Master's Thesis (Neuropsychology)

November 2006

A study on the short-term cognitive outcome of Percutaneous Transluminal Coronary Angioplasty with Intra-coronary Stenting

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ABSTRACT

This study explores the short term cognitive outcome of percutaneous transluminal coronary angioplasty with intra-coronary stenting. Participants were assessed cognitively using specific neuropsychological tests used to measure performance in the seven cognitive domains. Forty people took part in the study, with twenty of them making up the stented group, and twenty of them making up the control group. The stented group were assessed a few days before, and then a few weeks after their procedures. The control group were simply assessed whenever they agreed to participate, and then again a few weeks later. There were ten males and ten females in each group. The participants were all between the ages of 34 and 75, and the sample had an average age of 57. The researchers were given access to patients at Groote Schuur Hospital and Gatesville Medical Centre. Analysis of variance was used in order to assess differences between the groups with respect to changes in cognitive performance in all seven cognitive domains. Results indicated that there were not significant differences between the groups, with respect to changes in cognitive performance between the first and second interviews.

INTRODUCTION

Cardiovascular Disease

Cardiovascular disease, or coronary artery disease (CAD), is a condition which involves narrowing of the coronary arteries, which results in a restriction of blood flow to the heart (Brink, 1982). In brief, narrowing of the coronary arteries is a result of a strong tendency for the deposition of blood fats, and the consequent formation of fibrofatty atheromatous plaques on the inner walls of these arteries (Brink, 1982; Schoen,1989). These plaques cause a type of inflammation and connective tissue forms around them (Brink, 1982). This process is known as atherosclerosis, and causes the plaques to develop into hard, irregular lesions, which under certain circumstances, can enlarge, develop cracks, become pulpy, and even calcify (Brink, 1982). The factors that advance the above process constitute risk factors for CAD and

include hypercholesterolemia, hypertension, cigarette smoking and diabetes mellitus (Schoen, 1989). Narrowing of the coronary arteries can result in angina, and ultimately cardiac arrest (Pillai & Wright, 1999).

When patients present with angina, they usually undergo examination, cardiac catheterization and coronary angiography, which is a procedure used to establish the presence or absence of coronary artery disease (Bittl & Levin; 1980). This procedure is usually performed from the right femoral artery (in the groin), where an introducer sheath is inserted, usually using the Seldinger technique (Bittl & Levin; 1980). A hollow flexible tube called a guide catheter is inserted through this sheath, and with the help of X-ray images, is threaded up to the heart (Bittl & Levin; 1980). The tip of the catheter is pushed just inside the coronary artery that is being assessed and a small amount of radiographic contrast agent is injected through the catheter (Bittl & Levin; 1980). This contrast agent shows up clearly on the X-rays, which are recorded as a series of images called an angiogram (Bittl & Levin; 1980). On the angiogram, the doctor is able to see the exact site and severity of the narrowing of the coronary artery (Bittl & Levin; 1980).

When the doctor has studied the angiogram and confirmed that the patient has CAD, it is necessary to decide on the most appropriate treatment, which depends largely on the severity of the situation. Possible treatment options include medication, coronary angioplasty (PTCA) and bypass graft surgery (Bittl & Levin).

Percutaneous Transluminal Coronary Angioplasty (PTCA)

PTCA is one of the options available to patients diagnosed with CAD, and can achieve results that are comparable with bypass operations (Brink, 1982). This procedure is also performed by means of cardiac catheterization, and if appropriate, is conducted directly after the coronary angiography (discussed above), because the doctor needs to know the exact site of the coronary narrowing that needs to be targeted. With the guide catheter still in place from the coronary angiography, a smaller catheter, with a tiny deflated balloon at the tip, is inserted and is threaded through the narrowed artery and into the area that needs to be dilated (Schoen, 1989). The balloon is inflated for a variable period of time, and is then withdrawn, after

which another angiogram is performed to assess the result (Schoen; 1989). This process may be repeated, with levels of inflation pressure and sizes of balloons sometimes being varied (Schoen; 1989). Balloon inflation causes stretching and/or fracturing of the plaque formations in the coronaries, which leads to luminal expansion (Schoen; 1989). Once the artery has been successfully dilated, and the angiogram indicates satisfactory blood flow, the balloon and catheters are removed (Schoen; 1989). The two principal complications of this procedure are abrupt vessel closure and progressive re-narrowing or re-stenosis (Pillai & Wright, 1999).

Intra-coronary Stenting

The increasing awareness of the complications associated with PTCA lead to the conceptualization, research and development of a procedure known as intra-coronary stenting (Schoen; 1989). During intra-coronary stenting, after the coronary artery is dilated by the inflation of a balloon, a stent is deployed at the site of previous stenosis (Schoen; 1989). A stent is a small tubular mesh or coil device, usually constructed from stainless steel (Schoen; 1989). Some stents are self-expanding but most are mounted on a collapsed angioplasty balloon and are deployed by maximal balloon inflation, which causes these spring like structures to expand and lock (Pillai and Wright; 1999). Stents are designed to remain in arteries permanently, providing structural support, encouraging free blood flow and reducing the likelihood of future thromboses (Schoen; 1989). Although early complications made initial stenting results rather disappointing, modern stenting procedures overcome many of the limitations of PTCA and have become widely accepted practice (Pillai and Wright, 1999). In addition, although re-stenosis still remains a problem, recent advances in stent design are likely to further improve long term results (Pillai & Wright, 1999).

Cognitive effects of PTCA with intra-coronary stenting

Research into the cognitive effects of PTCA with intra-coronary stenting is extremely limited. However, several studies have focused on the cognitive effects of Coronary Artery Bypass Grafting (CABG), which is another surgical procedure used to treat individuals with CAD. According to Silbert *et al* (2004), short term post-operative cognitive decline is a common, important and debilitating complication of CABG,

and has been described extensively. In addition, although less common, the prevalence of long term post-operative cognitive decline in a certain percentage of CABG patients has been demonstrated in various studies (Borowicz *et al*, 1996; McKhann *et al*, 1997; Bruggemans *et al*, 1995). However, it should be noted that these long term effects are also commonly cited as being rare and relatively small (Savageau *et al*, 1982; Townes *et al*, 1989).

With respect to the nature of this cognitive impairment, McKhann *et al* (1997) reported short term and long term declines to be most common in the domains of visuoconstruction, language and verbal memory, with long term declines in executive function and attention also being relatively common. In addition, according to Selnes *et al* (1999), post-CABG cognitive changes are most prevalent in the cognitive domains of memory and visuoconstruction. However, a broad review of 35 studies on the long term and short term cognitive effects of CABG, concluded that memory, psychomotor speed and attention are the domains most commonly effected (Borowicz *et al*, 1996).

Short term cognitive decline following CABG may be related to the practice of using large doses of benzodiapines for anesthesia, post operative analgesia and sedation (Townes *et al*, 1989). However, drugs alone provide an incomplete explanation. Cognitive decline following CABG has also been attributed to perioperative hypoxia, as well as micro emboli, hypothermia and reduced cerebral blood flow during cardiopulmonary bypass (CPB) (Hlatky *et al*, 1997). CPB has also been associated with nonpulsatile blood flow, potentially inadequate perfusion pressure, extra cellular brain water and microscopic air bubbles, all of which may contribute to the cognitive decline following CABG (Wan *et al*, 2001). Thus, CPB is commonly implicated in the explanation of this decline.

