itself. All four trials were administered, which included simply reading the words printed in black ink on the first trial, simple colour naming of blocks on the second trial, and a less complex version of the final trial on the third trial. This ensures participants are prepared for the complex final trial, which was used as the measured task in this research.

- *Attention*

a) Digit Span (Weichsler Adult Intelligence Scale III - WAIS III). Participants are required to repeat an increasing series of numbers in the forward condition, and, in the backwards condition, repeat a second increasing series of numbers in reverse.

b) RAVLT (WMS – R). Trial 1 is used as an additional measure of attention.

- *Language*

Boston Naming Test (Short Form). A series of 30 line drawings are presented one at a time, and the participant is required to name these drawings upon confrontation.

**Assessment of Emotional State**

It is important to take into account that emotional state is considered an important predictor of cognitive change (Borowicz *et al.*, 1996; Murkin *et al.*, 1995). Anxiety has been well-documented in patients undergoing CABG surgery, and it is suggested that preoperative anxiety and depression have been associated with poorer cognitive performance (Dupuis *et al.*, 2006; Sendelbach, 2006). These variables are possible confounding variables in a study such as this, as fluctuations in mood state may lead to changes in cognitive test scores, leading one to be unsure as to whether a change in

test scores is as a result of emotional state or as a result of the OPCAB procedure. As a result, participants in both groups were administered both the Beck Depression Inventory (short form) and the Spielberger State-Trait Anxiety Inventory (STAI) at the same testing intervals as the neuropsychological battery in order to assess depression and anxiety as possible predictors of cognitive decline.

**Ethical Considerations**

All participants were informed, prior to assessment, of the nature of the study in which it was stressed that involvement was entirely voluntary, and were given an information sheet in which the research was explained in detail. The information sheet (Appendix A) ensured participants understood that they were able to withdraw from the study at any point without having to give a reason for withdrawal, and without their withdrawal affecting future treatment. The participants were assured of the confidentiality of their responses and identity. In addition, participants were informed of the contact details of the principal researcher in the event of questions and concerns regarding the research. It was explained that there were no anticipated risks involved in the study and that the research had been reviewed by the UCT Psychology Department Ethics Committee and the Faculty of Health Sciences Research Ethics Committee. The participants were required to sign a consent form (Appendix A) ensuring that they had understood the main aspects of the information sheet and gave consent for the information to be used for scientific purposes. The researcher ensured that all participant concerns had been addressed prior to commencement of the assessment. In addition, participants were informed that a copy of the results of the research would be made available to them should they require it.

**Statistical Methods**

In much of the literature (Hernandez *et al.*, 2007; Mahanna *et al.*, 1996; Van Dijk *et al.*, 2002), cognitive decline is defined as a decline in test scores of 20% or greater from baseline on at least 20% of the measures. This convention was followed in the present study. Primary data analysis involved running a two-way (2X2) mixed analysis of variance (ANOVA) with repeated measures, for eleven measures of cognitive function, spanning seven cognitive domains, namely verbal memory, visual memory, attention, visuoconstruction, executive function, language and psychomotor speed. In addition, a further two ANOVA analyses were conducted on the indicators of emotional state, namely depression and anxiety. The independent variables included a between groups factor, namely cardiac procedure, with two levels, OPCAB surgical group and non-surgical control group, and a within groups factor of time, with two levels, baseline and follow-up. This design assisted in determining cognitive change from baseline to one-month and establishing any difference in cognitive performance in the varying domains and between the groups. As a result of the numerous analyses conducted, the risk of Type 1 error rate was relatively high. This could not be avoided, as in order to gain an accurate idea of cognitive change, and indeed where that change occurs, it is necessary to evaluate each measure separately. Results significant at the 0.05 confidence level would have been interpreted with caution and Bonferroni corrections considered. Normal probability plots and Levene's tests were conducted to ensure that assumptions of normality and homogeneity of variance were upheld.

The secondary analysis was conducted using standard multiple regression, and aimed to assess whether a change in mood state could predict a change in cognitive performance in any of the measured domains, i.e. whether an improvement in depression or anxiety scores could predict an improvement in cognitive performance in any domain, and vice versa. Eleven multiple regression analyses were conducted. The independent variables included the mood state indicators, namely anxiety and depression change scores, whilst the dependent variable was the change score i.e. the calculated difference between the scores obtained on the baseline and follow-up assessment, for each measure of cognitive performance.

# RESULTS

The primary analysis was conducted using a mixed analysis of variance (ANOVA) design. As mentioned, this method of analysis assumes normally distributed data and homogeneity of variance, and Levene's tests and normal probability plots were conducted to ensure that these basic assumptions were upheld. The normal probability plots indicated that this assumption was upheld on all measures. Levene's test showed a significant p-value, and hence a violation of the assumption, on 3 of the 13 analyses. This was not deemed to be problematic, however, as ANOVA is robust in the face of violations of normality and homogeneity of variance, particularly with equal sample sizes (Howell, 2004).

Table 2 provides the analysis of variance results for each cognitive domain and highlights an improvement in cognitive performance from pre-operative to post-

operative assessment in both the surgical and control groups in the domains of language, psychomotor speed, executive function, and visual memory. In addition, results show that the control group performed significantly better than the surgical group on both assessments (pre-operative and post-operatve) in the domains of language, attention, psychomotor speed, executive function and verbal memory. The only domain failing to show significance, in terms of a difference between the groups or a difference over time, was visuoconstruction.

Table 2

*Analysis of Variance for All Cognitive Domains*

| Cognitive Domain | Source | df | F | p |
|---|---|---|---|---|
| **Language** (Boston Naming Test) | Cardiac Procedure (A) | 1 | 7.116 ** | 0.009 |
| | Time (B) | 1 | 21.917** | 0.001 |
| | Interaction (A*B) | 1 | 0.026 | 0.872 |
| **Attention** (Digit Span) | Cardiac Procedure (A) | 1 | 9.363** | 0.003 |
| | Time (B) | 1 | 0.315 | 0.576 |
| | Interaction (A*B) | 1 | 0.065 | 0.799 |
| **Attention** (RAVLT – trial 1) | Cardiac Procedure (A) | 1 | 4.067* | 0.048 |
| | Time (B) | 1 | 2.316 | 0.133 |
| | Interaction (A*B) | 1 | 0.019 | 0.890 |
| **Psychomotor Speed** (Digit Symbol) | Cardiac Procedure (A) | 1 | 10.960** | 0.001 |
| | Time (B) | 1 | 39.627** | 0.001 |
| | Interaction (A*B) | 1 | 1.705 | 0.196 |

*p<0.05, **p<0.01

| Cognitive Domain | Source | df | F | p |
|---|---|---|---|---|
| **Executive Function** (Similarities) | Cardiac Procedure (A) | 1 | 6.352* | 0.014 |
| | Time (B) | 1 | 6.072* | 0.016 |
| | Interaction (A*B) | 1 | 0.124 | 0.726 |
| **Executive Function** (Stroop Test - Time) | Cardiac Procedure (A) | 1 | 6.780* | 0.011 |
| | Time (B) | 1 | 5.988* | 0.017 |
| | Interaction (A*B) | 1 | 0.152 | 0.698 |
| **Executive Function** (Stroop Test - Errors) | Cardiac Procedure (A) | 1 | 3.523 | 0.065 |
| | Time (B) | 1 | 0.996 | 0.322 |
| | Interaction (A*B) | 1 | 0.713 | 0.401 |
| **Visuoconstruction** (Rey – Copy Administration) | Cardiac Procedure (A) | 1 | 2.640 | 0.108 |
| | Time (B) | 1 | 1.741 | 0.192 |
| | Interaction (A*B) | 1 | 0.000 | 0.959 |
| **Visual Memory** (Rey – Immediate recall) | Cardiac Procedure (A) | 1 | 0.334 | 0.565 |
| | Time (B) | 1 | 70.815** | 0.001 |
| | Interaction (A*B) | 1 | 0.002 | 0.967 |
| **Visual Memory** (Rey – Delayed recall) | Cardiac Procedure (A) | 1 | 0.715 | 0.401 |
| | Time (B) | 1 | 80.607** | 0.001 |
| | Interaction (A*B) | 1 | 1.032 | 0.313 |
| **Verbal Memory** (RAVLT – Total Recall) | Cardiac Procedure (A) | 1 | 5.965* | 0.017 |
| | Time (B) | 1 | 1.591 | 0.211 |
| | Interaction (A*B) | 1 | 2.346 | 0.130 |

*p<0.05, **p<0.01

In the domain of language, the analysis of variance on the Boston Naming Test yielded a statistically significant main between groups effect of cardiac procedure [$F_{(1, 72)} = 7.116$, $p = 0.009$]. This shows that at both baseline and follow-up assessment, the control group ($M = 26.486$) performed significantly better on the measure of language than the OPCAB surgical group ($M = 24.229$) (Table 3). The main effect of time was also shown to be significant [$F_{(1, 72)} = 21.917$, $p = 0.000$], highlighting that performance increased from baseline ($M = 24.854$) to the follow-up assessment ($M = 25.861$) in both the surgical and control group. In terms of effect size, eta squared ($\eta^2$) was calculated as a rough estimate of variance explained. 8.6% of the variance in cognitive performance in the domain of language, as measured by the Boston Naming Test, is explained by cardiac procedure ($\eta^2 = 0.086$) and 1.7% of the variance is explained by time ($\eta^2 = 0.017$), resulting in a total variance of 10% explained ($\eta^2 = 0.102$).

Within the cognitive domain of attention, both the Digit Span and the Rey Auditory Verbal Learning Test (RAVLT - trial 1), highlighted significant differences between the surgical and control group. In terms of Digit Span, the analysis of variance highlighted a significant effect of cardiac procedure [$F_{(1, 72)} = 9.363$, $p = 0.003$], demonstrating that control group performance ($M = 16.889$) was significantly better than the performance of the OPCAB surgical group ($M = 14.153$) at both baseline and follow-up assessments. A similar finding was shown in the RAVLT analysis, again highlighting a significant effect of cardiac procedure [$F_{(1, 72)} = 4.067$, $p = 0.048$], showing that the control group ($M = 5.750$) performed significantly better than the surgical group ($M = 5.000$) at both baseline and follow-up assessments. 10.9% of the variance in cognitive performance in the domain of attention, measured by Digit

Span, is explained by cardiac procedure ($\eta^2$ = 0.109). 4.3% of the variance in cognitive performance in the domain of attention, measured by RAVLT – trial 1, is explained by cardiac procedure ($\eta^2$ = 0.043).

Digit Symbol, a measure of psychomotor speed, showed both a significant difference between the groups [$F_{(1, 72)} = 10.960$, $p = 0.001$], and a significant effect of time [$F_{(1, 72)} = 39.627$, $p = 0.001$]. This illustrates that the control group ($M$ = 58.583) performed significantly better than the surgical group ($M$ = 46.958) in both assessments, and that both the surgical group and the control group performed significantly better over time from baseline ($M$ = 50.528) to follow-up assessment ($M$ = 55.014). 12.8% of the variance in cognitive performance on the measure of Digit Symbol, is explained by cardiac procedure ($\eta^2$ = 0.128) and 1.9% of the variance is explained by time ($\eta^2$ = 0.019), resulting in a total variance of 14.7% explained ($\eta^2$ = 0.147).

In the domain of executive function, 2 of the 3 tests yielded significant results, namely Similarities and Stroop Test – time. The test yielding non-significant results was Stroop Test – errors. In the Similarities analysis, the difference between the groups was shown to be significant [$F_{(1, 72)} = 6.352$, $p = 0.014$], and time was also shown to be significant [$F_{(1, 72)} = 6.072$, $p = 0.016$], demonstrating that the control group ($M$ = 22.083) performed significantly better than the OPCAB group ($M$ = 18.833) in both assessments, and that performance increased over time from baseline ($M$ = 19.972) to follow-up ($M$ = 20.944) in both groups. 7.6% of the variance in cognitive performance on the measure of Similarities, is explained by cardiac procedure ($\eta^2$ = 0.076) and 0.7% of the variance is explained by time ($\eta^2$ = 0.007), resulting in a total variance of 8.3% explained ($\eta^2$ = 0.083). Similar results were highlighted in the

Stroop – time analysis, with both the main effect of cardiac procedure [$F_{(1, 72)} = 6.780$, $p = 0.011$], and time [$F_{(1, 72)} = 5.988$, $p = 0.017$] showing significance. Again, this highlights that the control group ($M = 74.792$) performed significantly better, with faster time scores than the surgical group ($M = 92.667$) on both assessments, and that the performance of both groups increased over time, with faster time scores from baseline ($M = 86.653$) to follow-up ($M = 80.810$). 7.9% of the variance in cognitive performance on the measure of Stroop –time is explained by cardiac procedure ($\eta^2 = 0.079$) and 0.8% of the variance is explained by time ($\eta^2 = 0.008$), resulting in a total variance of 8.7% explained ($\eta^2 = 0.087$).

In terms of visual memory, both tests yielded significant results, namely Rey Complex Figure – immediate recall and Rey Complex Figure – delayed recall. The main within group effect of time was significant in both the Rey – immediate recall analysis [$F_{(1, 72)} = 70.815$, $p = 0.001$], and in the Rey – delayed recall analysis [$F_{(1, 72)} = 80.607$, $p = 0.001$]. This highlights that, in both tests, regardless of whether participants belonged to the surgical or control group, participants showed a better recall of the figure, from baseline to follow-up assessments, with means increasing from $M = 16.931$ to $M = 22.722$ in the Rey - immediate recall measure, and from $M = 16.410$ to $M = 21.750$ in the Rey – delayed measure. 14.4% of the variance in cognitive performance on the measure of Rey – immediate recall is explained by time ($\eta^2 = 0.144$). In addition, 12.9% of the variance in the domain of visual memory, on the measure of Rey-Delayed recall, is explained by time ($\eta^2 = 0.129$).