Consequently, it is widely assumed that PTCA with intra-coronary stenting, which is relatively non-invasive and which does not involve CPB, should not result in cognitive decline. However, as Wan *et al* (2001) explain, the causes for neuropsychological impairment following CABG are multifactorial, and CPB's exact role remains controversial. In fact, research has been unable to provide evidence demonstrating meaningful cognitive differences between patients following CABG

with CPB (on pump) and CABG without CPB (off pump) (Wan *et al*, 2001). Thus, the importance of CPB as an explanation of cognitive decline seems somewhat questionable.

Added to this, it should also be noted that PTCA with stenting, although non-invasive, is still a risky operation, and contains certain hypothetical risks. For example, this procedure could dislodge plaque build up on the inner walls of blood vessels, which could result in thrombi in the vessels of the brain or the heart. Alternatively, periods of ischaemia or fibrillation during the procedure could lead to stroke. In addition, cognitive decline could occur as a result of an unknown etiology (Williams, 2004). Therefore, the validity of assumptions about the safety of PTCA with intra-coronary stenting, with respect to the brain and its functions, is certainly open to question.

Whilst there is a scarcity of research on the cognitive effects of PTCA with intra-coronary stenting, some research has suggested that coronary angioplasty without stenting is not associated with short term or long term cognitive dysfunction (Blumenthal *et al*, 1991; Hlatky *et al*, 1997), while other research has suggested that it does sometimes result in impaired executive functioning (Sader *et al*, 2002). Studies that have focused on the cognitive effects of PTCA with intra-arterial stenting in other areas of the body have produced similarly inconclusive results. Research on the cognitive effects of carotid artery stenting has demonstrated that while most patients' cognitive performances remain unchanged, some patients do show significant improvements or deteriorations in single cognitive domains (Lehrner *et al*, 2005; Grunwald *et al*, 2006). In addition, research by Lee *et al* (1999) suggests that stenting of the extracranial cerebral arteries does not lead to a decline in cognitive performance (but there were only three participants in the study).

Only one study has actually investigated the cognitive effects of coronary angioplasty with intra-coronary stenting. This research was unable to demonstrate a significant difference between the pre-operative and post-operative neuropsychological performance of patients that underwent PTCA with intra-coronary stenting. (Wahrborg *et al*, 2004). However, while this study did not demonstrate cognitive changes in recipients of PTCA with intra-coronary stenting, it was also unable to demonstrate cognitive changes in recipients of CABG (Wahrborg *et al*, 2004), a

procedure that has often been shown to result in cognitive decline. This might be due to the fact that the study has certain limitations.

Firstly, the study did not utilize a control group, which is of course an essential part of an experimental design. Secondly, patients were only given 5 neuropsychological tests, which means that the functioning of many cognitive domains would not have been measured adequately, if at all. Thirdly, after being tested at baseline, patients were only tested again, 6 and 12 months after the procedure, which does not shed much light on the short term cognitive effects of PTCA with intra-coronary stenting. These effects are of obvious concern to anyone undergoing the procedure, and are certainly worth investigating. In addition, if PTCA with stenting does result in cognitive effects, one would expect them to be most apparent shortly after the procedure, and to become milder with time as a result of the healing process. Therefore, when considering how to investigate the potential cognitive effects of PTCA with stenting, it might be argued that a thorough study into the short term effects of the procedure would be a good way to start. Consideration of a further study into long term cognitive effects could be based on the results of the short term study.

AIM

The aim of this study was to investigate the short term cognitive effects of PTCA with intra-coronary stenting, while overcoming the limitations of existing research.

METHOD

Participants

This study utilized 40 participants divided into two groups of 20. The first group was comprised of patients admitted to the cardiac wards, that were found to have ischaemic heart disease, and that underwent PTCA with intra-coronary stenting as an intervention. The second group (control group) was comprised of willing participants with no diagnosis of ischaemic heart disease. Admittedly, the utilization of a control

group made up of patients with ischaemic heart disease, that did not undergo PTCA with stenting, would have been ideal. However, this was not possible for practical and ethical reasons. All the participants were between 34 and 75 years old, and the two groups were matched as closely as possible with regards to age. The mean age of the stented group was 57,3, while the mean age of the control group was 57,4. There were ten male patients and ten female patients in each group. The researchers were given access to patients in the C26 ward at Groote Schuur academic hospital, as well as patients of a private cardiologist practicing at Gatesville Medical Centre. The participants were all fluent in either English or Afrikaans, with the majority of them living in and around Cape Town.

Interviewers

This study is part of a larger study, that also involves patients undergoing the CABG procedure. The researchers involved are all post-graduate psychology students, trained to administer the neuropsychological tests that the study utilizes.

Ethical Considerations

Participation in this study was completely voluntary and participants were required to sign forms indicating their informed consent. The participants' involvement in the study did not cause them physical or emotional harm, and their individual test scores will remain confidential. This study was subject to scrutiny by both the psychology department and the medical school ethical review boards.

Measuring Cognitive Change

In order to measure the cognitive effects of PTCA with intra-coronary stenting, standardized neuropsychological tests were utilized. Patients were first administered these tests a day or two before they were stented. The researcher had originally wanted to conduct follow up testing exactly one month after intra-coronary stenting. However, practically, this was not always possible. As it turned out, the patients were all administered the tests for a second time within a month and a half of their operations. Similarly, control group participants were first tested when they agreed to

participate, and were then tested a second time within a month and a half of their first interview. Most of the testing took place at Groote Schuur hospital and Gatesville Medical Center, although a few of the follow up interviews were conducted in the homes of the participants.

As McKhann *et al* (1997) demonstrate, post-operative cognitive change varies by cognitive domain. Thus, in order for meaningful interpretation of 'cognitive decline' to be possible, it was important to separately test and analyze performance in all of these domains. This methodological feature gave the study the potential to gain some understanding about the nature of the cognitive decline (if it was found to occur), which would in turn provide some clues about the whereabouts and potential factors leading to the neural pathology responsible for the decline. The seven cognitive domains were assessed using the tests specified below:

1. Verbal Memory: Rey Auditory Verbal Memory Test (RAVLT), a word-list learning task, requiring 8 trials. Verbal learning, retention, and recognition memory are assessed. Alternative word lists were used in follow-up interviews.
2. Visual memory: Rey Complex Figure- Recall, used to assess the ability to recall a complex visual design previously copied. Taylor Complex Figure- this alternative to the Rey Complex figure was used in the follow-up interviews.
3. Language: Boston Naming Test (short form), a series of 30 line drawings that a patient must name on confrontation.
4. Attention: Digit Span forward and backward. The patient is asked to repeat/recall an increasing series of random digits. The patient is first asked to repeat these series forwards. Another series of digits is then provided, which the patient is asked to repeat backwards.
5. Visuoconstruction: Rey Complex Figure – Copy, used to assess the ability to copy a complex visual design. Taylor Complex Figure- alternative figure used in follow-up interviews.
6. Psychomotor speed: Symbol Digit, a timed measure of psychomotor speed in which the subject is required to reproduce a series of coded geometric symbols in blank boxes beneath randomly generated digits, according to a coding scheme for pairing digits and symbols.

7. Executive functioning:

a) Stroop Test, a timed task to measure response inhibition, where the subject is shown colour names. These words are all on one page and are printed in different coloured ink to what the written word actually denotes. For example, the word "red" may be typed in blue ink and then may appear later in green ink. To give an example, in one of the trials, the subject is required to go through each word, saying the colour the word is typed in and not what the word actually says.

b) Similarities subtest of WAIS III, a task used to investigate capacity for abstraction. The subject is given two words (for example, banana and apple). He/she is then required to explain what is similar about them (for example, a banana and an apple are both fruits). The pairs of words become increasingly difficult and more abstract (for example, what is similar about a statue and a poem?).