In the domain of verbal memory, the analysis of variance on the Rey Auditory Verbal Learning Scale (RAVLT – total recall) yielded a significant between groups effect of

cardiac procedure [$F_{(1, 72)} = 5.965$, $p = 0.017$]. This shows that the control group ($M$ = 8.875) performed significantly better than the OPCAB surgical group ($M$ = 6.903) on both assessments. 6.9% of the variance in cognitive performance, in the domain of verbal memory on the measure RAVLT – total recall is explained by cardiac procedure ($\eta^2 = 0.069$).

Table 3

*Descriptive Statistics of All Cognitive Domains*

| | | | Baseline | Follow-up | Marginal Means |
|---|---|---|---|---|---|
| **Language** (Boston Naming Test) | OPCAB (n = 36) | M | 23.708 | 24.750 | 24.229 |
| | | SD | 4.026 | 3.881 | |
| | Control (n = 36) | M | 26.000 | 26.972 | 26.486 |
| | | SD | 3.629 | 3.229 | |
| | Marginal Means | | 24.854 | 25.861 | |
| **Attention** (Digit Span) | OPCAB (n = 36) | M | 14.111 | 14.194 | 14.153 |
| | | SD | 3.511 | 3.616 | |
| | Control (n = 36) | M | 16.778 | 17.000 | 16.889 |
| | | SD | 4.428 | 4.229 | |
| | Marginal Means | | 15.444 | 15.597 | |
| **Attention** (RAVLT – Trial 1) | OPCAB (n = 36) | M | 5.167 | 4.833 | 5.000 |
| | | SD | 1.648 | 1.298 | |
| | Control (n = 36) | M | 5.889 | 5.611 | 5.750 |
| | | SD | 1.924 | 2.181 | |
| | Marginal Means | | 5.528 | 5.222 | |

*Note*: M = mean, SD = standard deviation

| | | | Baseline | Follow-up | Marginal Means |
|---|---|---|---|---|---|
| **Psychomotor Speed** (Digit Symbol) | OPCAB (n = 36) | M | 44.250 | 49.667 | 46.958 |
| | | SD | 15.902 | 14.980 | |
| | Control (n = 36) | M | 56.806 | 60.361 | 58.583 |
| | | SD | 15.538 | 14.341 | |
| | Marginal Means | | 50.528 | 55.014 | |
| **Executive Function** (Similarities) | OPCAB (n = 36) | M | 18.278 | 19.389 | 18.833 |
| | | SD | 4.995 | 5.222 | |
| | Control (n = 36) | M | 21.667 | 22.500 | 22.083 |
| | | SD | 6.174 | 6.372 | |
| | Marginal Means | | 19.972 | 20.944 | |
| **Executive Function** (Stroop Test - Time) | OPCAB (n = 36) | M | 96.056 | 89.278 | 92.667 |
| | | SD | 40.270 | 34.100 | |
| | Control (n = 36) | M | 77.250 | 72.333 | 74.792 |
| | | SD | 22.580 | 22.580 | |
| | Marginal Means | | 86.653 | 80.810 | |
| **Executive Function** (Stroop Test - Errors) | OPCAB (n = 36) | M | 4.806 | 4.750 | 4.778 |
| | | SD | 4.553 | 4.365 | |
| | Control (n = 36) | M | 3.556 | 2.889 | 3.222 |
| | | SD | 3.264 | 2.906 | |
| | Marginal Means | | 4.181 | 3.819 | |

*Note*: M = mean, SD = standard deviation

| | | | Baseline | Follow-up | Marginal Means |
|---|---|---|---|---|---|
| **Visuoconstruction** (Rey – Copy) | OPCAB (n = 36) | M | 32.750 | 33.306 | 33.028 |
| | | SD | 4.287 | 2.400 | |
| | Control (n = 36) | M | 33.792 | 34.306 | 34.049 |
| | | SD | 3.510 | 1.939 | |
| | Marginal Means | | 33.271 | 33.806 | |
| **Visual Memory** (Rey – Immediate Recall) | OPCAB (n = 36) | M | 16.472 | 22.292 | 19.382 |
| | | SD | 6.764 | 6.486 | |
| | Control (n = 36) | M | 17.389 | 23.153 | 20.271 |
| | | SD | 7.550 | 7.731 | |
| | Marginal Means | | 16.931 | 22.722 | |
| **Visual Memory** (Rey – Delayed Recall) | OPCAB (n = 36) | M | 15.458 | 21.403 | 18.431 |
| | | SD | 6.797 | 5.921 | |
| | Control (n = 36) | M | 17.361 | 22.097 | 19.729 |
| | | SD | 7.594 | 7.511 | |
| | Marginal Means | | 16.410 | 21.750 | |
| **Verbal Memory** (RAVLT– Total Recall) | OPCAB (n = 36) | M | 6.861 | 6.944 | 6.903 |
| | | SD | 3.322 | 3.480 | |
| | Control (n = 36) | M | 9.306 | 8.444 | 8.875 |
| | | SD | 3.725 | 4.095 | |
| | Marginal Means | | 8.083 | 7.694 | |

*Note*: M = mean, SD = standard deviation

**Indicators of Emotional State**

Table 4 provides the analysis of variance results for the indicators of emotional state. Results highlight a significant decrease in both depression and anxiety for the surgical group from baseline to follow-up assessment. The analysis of variance on depression scores yielded a significant interaction effect [$F_{(1, 72)} = 10.058$, $p = 0.002$], showing that one level of the independant variable depends on the level of the other independant variable. A cell mean plot of the interaction (Appendix B) shows that the interaction is disordinal, which is the reason that one would be wary of interpreting the significant main effect of time [$F_{(1, 72)} = 9.562$, $p = 0.003$]. A post-hoc Tukeys analysis was conducted, demonstrating a significant decrease in scores from baseline ($M = 3.528$) to follow up assessment ($M = 1.333$) (Table 5). This highlights a significant decrease in depression in the OPCAB surgical group from pre-operative to post-operative assessment. 3.9% of the variance in cognitive performance on the measure of emotional state, in terms of depression, is explained by time ($\eta^2 = 0.039$) and 4.1% of the variance is explained by the interaction ($\eta^2 = 0.041$), resulting in a total variance of 8.0% explained ($\eta^2 = 0.080$).

In terms of anxiety, the analysis of variance yielded a significant interaction effect [$F_{(1, 72)} = 11.363$, $p = 0.001$]. Highlighting a similar pattern to that of the depression analysis mentioned above, the cell mean plot for anxiety (Appendix B) showed a disordinal interaction, again leading one to be wary of interpreting the significant main effect of time [$F_{(1, 72)} = 14.700$, $p = 0.001$]. A post-hoc Tukeys analysis highlighted a significant decrease in anxiety scores from baseline ($M = 25.694$) to follow-up ($M = 21.806$), showing that there was a significant decrease in anxiety in

the OPCAB surgical group from baseline to follow-up assessment. 3.3% of the variance in cognitive performance on the measure of emotional state, in terms of anxiety, is explained by time ($\eta^2 = 0.033$) and 2.5% of the variance is explained by the interaction ($\eta^2 = 0.025$), resulting in a toal variance of 5.8% explained ($\eta^2 = 0.058$).