The ability of neuropsychological tests to detect post-operative cognitive decline depends heavily on their sensitivity, with respect to the detection of change in cognitive function over time. The above tests have features, such as high test-retest reliability and small or non-existent practice effects, that make them useful for repeated administration, and therefore, for detection of change (Silbert, 2004).

Other Measures

Depression is a widely reported post-operative concern, which can influence cognitive test scores (Borowicz, 1996). In addition, anxiety, which becomes a factor for many patients just before a surgical procedure, can also greatly undermine cognitive performance. Thus, it was important to consider the possibility, that an increase or decrease in the stented group's level of depression or anxiety (as a result of the procedure) between first and second interviews, could lead to a change in cognitive performance between these interviews, thereby confounding the results of the study. As a result, in addition to the cognitive measures, all participants were administered the Centre for Epidemiological Study of Depression (CES-D) during both interviews to allow for the consideration of the possibility that changes in levels of depression could be responsible for cognitive changes between interviews. Similarly, they were

administered the Spielberger State-Trait Anxiety Inventory (STAI-T) during both interviews to allow for the consideration of the possibility that changes in levels of anxiety could be responsible for cognitive changes between interviews.

Statistical Methods

In order to analyse the data, simple one-way analysis of variance was utilized. The independent variable (group variable) varied with respect to whether the participant underwent PTCA with intra-coronary stenting, or whether he/she was a member of the control group. The dependant variables took the form of the calculated differences between the scores obtained in the first and second interviews, for the tests used to measure the participants' performances in the seven cognitive domains. The other two relevant variables, were the calculated differences between scores obtained in the first and second interviews, for the measures of depression and anxiety, which were thought to be possible confounding variables.

Overall, nine separate analyses were conducted. Whilst, this increased the risk of type one error, it was necessary to analyze the cognitive domains separately, for reasons that have already been explained. If any results were significant at the 0,05 confidence level, they would have been reported cautiously, and Bonferroni corrections would have been considered. The validity of assumptions regarding normality, as well as homogeneity of variances, were assessed using plots of the dependant variable residuals around the regression line, and Levene's tests respectively.

In the first two analyses, one-way ANOVA was used in order to determine whether there were significant differences between the two groups, with respect to the calculated differences between scores obtained in the first and second interviews, for measures of depression and anxiety. The rest of the analyses used one-way ANOVA to determine whether there were significant differences between the two groups, with respect to the calculated differences between scores obtained in the first and second interviews, for the tests used to measure the participants' performances in the seven cognitive domains.

If either of the first two analyses were found to be significant (and one of the subsequent analyses was found to be significant), an analysis of covariance (ANCOVA) using the general linear model would have been utilized. This method provides a useful way of removing the variance of the dependent variable that can be attributed to a covariate (confounding variable). In other words, this method is useful as a means of controlling for the effect of an extraneous variable, and gaining a more accurate idea about the amount of variance that can be attributed to the independent variable of interest (the group variable).

RESULTS

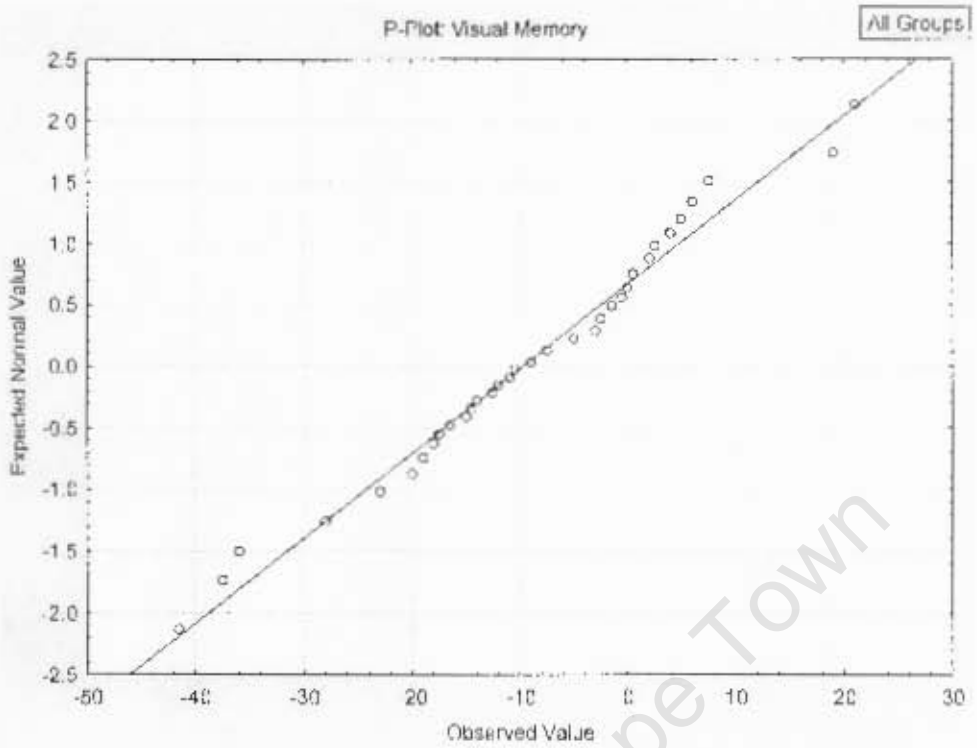
The method of statistical analysis that was used to analyze the data collected in this study (simple one-way analysis of variance), assumes normality, as well as homogeneity of variances. For all nine analyses, plots of the dependant variable residuals showed that most of them were close to the respective regression lines. Whilst they are a somewhat rough guide, these plots indicate that the data is acceptable with regards to the assumption of normality. In addition, Levene's tests did not yield significant results for any of the analyses. Thus, it can be concluded that the nature of the data does not violate assumptions regarding homogeneity of variances. The Levene's test results (Table 1) and normality plot (Figure 1) for the analysis pertaining to the cognitive domain of visual memory, are shown below as examples of the results of the tests that were done to check the assumptions of the ANOVA technique. The Levene's test results and normality plots for the rest of the analyses are included in the appendix.

Table 1

	Levene's Test for Homogeneity of Variances (Thesis Datafile sta) Effect: Group Degrees of freedom for all F's: 1, 38			
	MS Effect	MS Error	F	p
Visual Memory	55.10756	69.63822	0.791341	0.379292

Note that the p-value is greater than 0.05, indicating insignificance.

Figure 1



Note that the residuals are scattered closely around the regression line, indicating normality.

The first two analyses were conducted in order to determine whether changes with respect to levels of depression and anxiety, were in any way dependant on the group variable. If changes in levels of depression or anxiety were found to be dependant on the group variable, these variables would not have been able to be ruled out as possible confounding variables (assuming that cognitive performance was found to be dependent on the group variable). For example, results may have reflected that the stenting procedure was associated with an increase in depression. In such a case, if it was also found that the stenting procedure was associated with a decline in performance on verbal memory, one could not say whether the decline was a result of the stenting procedure, or of its associated increase in levels of depression. As a result, an analysis of covariance using the general linear model would have been necessary in order to control for the confounding variable.

However, while the results do indicate that participants' depression scores decreased marginally more for the stented group than the control group between interviews

(Table 2), the difference was far from being significant (Table 3). This means that participant changes with respect to levels of depression, can be assumed to be independent of the group variable, which means that further consideration of the possibility of changes in levels of depression being a confounding variable, is unnecessary.