Table 4

*Analysis of Variance for Indicators of Emotional State*

| Cognitive Domain | Source | df | F | p |
|---|---|---|---|---|
| **Depression** (BDI) | Cardiac Procedure (A) | 1 | 0.345 | 0.559 |
| | Time (B) | 1 | 9.562** | 0.003 |
| | Interaction (A*B) | 1 | 10.058** | 0.002 |
| **Anxiety** (STAI) | Cardiac Procedure (A) | 1 | 0.160 | 0.690 |
| | Time (B) | 1 | 14.700** | 0.001 |
| | Interaction (A*B) | 1 | 11.363** | 0.001 |

*p<0.05, **p<0.01

Table 5

*Descriptive Statistics of Indicators of Emotional State*

| | | | Baseline | Follow-up | Marginal Means |
|---|---|---|---|---|---|
| **Depression** (BDI) | OPCAB (n = 36) | M | 3.523 | 1.333 | 2.431 |
| | | SD | 3.574 | 2.056 | |
| | Control (n = 36) | M | 2.111 | 2.138 | 2.125 |
| | | SD | 2.108 | 2.620 | |
| | Marginal Means | | 2.819 | 1.736 | |

*Note*: M = mean, SD = standard deviation

| | | | Baseline | Follow-up | Marginal Means |
|---|---|---|---|---|---|
| **Anxiety** (STAI) | OPCAB (n = 36) | M | 25.694 | 21.806 | 23.750 |
| | | SD | 6.541 | 4.821 | |
| | Control (n = 36) | M | 23.389 | 23.139 | 23.264 |
| | | SD | 5.778 | 5.287 | |
| | Marginal Means | | 24.542 | 22.472 | |

*Note*: M = mean, SD = standard deviation

The secondary statistical analysis, conducted using a standard multiple regression analyses, yielded significant results in two tests, namely language (Boston Naming Test) and attention (RAVLT – trial 1). In terms of diagnostics, a residual analysis was conducted for each multiple regression analysis to ensure that the assumptions of multivariate normality and linearity were upheld. The histograms of raw residuals appeared normal in all analyses thereby satisfying the assumption of multivariate normality, whilst scatterplots of predicted versus raw residuals showed a random distribution in all analyses, thereby satisfying the assumption of linearity. In addition, Cooks Distances were assessed, as a measure of influence on determining regression results, which showed no evidence of multivariate outliers in any of the 11 analyses.

The regression analysis conducted with language (Boston Naming Test) as the dependent variable, showed depression to be a statistically significant predictor in terms of both surgical and control groups with an associated beta coefficient of -.328 ($p$ = 0.009) (Table 8). The model as a whole was statistically significant [$F_{(2, 69)}$ = 3.68, $p$ = 0.030], and in terms of practical significance, $R^2$ = 0.10 and adjusted $R^2$ = 0.07, suggesting that 10% (or more conservatively, 7%) of the variance in the change in language scores is explained by the change in the predictor, depression (Table 9).

Table 8

*Regression Coefficients – Language (n = 72)*

| | Beta | Std Err. Beta | B | Std. Err B | t(69) | p-level | Tolerance |
|---|---|---|---|---|---|---|---|
| Depression | -0.328 | 0.122 | -0.189 | 0.070 | -2.68 | 0.009** | 0.87 |
| Anxiety | 0.160 | 0.122 | 0.059 | 0.045 | 1.31 | 0.196 | 0.87 |

*Note:* Dependent Variable: BNT, *p<0.05, **p<0.01

Table 9

*Regression Summary – Language (n = 72)*

| Multiple R | Multiple $R^2$ | Adjusted $R^2$ | F | p-value | Std.Err.Estimate |
|---|---|---|---|---|---|
| 0.310 | 0.096 | 0.070 | 3.675 | 0.030* | 1.748 |

*Note:* Predictor: Depression, *p<0.05, **p<0.01

In terms of multicollinearity (Table 8), the depression variable displayed a high level of tolerance (0.87) suggesting that it is highly independent of the other independent variable, anxiety, as a predictor. Indeed the correlation between anxiety and depression was r = 0.35, which although appears relatively strong in comparison to the interrelations between other variables, is a far weaker correlation than one might expect with these indicators of mood state (Appendix B). The regression analysis illustrates that as depression scores decrease ($M$ = -1.08), language scores increase ($M$ = 1.01) (Table 11).

The regression analysis conducted with attention as the dependent variable (RAVLT – trial 1), showed anxiety to be a statistically significant predictor in both groups with an associated beta coefficient of .264 ($p$ = 0.037) (Table 12). The model as a whole was statistically significant [$F_{(2, 69)} = 2.659$, $p = 0.023$], and $R^2 = 0.07$, and adjusted $R^2 = 0.05$ suggesting that 7% (or more conservatively, 5%) of the variance in the change of attention scores is explained by the change in the predictor, anxiety (Table 13). The regression analysis highlights that as anxiety scores decrease ($M$ = -2.07), attention scores decrease ($M$ = -0.31).

Table 12

*Regression Coefficients – Attention (n = 72)*

| | Beta | Std Err. Beta | B | Std. Err B | t(69) | p-level | Tolerance |
|---|---|---|---|---|---|---|---|
| Depression | 0.010 | 0.124 | 0.005 | 0.066 | 0.080 | 0.936 | 0.87 |
| Anxiety | 0.264 | 0.124 | 0.091 | 0.043 | 2.127 | 0.037* | 0.87 |

*Note:* Dependent Variable: RAVLT – trial 1, *p<0.05, **p<0.01

Table 13

*Regression Summary – Attention (n = 72)*

| Multiple R | Multiple $R^2$ | Adjusted $R^2$ | F | p-value | Std.Err.Estimate |
|---|---|---|---|---|---|
| 0.268 | 0.072 | 0.045 | 2.659 | 0.037* | 1.654 |

*Note*: Predictor: Anxiety, *p<0.05, **p<0.01

Table 11

*Descriptive Statistics*

| Change Scores | Mean | Std.Dev. | N |
|---|---|---|---|
| Depression | -1.08 | 3.16 | 72 |
| Anxiety | -2.07 | 4.90 | 72 |
| Boston Naming Test (BNT) | 1.01 | 1.81 | 72 |
| Rey Copy Administration | 0.53 | 3.42 | 72 |
| Rey Immediate Recall | 5.79 | 5.80 | 72 |
| Rey Delayed Recall | 5.34 | 5.05 | 72 |
| Digit Span | 0.15 | 2.29 | 72 |
| RAVLT – attention (RAVLT-Att) | -0.31 | 1.69 | 72 |
| RAVLT – total recall (RAVLT- Tot.R) | -0.39 | 2.64 | 72 |
| Similarities | 0.97 | 3.33 | 72 |
| Stroop Test - Time | -5.85 | 20.15 | 72 |
| Stroop Test – Error | -0.35 | 3.08 | 72 |
| Digit Symbol | 4.49 | 6.08 | 72 |

# DISCUSSION

This research forms part of a larger study in which the cognitive effects of OPCAB surgery are compared to the effects of the conventional CABG group. The purpose of this particular research project was to gain an accurate picture of the short-term cognitive effects of OPCAB surgery in comparison to a healthy control group. Although the literature appears contradictory, providing no definitive answers regarding the superiority of the OPCAB procedure over the conventional CABG procedure in terms of cognitive outcomes, it is clear that a large proportion of authors believe that OPCAB is likely to be yield safer neurocognitive results, largely as a result of the avoidance of aortic cannulation and CPB (Al-Ruzzeh *et al.*, 2006; Ascione & Angelini, 2003; Lee, 2003; Zamvar *et al.*, 2002; Zangrillo *et al.*, 2005).