Table 2

	Descriptive Statistics (Thesis Datafile.sta)						
Effect	Level of Factor	N	Depression Mean	Depression Std.Dev.	Depression Std.Err	Depression -95.00%	Depression +95.00%
Total		40	1.000000	2.698528	0.426675	0.136969	1.863031
Group	stented	20	1.200000	2.284962	0.510933	0.130605	2.269395
Group	control	20	0.800000	3.105174	0.694338	-0.653266	2.253266

To help make the descriptive statistics tables such as the one above more understandable, consider the following example. The 'Depression Mean' for the stented group (1.2), is essentially obtained by subtracting the group's mean depression score for the 2nd interview, from the group's mean depression score for the 1st interview. Hence, it can be concluded that the stented group's depression scores decreased by an average of 1.2 points between interviews. Similarly, it can be concluded that the control group's depression scores decreased by an average of 0.8 points between interviews.

Table 3

	Univariate Tests of Significance for Depression (Thesis Datafile.sta) Sigma-restricted parameterization Effective hypothesis decomposition				
Effect	SS	Degr. of Freedom	MS	F	p
Intercept	40.0000	1	40.00000	5.382436	0.025809
Group	1.6000	1	1.60000	0.215297	0.645294
Error	282.4000	38	7.43158		

Note that the group p-value in the above table is greater than 0.05, which indicates that the difference between the 'Depression Means' of the two groups (discussed above), is statistically insignificant. In other words, the difference between the two groups, with respect to their average differences on scores of depression between interviews, is insignificant

In addition, the results indicate that participants' anxiety scores decreased marginally less for the stented group than the control group between interviews (Table 4). However, once again, the difference was marginal and insignificant (Table 5), which means that participant changes with respect to levels of anxiety can also be assumed to be independent of the group variable. Thus, further consideration of the possibility of changes in levels of anxiety being a confounding variable, is also unnecessary.

Table 4

	Descriptive Statistics (Thesis Datafile.sta)						
Effect	Level of Factor	N	Anxiety Mean	Anxiety Std.Dev.	Anxiety Std.Err	Anxiety -95.00%	Anxiety +95.00%
Total		40	1.350000	3.919380	0.619708	0.096522	2.603478
Group	stented	20	0.800000	3.533300	0.790070	-0.853635	2.453635
Group	control	20	1.900000	4.290749	0.959441	-0.108132	3.908132

Note that the stented group's anxiety scores decreased by an average of 0.8 points between interviews. The control group's anxiety scores decreased by an average of 1.9 points between interviews.

Table 5

	Univariate Tests of Significance for Anxiety (Thesis Datafile.sta) Sigma-restricted parameterization Effective hypothesis decomposition				
Effect	SS	Degr. of Freedom	MS	F	p
Intercept	72.9000	1	72.90000	4.719250	0.036132
Group	12.1000	1	12.10000	0.783305	0.381698
Error	587.0000	38	15.44737		

Note that the group p-value is greater than 0.05, indicating that the above difference (Table 4) is insignificant.

Due to the nature of the above results, the planned ANCOVA was not needed, and the rest of the data could simply be analyzed using ANOVA.

Overall, participants' scores on measures of visual memory and visuoconstruction increased between the first and second interviews. However, these scores increased more for the stented group than the control group (Tables 6 and 7).

Table 6

	Descriptive Statistics (Thesis Datafile.sta)						
Effect	Level of Factor	N	Visual Memory Mean	Visual Memory Std.Dev.	Visual Memory Std.Err	Visual Memory -95.00%	Visual Memory +95.00%
Total		40	-9.6875	14.02593	2.217695	-14.1732	-5.20179
Group	stented	20	-11.6500	12.86478	2.876653	-17.6709	-5.62910
Group	control	20	-7.7250	15.17223	3.392615	-14.8258	-0.62418

Note that the stented group's visual memory scores increased by an average of 11.65 points between interviews. The control group's visual memory scores increased by an average of 7.725 points between interviews.

Table 7

Effect	Descriptive Statistics (Thesis Datafile.sta)						
	Level of Factor	N	Visuo-construction Mean	Visuo-construction Std.Dev	Visuo-construction Std.Err	Visuo-construction -95.00%	Visuo-construction +95.00%
Total		40	-1.23750	4.133955	0.653636	-2.55960	0.084603
Group	stented	20	-2.15000	4.853376	1.085248	-4.42145	0.121450
Group	control	20	-0.32500	3.125763	0.698942	-1.78790	1.137902

Note that the stented group's visuoconstruction scores increased by an average of 2.15 points between interviews. The control group's visuoconstruction scores increased by an average of 0.325 points between interviews.

Participant scores for language, psychomotor speed and executive functioning also increased between the first and second interviews. However, in these domains, scores increased less for the stented group than the control group (Tables 8, 9 and 10).

Table 8

Effect	Descriptive Statistics (Thesis Datafile.sta)						
	Level of Factor	N	Language Mean	Language Std.Dev	Language Std.Err	Language -95.00%	Language +95.00%
Total		40	-0.700000	1.963774	0.310500	-1.32805	-0.071954
Group	stented	20	-0.650000	1.980829	0.442927	-1.57706	0.277057
Group	control	20	-0.750000	1.996708	0.446477	-1.68449	0.184488

Note that the stented group's language scores increased by an average of 0.65 points between interviews. The control group's language scores increased by an average of 0.75 points between interviews.

Table 9

Effect	Descriptive Statistics (Thesis Datafile.sta)						
	Level of Factor	N	Psycho-motor Speed Mean	Psycho-motor Speed Std.Dev	Psycho-motor Speed Std.Err	Psycho-motor Speed 95.00%	Psycho-motor Speed +95.00%
Total		40	-2.75000	8.381145	1.325175	-5.43042	0.069580
Group	stented	20	-1.35000	7.442941	1.664292	-4.83340	2.133404
Group	control	20	-4.15000	9.201115	2.057432	-8.45625	0.156255

Note that the stented group's psychomotor speed scores increased by an average of 1.35 points between interviews. The control group's psychomotor speed scores increased by an average of 4.15 points between interviews.

Table 10

Effect	Descriptive Statistics (Thesis Datafile.sta)						
	Level of Factor	N	Executive Functioning Mean	Executive Functioning Std.Dev.	Executive Functioning Std.Err	Executive Functioning -95.00%	Executive Functioning +95.00%
Total		40	-2.77500	4.833046	0.764172	-4.32068	-1.22932
Group	stented	20	-2.00000	5.370485	1.200877	-4.51346	0.51346
Group	control	20	-3.55000	4.223680	0.944444	-5.52674	-1.57326

Note that the stented group's executive function scores increased by an average of 2 points between interviews. The control group's executive function scores increased by an average of 3.55 points between interviews.

Overall, participants scores on measures of attention increased between the first and second interviews. However these scores increased for the stented group, and actually decreased marginally for the control group (Table 11).

Table 11

Effect	Descriptive Statistics (Thesis Datafile.sta)						
	Level of Factor	N	Attention Mean	Attention Std.Dev.	Attention Std.Err	Attention -95.00%	Attention +95.00%
Total		40	-0.175000	2.110869	0.333758	-0.85009	0.500089
Group	stented	20	-0.400000	2.233713	0.499473	-1.44541	0.645410
Group	control	20	0.050000	2.012461	0.450000	-0.89186	0.991861

Note that the stented group's attention scores increased by an average of 0.4 points between interviews. The control group's attention scores decreased by an average of 0.05 points between interviews

Participants' scores on measures of verbal memory decreased between the first and second interviews. However, these scores decreased more for the stented group than the control group (Table 12).