The results of this research do not demonstrate any evidence of cognitive decline following the OPCAB surgical procedure. Instead, the results show that cognitive performance increased in the post-operative assessment as opposed to decreased. This result was counter-intuitive, as it was expected that some form of decline, albeit perhaps mild, was likely to occur, in light of the literature on the topic, in which it has been suggested that the risk of cognitive injury, although lessened, is not eliminated by the OPCAB procedure (Keenan *et al.*, 2005; Zangrillo *et al.*, 2005).

The results in this research show that cognitive performance in the surgical group increased from baseline to follow-up assessment in all measured cognitive domains, apart from one measure of attention (RAVLT – trial 1) which decreased slightly

although not significantly so. This increase in cognitive performance was shown to be significant in the domains of language, psychomotor speed and visual memory. In addition, a significant increase in performance was shown on two of the three measures of executive functioning (Similarities and Stroop – Time). The third measure of executive functioning (Stroop – Errors) did not demonstrate a significant change, despite showing a slightly lower error rate (increased performance) on postoperative assessment. The domains of verbal memory, visuoconstruction and attention failed to show significant change over time, although it is important to note that a slight increase in scores did occur.

It is vitally important to note, however, that a significant increase in cognitive performance was clearly not limited to the surgical group. Results demonstrate that the control group performance increased on almost all measures, with the exception of verbal memory and the same measure of attention as the surgical group (RAVLT – trial 1) which, as in the surgical group, decreased slightly but not significantly so. The fact that the control group also showed an increase in performance, and that this improvement was of an approximately equal amount to that of the surgical group on each measure, is a striking and indeed problematic finding in light of the literature in this field (Keenan *et al.*, 2005; Zangrillo *et al.*, 2005). Indeed, an improvement occurred on ten of the eleven measures in both the surgical and control groups, suggesting that this is not merely a result of random fluctuation. It would appear, therefore, that the increased performance seen in the results is due to the influence of factors other than surgical procedure. As a result, one would be likely to suggest that practice effects are involved, whereby participants show an improved performance as a result of repeated exposure to the same neuropsychological tests (Selnes, Pham,

Zeger & McKhann, 2006). However, the tests used in this research were selected on the basis that they had non-existent practice effects and high test-retest reliability (Mahanna *et al*, 1996; Silbert *et al.*, 2004). Indeed practice effects reported in the standardised literature regarding the tests used in this study (See Lezak, Howieson & Loring, 2004) are non-existent or at most, extremely small, and therefore, clearly do not lend sufficient evidence to suggest that they are the reason for the dramatic picture seen in these results. High test-retest reliability was also shown the selected tests (See Lezak *et al.*, 2004), which is an important factor in determining whether a true change in cognitive performance has occurred (Hanning, 2005). Lezak *et al.* (2004) does however mention that "most studies have found the Rey figure to be harder to recall than the Taylor which typically elicits scores several points higher than the Rey." This perhaps offers a possible explanation for an increase in scores in that specific test. However, this explanation does not assist in providing an accurate description of what is really occurring in the results, as an increase was seen in the majority of the tests, all of which are reported to have non-existent practice effects and equivalent alternate forms.

Clearly, it is also important to note that in addition to an increase in performance in each group, the control group performed consistently better on all measures, at both baseline and follow-up assessments, when compared to the surgical group. This difference was significant in the domains of language, attention, psychomotor speed, executive function and verbal memory, whilst the domains of visual memory and visuoconstruction, although highlighting superior control group scores on both assessments, failed to show a significant difference. It is indeed logical to assume that the control group may perform better than the surgical group pre-operatively due to

the fact that the surgical group had been diagnosed with CAD, was experiencing reduced brain perfusion, and indeed, an increased level of anxiety and depression at baseline due to the impending surgery, as is shown in the results. However, upon post-operative assessment, one would expect the difference between the two groups to have lessened as a result of a successful surgery, increased brain perfusion, and a decreased level of depression and anxiety in the surgical group, which was again shown in the results. However, this was clearly not the case, as it is evident that the difference between the groups remained approximately equal from baseline to follow-up assessment, which is a striking finding. This, firstly, reinforces the notion that what we are seeing in the results is due to factors other than surgical procedure, as both groups showed improved performance despite the fact that only one group underwent the surgical procedure. Secondly, it is clear that emotional state is also unable to provide an adequate explanation of the results. It was clear that the surgical group showed significantly higher levels of depression and anxiety at baseline, but that at follow-up, the surgical group were showing lower levels of depression and anxiety than the non-surgical controls. Although this would provide a neat explanation for an increase in performance of the surgical group, it clearly does not explain the entire picture that is seen in the results as the emotional state of the controls remained constant, and yet their performance increased by approximately the same amount as the surgical group, and in the same domains.

Diegeler *et al.* (2000) suggest that "the perioperative mental (and physical) stress due to hospitalization, operation, and inhabitual environment has to be recognized as an important phenomenon affecting intellectual performance." Bearing this in mind, one might suggest that the setting in which the assessments were conducted may provide a

possible explanation for the increase in cognitive performance. This is due to the fact that the surgical group were largely assessed at the bedside in the various clinical settings at baseline as a result of last minute admissions and the difficulty of gaining access to participants prior to admission. This was often a noisy environment, and indeed a fractured assessment with many interruptions by hospital staff. On follow-up, the surgical group were often assessed in quieter environments such as consultation rooms or at the homes of the patients. As a result, one might expect the performance in the surgical group to increase on post-operative assessment as a result of a more conducive environment for testing. However, once again, this explanation does not appear to be adequate in explaining the results, as the control participants were assessed predominantly in their homes at both baseline and follow-up as a result of the group comprising community-dwelling participants that were not sourced in the hospital setting. The control group therefore generally experienced a quieter assessment environment in both assessments, which could possibly aid in explaining their better performance in comparison to the surgical group. However, this clearly does not provide an explanation for the increase in performance that was witnessed in both groups from baseline to follow-up assessment, as the control participants scores also increased despite the fact that they were being assessed in the exact same location as baseline.

Additionally, although the surgical and control group were not matched in terms of gender, this is unlikely to assist in providing an explanation for the results, as it is known that there is no significant difference between men and women in terms of neurological outcomes following OPCAB surgery (Newman *et al.*, Patel, Smith & Engel, 2006). The sample was matched in terms of age, education and pre-morbid IQ,

which ensured that these variables would not impact on the results gained in this study.

These results are clearly problematic, as no adequate explanation for the entire picture is forthcoming. The difficulty lies in explaining the reason for an equal increase in performance scores in the control group as is seen in the surgical group, considering that practice effects have been reported as small or non-existent. The explanations mentioned above would serve well in explaining an increase in cognitive performance in the surgical group, should the control group had remained constant. However, it is clear that there must be some unexplained factor which is influencing cognitive performance in both groups in order for these results to have emerged. Indeed Dupuis *et al.* (2006) report a similar result, finding, on average, an improvement rather than a decline after CABG surgery. In addition, Selnes *et al.* (2003) found that both surgical and control groups improved from baseline to 3 months. However, these improvements were noted after CABG surgery as opposed to OPCAB surgery, and although a similar mechanism might be involved, one can not say with confidence that this is indeed the case. Nonetheless, it is abundantly clear that further research is necessary in order to gain an accurate explanation of the phenomenon that emerged in this particular research.

The secondary analysis was conducted as a result of the notion that mood state is often considered an important predictor of cognitive change (Borowicz *et al.* 1996; Dupuis *et al.*, 2006; Murkin *et al.* 1995; Sendelbach, 2006). It was decided to assess whether a change in emotional state, either depression or anxiety, could predict a change in any of the measured domains, considering the fact that no cognitive decline

had been found. The results showed that a change in depression is able to predict a change in the domain of language as measured by the Boston Naming Test, and as depression scores decrease, naming scores increase. Additionally, results showed that a change in anxiety is able to predict a change in the domain of attention, as measured by the RAVLT –trial 1, and as anxiety scores decrease, attention scores decrease. One might begin to theorise in terms of possible explanations for these findings. However, it is important to note that the results were shown to be non-significant for the majority of the measures analysed, perhaps suggesting that a change in emotional state is not a reliable predictor of cognitive change, a finding which has also been supported in the literature (Andrew *et al.*, 2000; Selnes & McKhann, 2005).

Indeed, it appears logical that a decrease in depression may result in better test scores, but should this link exist, then one would expect this trend to be evident in almost all of the measures, instead of simply in naming ability. Additionally, in terms of attention, it was shown that a decrease in anxiety is a predictor of decreased attention. Again, one may theorise that if a subject is less anxious, they perhaps are feeling more relaxed in the testing setting and are feeling less concerned about paying close attention. However, it is important to note that this is mere speculation, and once looking at these results against the majority of non-significant results, one may suggest that these results achieved significance as a result of some random occurrence. It is indeed difficult to interpret these results with confidence in light of the small sample size, but, at the very least, this analysis attempts to provide information about areas that may emerge as important once a larger sample is employed.

**Limitations of the Research**

This study attempted to overcome some of the limitations of previous research that have been mentioned in the literature as highly important in gaining an accurate illustration of cognitive change, by including a non-surgical control group, by matching the samples in terms of age and education and baseline functioning, by thoroughly assessing emotional state indicators (depression and anxiety) pre-operatively and post-operatively and by ensuring that a recommended test battery was employed that assesses a wide range of domains in cognitive functioning (Borowicz *et al.*, 1996; Dupuis *et al.*, 2006; Eagle & Guyton *et al.*, 2004; Haddock *et al.*, 2003; Hogue *et al.*, 2007; McKhann *et al.*, 1997; Murkin *et al.*, 1995; Selnes *et al.* 2003).

Despite this, however, there were limitations inherent in the present research. Firstly, although the researcher aimed to obtain a large and representative sample, this was unfortunately not possible due to practical reasons. As a result of OPCAB surgery not being as commonly performed as the conventional CABG procedure, it was difficult to gain a large number of surgical participants for the sample. In addition to this, as a result of the subjects being medically unwell and about to undergo major surgery, many of the prospective subjects were unwilling to participate in the research. Patient attrition was indeed a limitation in this study in that, in addition to the participants that were disinterested or those that completed a pre-operative assessment and were disinterested in completing the post-operative assessment, were those patients that were unable to complete the follow-up assessment due to death, or medical reasons, such as stroke. Although the sample appears reasonable (n = 72), it is relatively small in comparison to the sample sizes that have been employed in much of the literature

using a few hundred participants (Dupuis *et al.*, 2006; Angelini *et al.*, 2002; Van Dijk *et al.*, 2002), and as a result, has limited statistical power, and it is problematic to generalise the results of this study with any large degree of confidence.

In addition, in order for results to be generalised to the larger OPCAB community, one needs to employ a sample that is representative of this community. It has been suggested that a limitation inherent in this type of research is that an inadvertent biasing of the population tends to occur (Borowicz *et al.*, 1996). As mentioned above, this may be as a result of participant disinterest and subject attrition for various reasons. Although these factors are random, and a systematic bias may not exist, it nonetheless leads to a sample in which a large portion of patients undergoing this specific procedure are not represented, and who may well have had a significant impact on the research.

It is also important to note that this study included a sample heavily weighted towards male patients, with 29 male subjects and only 7 female subjects. It was found that the population of cardiac patients at all of the various treatment centres was largely male, and hence, perhaps the sample is able to be considered as representative of the South African cardiac population. Nonetheless, it is an important consideration to take into account in generalising the results of this study. The sample also included only English and Afrikaans speaking participants, as a result of the researcher not being fluent in Xhosa, and the lack of an interpreter. However, the cardiac population tended to consist almost completely of English and Afrikaans speaking individuals, and therefore the exclusion of Xhosa speaking individuals may perhaps not be a major cause for concern.

Another limitation involves the assessment procedure itself. It became clear that many participants found the test battery to be too lengthy. The battery required roughly 60 - 90 minutes to administer, depending on the individual concerned. The surgical group, as a result of being unwell, and often in great pain, tended to become less focused and pay less attention during the course of the assessment, which will have impacted heavily on the testing measures. It was attempted to use shorter forms of some of the tests (i.e. Boston Naming Test), but the difficulty came in attempting to strike a balance between a manageable assessment for the participant, and a battery that does indeed assess all aspects of cognitive function. In addition to this, as mentioned above, a limitation involved the testing setting which was largely different for the surgical and control groups, and was often not conducive to gaining an accurate measure of cognitive ability, as a result of noise, discomfort and the fractured nature of the assessment due to continual interruptions.

A large limitation in this research is that the researcher was not blind to the group in which the patient belonged, which is likely to have resulted in researcher bias. At the start of this particular study, participants were sourced and identified by the principal researcher and allocated to the various researchers involved, allowing the researchers to remain blind to whether the participant was a surgical or control group member, and indeed, to which surgical group they belonged. However, unforeseen complications occurred, unfortunately resulting in this aspect having to be abandoned. It is nonetheless an important factor to take into account in considering the results that emerged from this research.