Table 12

Effect	Descriptive Statistics (Thesis Datafile.sta)						
	Level of Factor	N	Verbal Memory Mean	Verbal Memory Std.Dev.	Verbal Memory Std.Err	Verbal Memory -95.00%	Verbal Memory +95.00%
Total		40	1.525000	12.27670	1.941116	-2.40128	5.451278
Group	stented	20	2.750000	9.75961	2.182315	-1.81764	7.317638
Group	control	20	0.300000	14.52439	3.247752	-6.49762	7.097624

Note that the stented group's verbal memory scores decreased by an average of 2.75 points between interviews. The control group's verbal memory scores decreased by and average of 0.3 points between interviews.

Having said all this, none of the above differences were significant. In other words there were no statistically significant differences between the groups with respect to changes in cognitive performance between interviews. The difference between groups with respect to changes on scores of visuoconstruction between interviews, was the closest difference to being significant. However, even this result wasn't particularly close to significance, and as shown below (Tables 13 to 19), most of the results were far from being significant.

Table 13

Effect	Univariate Tests of Significance for Verbal Memory (Thesis Datafile.sta) Sigma-restricted parameterization Effective hypothesis decomposition				
	SS	Degr. of Freedom	MS	F	p
Intercept	93.025	1	93.0250	0.607594	0.440523
Group	60.025	1	60.0250	0.392054	0.534965
Error	5817.950	38	153.1039		

Note that the group p-value is greater than 0.05, indicating statistical insignificance.

Table 14

Effect	Univariate Tests of Significance for Visual Memory (Thesis Datafile.sta) Sigma restricted parameterization Effective hypothesis decomposition				
	SS	Degr. of Freedom	MS	F	p
Intercept	3753.906	1	3753.906	18.97353	0.000097
Group	154.056	1	154.056	0.77865	0.383102
Error	7518.287	38	197.850		

Note that the group p-value is greater than 0.05, indicating statistical insignificance

Table 15

Effect	Univariate Tests of Significance for Language (Thesis Datafile.sta) Sigma-restricted parameterization Effective hypothesis decomposition				
	SS	Degr. of Freedom	MS	F	p
Intercept	19.6000	1	19.60000	4.955422	0.032016
Group	0.1000	1	0.10000	0.025283	0.874507
Error	150.3000	38	3.95526		

Note that the group p-value is greater than 0.05, indicating statistical insignificance.

Table 16

Univariate Tests of Significance for Visuoconstruction (Thesis Datafile.sta)
Sigma-restricted parameterization
Effective hypothesis decomposition

Effect	SS	Degr. of Freedom	MS	F	p
Intercept	61.2562	1	61.25625	3.676221	0.062734
Group	33.3062	1	33.30625	1.998835	0.165561
Error	633.1875	38	16.66283		

Note that the group p-value is greater than 0.05, indicating statistical insignificance.

Table 17

Univariate Tests of Significance for Attention (Thesis Datafile.sta)
Sigma-restricted parameterization
Effective hypothesis decomposition

Effect	SS	Degr. of Freedom	MS	F	p
Intercept	1.2250	1	1.225000	0.271033	0.605660
Group	2.0250	1	2.025000	0.448035	0.507316
Error	171.7500	38	4.519737		

Note that the group p-value is greater than 0.05, indicating statistical insignificance.

Table18

Univariate Tests of Significance for Psychomotor Speed (Thesis Datafile.sta)
Sigma-restricted parameterization
Effective hypothesis decomposition

Effect	SS	Degr. of Freedom	MS	F	p
Intercept	302.500	1	302.5000	4.319642	0.044475
Group	78.400	1	78.4000	1.119537	0.296698
Error	2661.100	38	70.0289		

Note that the group p-value is greater than 0.05, indicating statistical insignificance.

Table 19

Univariate Tests of Significance for Executive Functioning (Thesis Datafile.sta)
Sigma-restricted parameterization
Effective hypothesis decomposition

Effect	SS	Degr. of Freedom	MS	F	p
Intercept	308.0250	1	308.0250	13.19685	0.000825
Group	24.0250	1	24.0250	1.02931	0.316736
Error	886.9500	38	23.3408		

Note that the group p-value is greater than 0.05, indicating statistical insignificance.

DISCUSSION

Although the measures used in this study, have features such as high test-retest reliability and small or non-existent practice effects (Silbert, 2004), the results show that there were differences between scores obtained in the first and second interviews, in both the stented and the control groups. This illustrates the value of using a design that includes a control group, and not assuming that the measures are perfectly accurate and reliable. Thus, when interpreting the results, the overall change in test scores between interviews is unimportant. To find meaning in the results, it is crucial to focus on the change in the scores of the stented group relative to the change in the scores of the control group.

For instance, the results indicate that on average, the stented group's depression levels decreased more between interviews than those of the control group. This result is not in line with expectations about the possibility of post-operative depression, which would have resulted in the stented group's post operative depression scores increasing more than the control group's scores, or at least decreasing less than the control group's scores. In any event, this result might indicate that the stented group was more depressed than the control group to begin with, possibly due to stressful pre-operative circumstances. Alternatively, or in addition, it might indicate that the stented group was less depressed (more happy) than the control group when interviewed the second time, possibly due to a sense of relief about the operation being over, or renewed hopefulness and optimism about the future as a result of the success of the procedure in alleviating the unpleasant, debilitating symptoms of CAD.

Looking at the rest of the results, it would seem that relative to control group scores, the stenting procedure resulted in higher levels of anxiety, better performance in the cognitive domains of visual memory, visuoconstruction and attention, and worse performance in the cognitive domains of language, psychomotor speed, executive functioning and verbal memory. Thus, without further interpretation the effects of PTCA with stenting seem rather mixed and unclear. However, whilst it would be possible to look at each analysis (as has been done with the one on depression), and to

theorize about reasons for the results, considering the insignificance of these results, this would be unnecessary and pointless.

The brief interpretation of the results of group depression scores, was done in order to illustrate how significant results could have been interpreted, and should not be taken to indicate anything more than that. The results show that the differences between the two groups with respect to changes in scores on all of the measures, were marginal and statistically insignificant. This means that further interpretation of these differences should not be carried out, due to the likelihood that all these differences occurred due to random or chance fluctuations. The only interpretation that can be made safely, is that based on these results, it cannot be said that PTCA with intra-coronary stenting has any short term effect on cognitive performance, or on levels of depression or anxiety.

The results of this study are not entirely unexpected, and are in line with the results of the extremely limited prior research. This study has demonstrated that the short term cognitive effects of PTCA with intra-coronary stenting (if there are any) are not particularly obvious, and has added support to the hypothesis that the procedure is safe with respect to patients' neurocognitive well-being. However this does not mean that PTCA with intra-coronary stenting does not result in cognitive effects. The main reason that such a claim can not yet be made with confidence, is due to the small sample size of the study.

When this study was planned, the researcher was aiming to obtain a larger sample. However, unforeseen problems and complications that occurred during data collection resulted in the formulation of more modest goals. These problems occurred due to the nature of the process that the patients undergo in the cardiac wards. Some of the patients that end up in these wards are sent for cardiac catheterization. However, this is often only decided after examination by the doctors, which can go on late into the night before the day that catheterizations take place. This means that many patients had to be seen before the doctors decided on a course of action, and before the researcher knew whether they were going to be catheterized, and of course, many of them weren't catheterized.