Lastly, as the literature has highlighted the multifactorial nature of postoperative neuropsychological impairment (Royter *et al.*, 2004; Wan & Yim, 2001), it was planned to gain information from the participants at the time of their assessments regarding factors such as a history of diabetes mellitus, smoking and alcohol usage, a history of thyroid disease, current medication usage, syncope and cholesterol levels. Although information was elicited from some participants, it was not always practical to gain accurate information from all participants. In terms of smoking and alcohol usage, participants were often vague and, without collateral information from a family member, one was unsure as to the accuracy of the information given. With the resultant information that was gained in this research, it was not possible to conduct a meaningful analysis on the data, which is clearly a limitation.

**Recommendations for Future Research**

As mentioned above, it is clear that a larger sample is required if one is to gain meaningful results regarding postoperative neuropsychological decline and indeed, to be able to generalise the results gained in this research to a larger cardiac population. The results gained in this research were counter-intuitive, and it would be beneficial to conduct a rigorous study with a large sample in order to investigate the phenomenon that emerged more fully. In addition, it is essential that detailed demographic information regarding factors such as alcohol usage, medication, history of diabetes mellitus and thyroid disease be attained in a thorough manner in order to control for possible alternative explanations of cognitive change.

In order to fully discount the effects of emotional state on cognitive performance scores, it may also be beneficial to ensure that a baseline assessment is conducted at an earlier point, perhaps a week preoperatively, as opposed to the day before surgery when the participants are experiencing extreme stress, in order to ensure that one gains a clear and accurate measure of cognitive functioning. It is vital that this assessment, and that of the follow-up assessment, be conducted in a quiet area that is comfortable and conducive to assessment.

An important recommendation for future research, as a result of the contradictory literature regarding short-term and long-term postoperative effects on neuropsychological function, would be to include an additional long-term follow-up assessment (Hernandez *et al.*, 2007; Stroobant *et al.*, 2002; Van Dijk *et al.*, 2002; Van Dijk *et al.*, 2004). Although the researcher did originally plan to include long-term follow up assessments, for practical reasons in terms of gaining an adequate sample size, this was simply not possible. In addition, it is important to take into account that the design of this study assesses change in cognitive performance over time by looking at only two measurement points, baseline and follow-up assessment. As a result, this does not allow for a detailed analysis of changes in cognitive performance along the time course, but limits one to an evaluation of the participants' entire cognitive picture on the basis of two static assessments (Dupuis *et al.*, 2006). As this study is simply assessing short-term cognitive effects, it is perhaps not highly problematic to assess participants on two time points as the time course involved is only 1 month. In a long term study, however, it would be necessary to assess participants on numerous occasions if one is to gain an accurate picture of the participants' cognitive status and change over time.

# CONCLUSION

Numerous studies have reported a significant cognitive decline following the CABG procedure (Alhgren *et al.*, 2003; Keenan *et al.*, 2005; Andrew *et al.*, 2000; McKhann *et al.*, 1997; Newman *et al.*, 2001; Royter *et al.*, 2004; Selnes *et al.*, 1999; Selnes *et al.*, 2003; Van Dijk *et al.*, 2000; Währborg *et al*, 2004). As this procedure has become the most common form of treatment for patients with CAD (Wan & Yim, 2001), there are major implications for the patient population. It has been suggested that the OPCAB procedure may result in superior outcomes in terms of neurocognitive injury (Hernandez *et al.*, 2007). However, the investigation into postoperative cognitive change following OPCAB surgery is an area in which contradictory research continually arises and it is clear that the prevalence of postoperative deficits reported varies greatly (Dupuis *et al.*, 2006). The results of this study are important as they highlight an overwhelming absence of cognitive decline following OPCAB surgery, in the domains of language, visual memory, verbal memory, visuoconstruction, executive function, psychomotor speed and attention, and indeed show a marked improvement in cognitive performance in both the surgical and control groups in almost all measured domains. Despite the limitations of this study, it nonetheless provides important information surrounding the effects of OPCAB surgery on cognitive performance and contributes to the theoretical base of cardiac knowledge. It is vital that further research be conducted in a solid manner to provide definitive information regarding the superiority of the OPCAB procedure over the CABG procedure, and in order to be able to inform patients of the risks and benefits attached to OPCAB surgery with confidence.

# ACKNOWLEDGEMENTS

Firstly I would like to thank my supervisor, Prof. Mark Solms for his support and guidance in this research. In addition, I would like to express my heartfelt gratitute to Dr. Dave Harris, and to Prof. Johan Brink for their continued assistance and support in the sourcing of participants. I would like to thank Cara Williams for her advice and input throughout the study. Additional thanks are due to the staff in the Cardiac Clinic and Cardiothoracic Surgery Ward at Groote Schuur Hospital, and the surgical wards at N1 City Hospital, Kuilsriver Hospital and Gatesville Medical Centre for their continued patience and willing assistance. I also wish to thank Susan Malcolm-Smith and Greg Distiller for their statistical advice and support. Final words thanks are due to the participants, both surgical and control, for their cooperation, enthusiasm and kind assistance, without whom this research would not have been possible.

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# APPENDIX A:

## ETHICAL CONSIDERATIONS:

## INFORMED CONSENT FORM AND PATIENT

## INFORMATION SHEET

# CONSENT FORM

## TITLE OF PROJECT:

**Study into the Short-term and Long-term Effects of Three Cardiac Procedures on Cognitive Performance**

*Please cross out as necessary*

Have you read the Subject Information Sheet? YES/NO

Have you had an opportunity to ask questions and discuss the study? YES/NO

Have you received satisfactory answers to all your questions? YES/NO

Have you received enough information about the study? YES/NO

Who have you spoken to? Dr/Mr/Mrs/Ms/Prof. .....

Do you understand that you are free to withdraw from the study:

-at any time
-without having to give a reason for withdrawing
-and without affecting your future treatment? YES/NO

Do you understand that some of your answers in the study may be audio-taped? YES/NO

Do you consent to the unattributed and confidential use of these recordings for scientific purposes? YES/NO

**Name (in BLOCK LETTERS):**

**Signature:** **Date:**

# PARTICIPANT INFORMATION SHEET

## TITLE OF PROJECT:

**Study into the Short-term and Long-term Effects of Three Cardiac Procedures on Cognitive Performance**

- You are invited to participate in a neuropsychological study conducted in the cardiac clinic and cardiothoracic surgery at Groote Schuur Hospital and Gatesville Medical Centre. Please read this information sheet carefully and do not hesitate to ask the researcher for any additional information.

- The overall purpose of the study is to investigate and compare cognitive performance following three different cardiac procedures.

- You are asked to take part in this study by participating in three, maybe four interviews, designed to assess your cognitive functioning. The interviews may be audio-taped and sessions will last approximately 1-hour, and some of your relatives may also be asked to participate in the study on separate occasions.

- There are no anticipated risks involved in this research, but if you should experience mental and/or physical fatigue, or any form of psychological distress please be aware that you can inform the researcher immediately.

- It is up to you to decide whether or not you take part. If you decide to take part you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part you are still free to withdraw from the study at any time, without having to give a reason and without this affecting future treatment.

- The confidentiality of your answers and your identity will be protected. All data recordings made will be suitably anonymous, securely stored, made accessible only to the researchers.