In addition, besides coronary angiographs, cardiac catheterization also allows for other investigations into the functioning of the heart. On the basis, of all these investigations, the doctors make decisions about how to treat the patient. This means that before the cardiac catheterization, there was no way of telling whether the patient would end up undergoing PTCA with stenting, whether he/she would be diagnosed with and treated for some other cardiac problem, or whether he/she would be treated for CAD, but using a different method of intervention deemed more appropriate. As a result, many of the interviewed patients, even when they did end up getting catheterized, did not undergo PTCA with stenting. Thus, the data collection process was extremely inefficient and would be well described as a 'hit and miss situation', with many hours and interviews being wasted.

Studies on the cognitive effects of the CABG procedure have consistently demonstrated that cognitive decline (especially short term decline), is a reality. One of the reasons that these studies were able to do this, was that many of them used samples of a fair size, which gave them the ability to elicit significant results and to be confident when drawing conclusions. For example, the studies by Silbert *et al*, Bruggemans *et al*, Townes *et al* and Savageau *et al*, had sample sizes of 50, 63, 65 and 227 respectively. Results of studies on the cognitive effects of PTCA without stenting, and stenting in other areas of the body, have been less conclusive. This might have something to do with the fact that they seem to have used smaller samples. For example, studies by Lee *et al*, Grunwald *et al*, Sader *et al* and Lehrner *et al*, used sample sizes of 3, 10, 16 and 20 respectively.

Only twenty stented patients were interviewed in this study. The fact that there were no statistically significant short term cognitive changes in these patients, does suggest that the procedure is safe with respect to the integrity of brain function, but is certainly not conclusive. Theoretically, PTCA with intra-coronary stenting might lead to an average change in cognitive performance (as calculated when using ANOVA), that is too marginal to be statistically significant with such a small sample. For example, the procedure could lead to relatively widespread but subtle cognitive change, which would result in a low calculated average for cognitive change, which would only emerge as being statistically significant with a larger sample (depending on the subtlety of the decline). Alternatively, the procedure might only lead to

cognitive change (which could be quite drastic), in a small percentage of people. In such a case, the calculated average for cognitive change would again be low, and a larger sample would be required in order to attain a statistically significant result.

Thus, there is a chance that subtle or rare short term cognitive change does occur as a result of PTCA with intra-coronary stenting, and that this study, due to its small sample size, was unable to expose this change. Therefore, it must be noted, that a larger sample would have greatly strengthened this study. Future studies should aim to obtain samples as large as possible, so that stronger conclusions can be drawn from the results.

CONCLUSION

CAD is the most common form of heart disease in industrialized nations (Gersh *et al*, 1980). However, some of the surgical procedures performed in order to alleviate this disease have been associated with post-operative cognitive decline (Silbert et al, 2004). While the cognitive effects of the CABG on-pump procedure are fairly well documented, the effects of the CABG off-pump procedure are less well documented, and the effects of PTCA with intra-coronary stenting are hardly documented at all. Although it has its limitations, this study has made an important contribution to our extremely limited knowledge regarding the cognitive consequences of PTCA with intra-coronary stenting. In future, patients can be assured that there is no evidence to suggest that PTCA with stenting causes any change in cognitive performance, and that if the procedure does cause cognitive changes, they have not been detected because they are subtle, rare or both.

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APPENDIX– Levene's test results and normality plots.

Table 20

	Levene's Test for Homogeneity of Variances (Thesis Datafile.sta) Effect: Group Degrees of freedom for all F's: 1, 38			
	MS Effect	MS Error	F	p
Verbal Memory	56.40625	68.00625	0.829427	0.368179

Note that the p-value is greater than 0.05, indicating insignificance.

Table 21

	Levene's Test for Homogeneity of Variances (Thesis Datafile.sta) Effect: Group Degrees of freedom for all F's: 1, 38			
	MS Effect	MS Error	F	p
Language	0.110250	1.349461	0.081699	0.776560

Note that the p-value is greater than 0.05, indicating insignificance.

Table 22

	Levene's Test for Homogeneity of Variances (Thesis Datafile.sta) Effect: Group Degrees of freedom for all F's: 1, 38			
	MS Effect	MS Error	F	p
Visuoconstruction	20.16400	6.971671	2.892276	0.097176

Note that the p-value is greater than 0.05, indicating insignificance.

Table 23

	Levene's Test for Homogeneity of Variances (Thesis Datafile.sta) Effect: Group Degrees of freedom for all F's: 1, 38			
	MS Effect	MS Error	F	p
Attention	2.450250	1.718250	1.426015	0.239817

Note that the p-value is greater than 0.05, indicating insignificance.

Table 24

	Levene's Test for Homogeneity of Variances (Thesis Datafile.sta) Effect: Group Degrees of freedom for all F's: 1, 38			
	MS Effect	MS Error	F	p
Psychomotor Speed	28.90000	33.85789	0.853568	0.361375

Note that the p-value is greater than 0.05, indicating insignificance.

Table 25

	Levene's Test for Homogeneity of Variances (Thesis Datafile.sta) Effect: Group Degrees of freedom for all F's: 1, 38			
	MS Effect	MS Error	F	p
Executive Functioning	4.225000	9.013158	0.468759	0.497714

Note that the p-value is greater than 0.05, indicating insignificance.

Table 26

	Levene's Test for Homogeneity of Variances (Thesis Datafile.sta) Effect: Group Degrees of freedom for all F's: 1, 38			
	MS Effect	MS Error	F	p
Depression	1.024000	3.684211	0.277943	0.601117

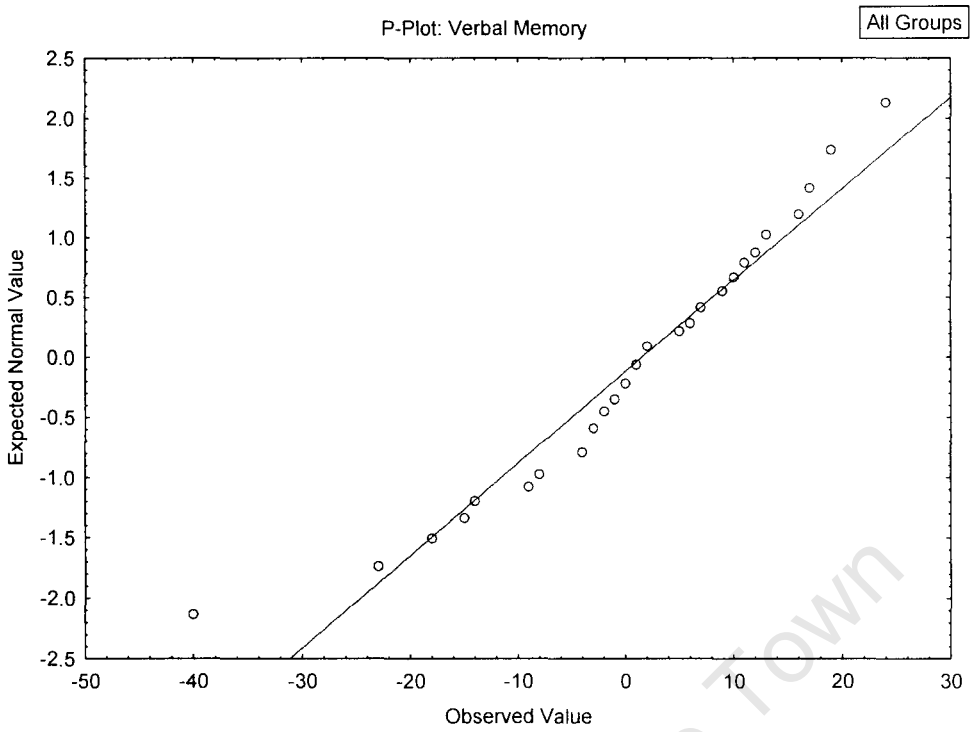
Note that the p-value is greater than 0.05, indicating insignificance.