- This study is an educational project, forming part of a Ph.D. thesis at the University of Cape Town (UCT). The research will be carried out by researchers from UCT and will be funded by the same university.

- The study has been reviewed by the UCT Psychology Department's ethics committee and the Faculty of Health Sciences Research Ethics Committee.

- If you have any questions regarding this study, or concerns regarding the manner in which the study was conducted, or would like to be informed of the results when the study is completed, please feel free to contact the principal researcher.

- Address for communications:
  Professor Mark Solms Ph. (021) 650-3435
  Department of Psychology
  University of Cape Town, Rondebosch 7701

# APPENDIX B:

## ADDITIONAL STATISTICAL MATERIAL

Figure 1

*Cell Mean Plot of Significant Interaction Effect for Depression*

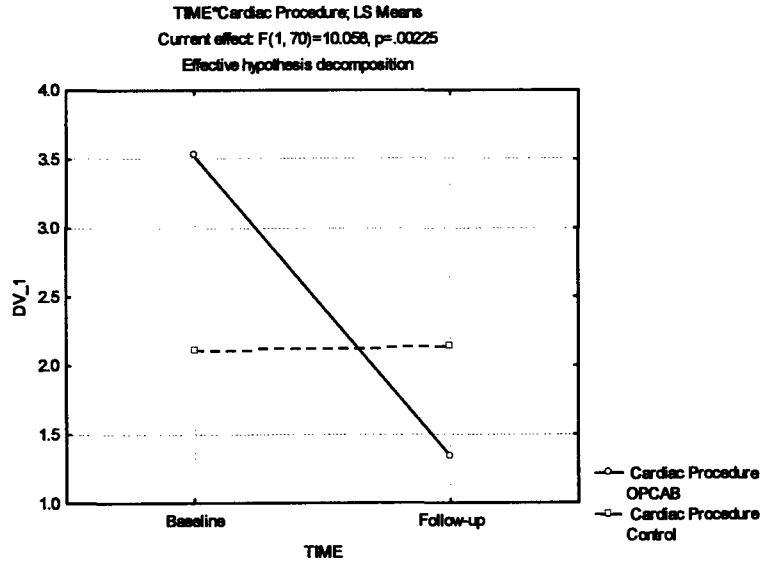


Figure 2

*Cell Mean Plot of Significant Interaction Effect for Anxiety*

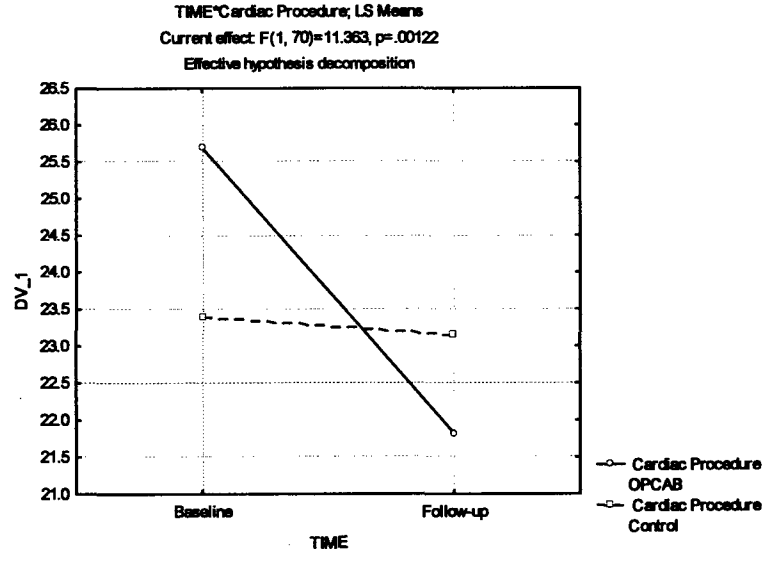

Table 10

*Intercorrelation Matrix*

| | Dep | Anx | BNT | ReyI | ReyD | DSp | Ravlt A | Ravlt TR | Simil | D Sym | Stroop T | Stroop E | Rey C |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dep | 1.00 | 0.35 | -0.27 | 0.01 | -0.07 | 0.10 | 0.10 | 0.05 | -0.04 | -0.21 | 0.15 | 0.24 | 0.38 |
| Anx | 0.35 | 1.00 | 0.04 | -0.03 | -0.24 | -0.09 | 0.27 | 0.03 | -0.10 | -0.21 | 0.21 | 0.15 | -0.08 |
| BNT | -0.27 | 0.04 | 1.00 | 0.02 | -0.10 | -0.13 | 0.01 | -0.07 | 0.19 | 0.08 | 0.03 | 0.00 | -0.40 |
| ReyI | 0.01 | -0.03 | 0.02 | 1.00 | 0.73 | 0.05 | 0.15 | -0.04 | -0.08 | 0.06 | -0.05 | 0.02 | 0.30 |
| ReyD | -0.07 | -0.24 | -0.10 | 0.73 | 1.00 | -0.05 | 0.04 | 0.15 | 0.11 | 0.21 | -0.13 | -0.04 | 0.31 |
| DSp | 0.10 | -0.09 | -0.13 | 0.05 | -0.05 | 1.00 | -0.02 | 0.02 | -0.02 | 0.10 | -0.01 | 0.04 | 0.08 |
| RavltA | 0.10 | 0.27 | 0.01 | 0.15 | 0.04 | -0.02 | 1.00 | 0.22 | -0.11 | -0.07 | 0.18 | -0.03 | 0.20 |
| RavltTR | 0.05 | 0.03 | -0.07 | -0.04 | 0.15 | 0.02 | 0.22 | 1.00 | -0.05 | -0.00 | 0.11 | -0.08 | 0.17 |
| Simil | -0.04 | -0.10 | 0.19 | -0.08 | 0.11 | -0.02 | -0.11 | -0.05 | 1.00 | 0.22 | -0.00 | -0.05 | -0.16 |
| DSym | -0.21 | -0.21 | 0.08 | 0.06 | 0.21 | 0.10 | -0.07 | -0.00 | 0.22 | 1.00 | -0.11 | 0.04 | -0.03 |
| StroopT | 0.15 | 0.21 | 0.03 | -0.05 | -0.13 | -0.01 | 0.18 | 0.11 | -0.00 | -0.11 | 1.00 | -0.17 | 0.08 |
| StroopE | 0.38 | -0.08 | -0.40 | 0.30 | 0.31 | 0.08 | 0.20 | 0.17 | -0.16 | -0.03 | 0.08 | 1.00 | 0.28 |
| ReyC | 0.24 | 0.15 | 0.00 | 0.02 | -0.04 | 0.04 | -0.03 | -0.08 | -0.05 | 0.04 | -0.17 | 0.28 | 1.00 |

*Note*: "Dep" = depression, "Anx" = anxiety, "BNT" = Boston Naming Test, "ReyI" = Rey immediate recall, "ReyD" = Rey delayed recall, "Dsp" = Digit Span, "Simil" = Similarities, "DSym" = Digit Symbol, "StroopT" = Stroop Test – Time, "StroopE" = Stroop Test – Error, "ReyC" = Rey Copy Administration