Table 27

	Levene's Test for Homogeneity of Variances (Thesis Datafile.sta) Effect: Group Degrees of freedom for all F's: 1, 38			
	MS Effect	MS Error	F	p
Anxiety	0.841000	9.686053	0.086826	0.769856

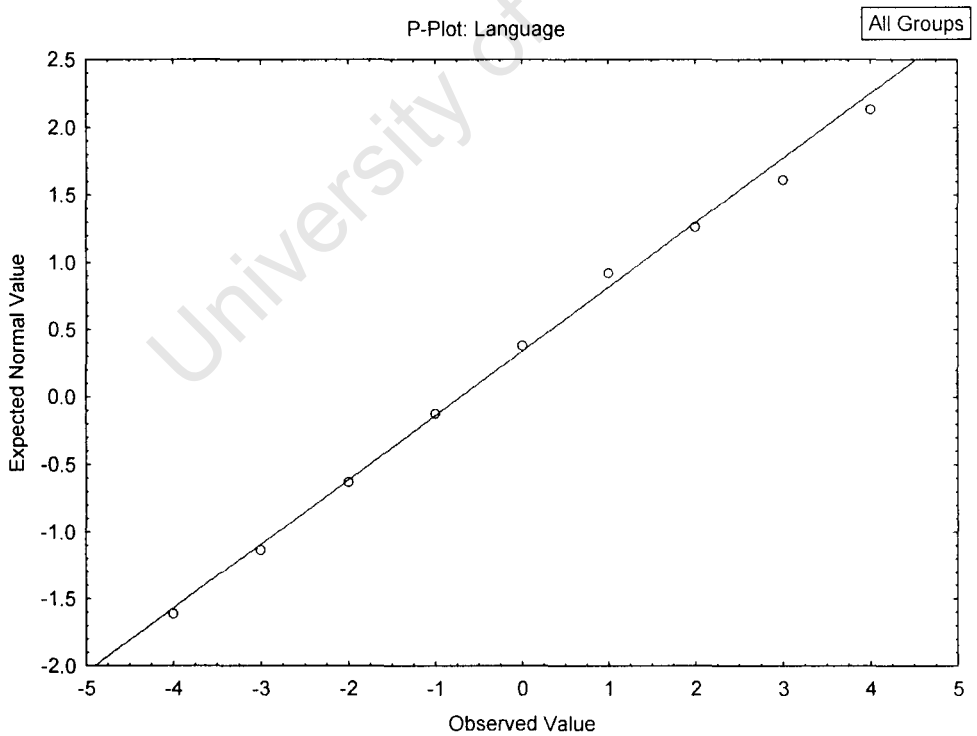
Note that the p-value is greater than 0.05, indicating insignificance.

Figure 2



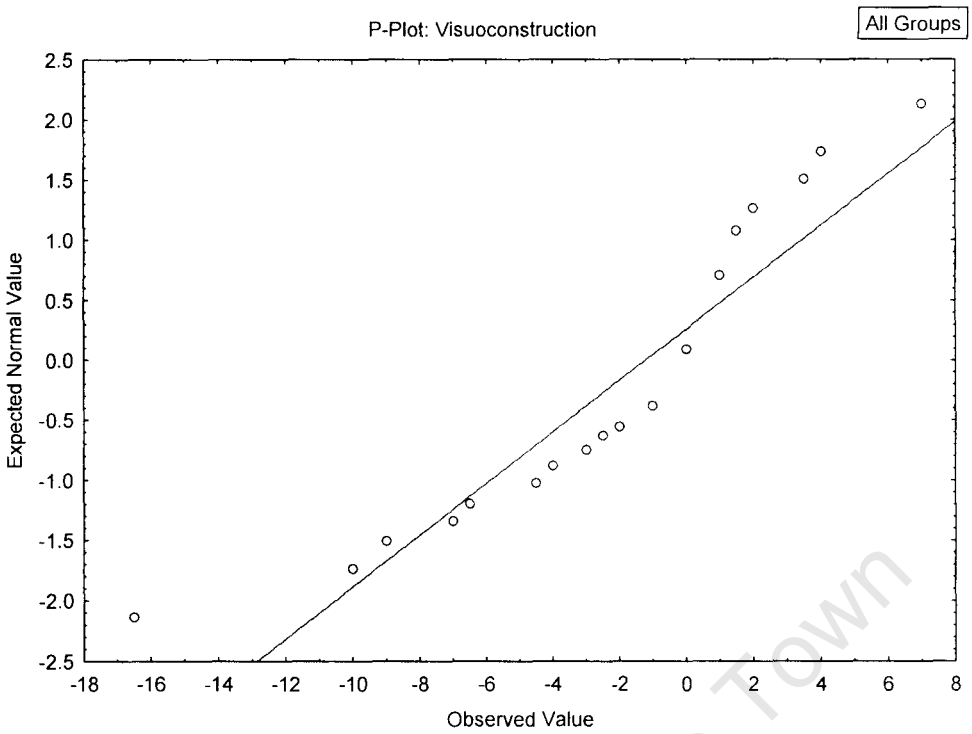
Note that the residuals are scattered closely around the regression line, indicating normality.

Figure 3



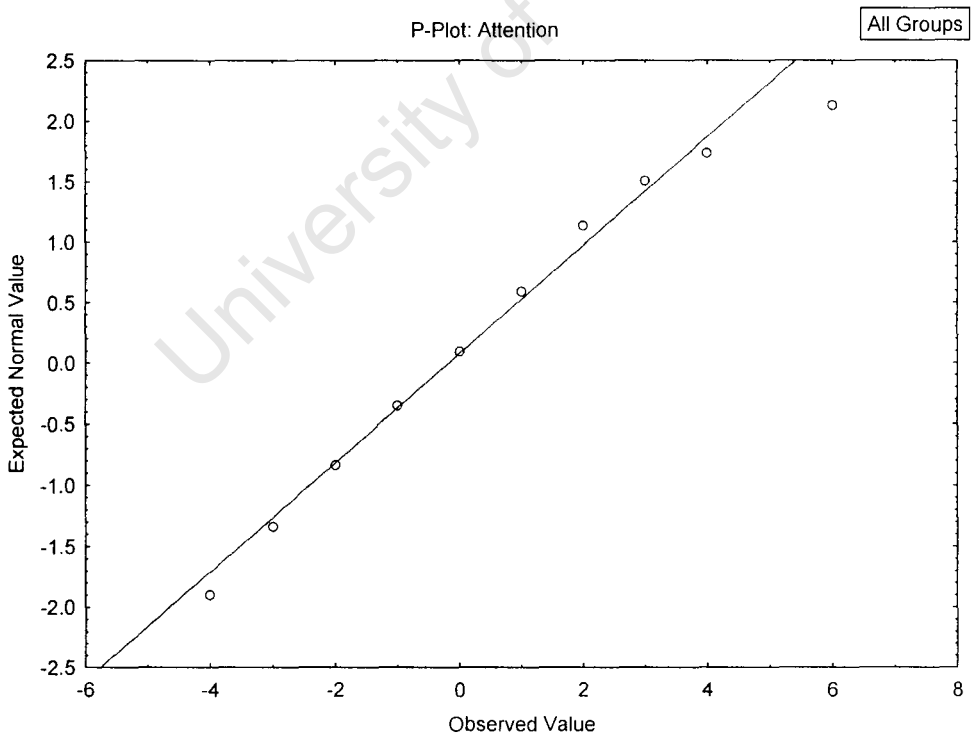
Note that the residuals are scattered closely around the regression line, indicating normality.

Figure 4



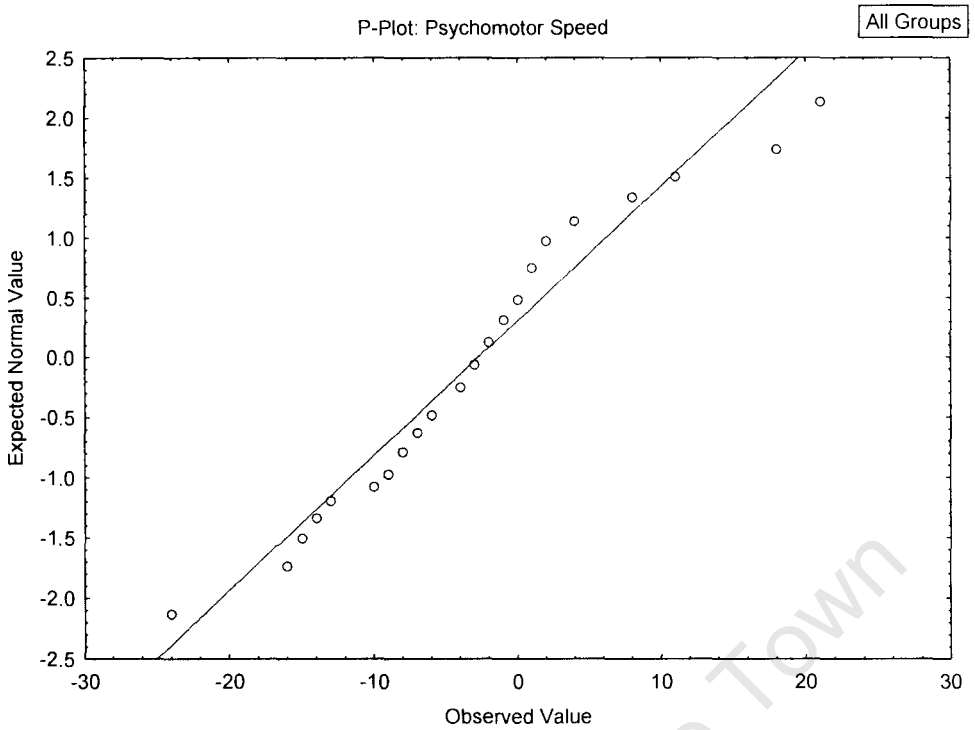
Note that the residuals are scattered closely around the regression line, indicating normality.

Figure 5



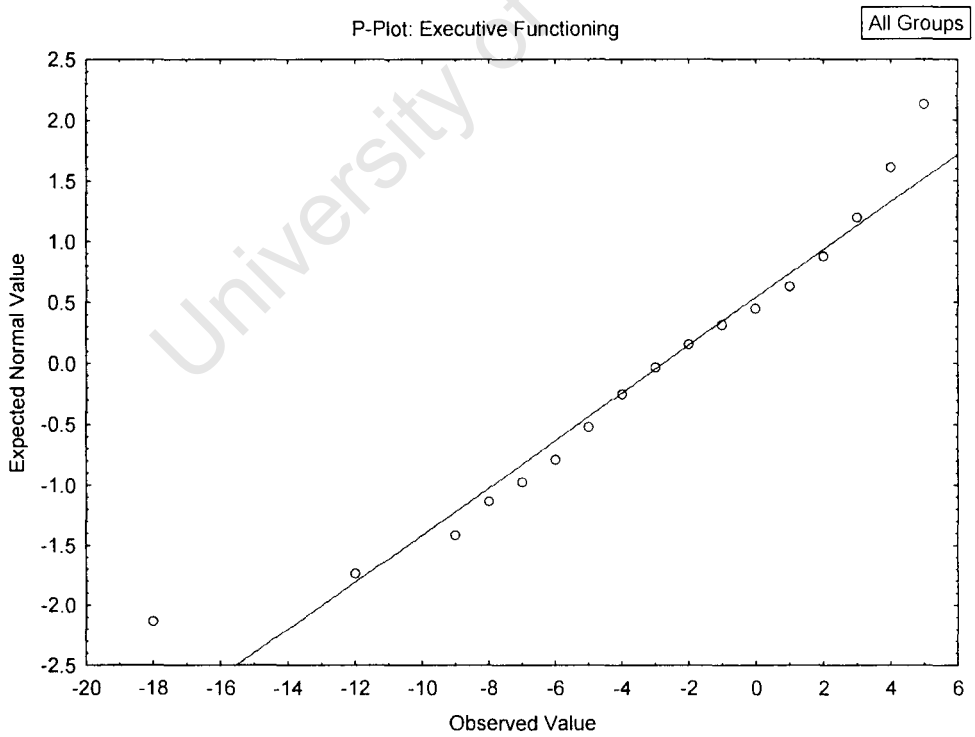
Note that the residuals are scattered closely around the regression line, indicating normality.

Figure 6



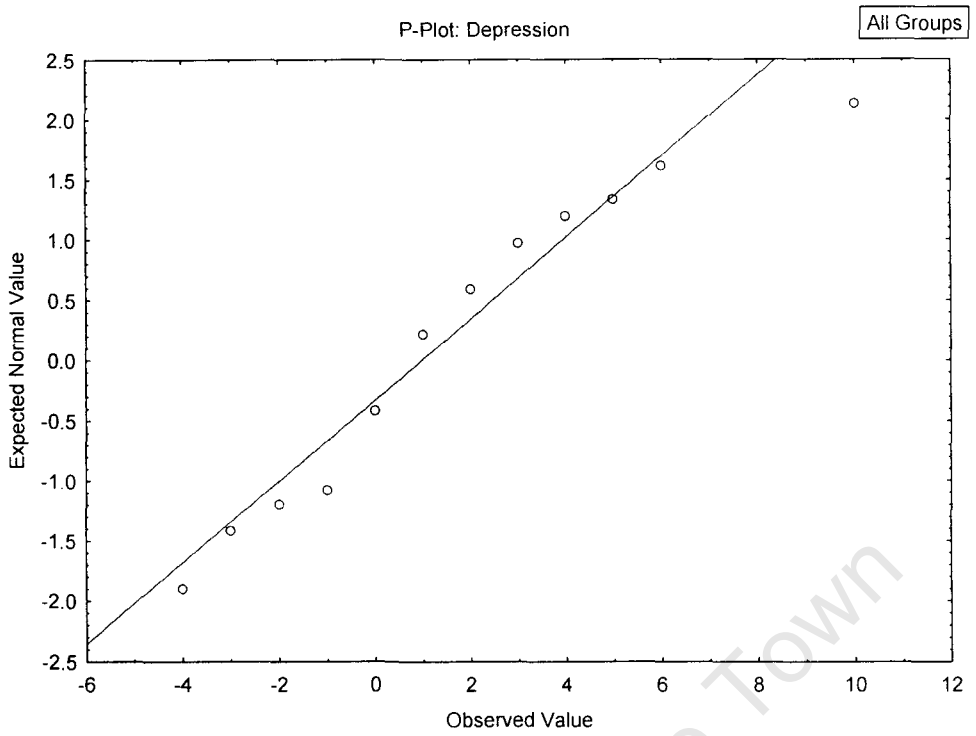
Note that the residuals are scattered closely around the regression line, indicating normality.

Figure 7



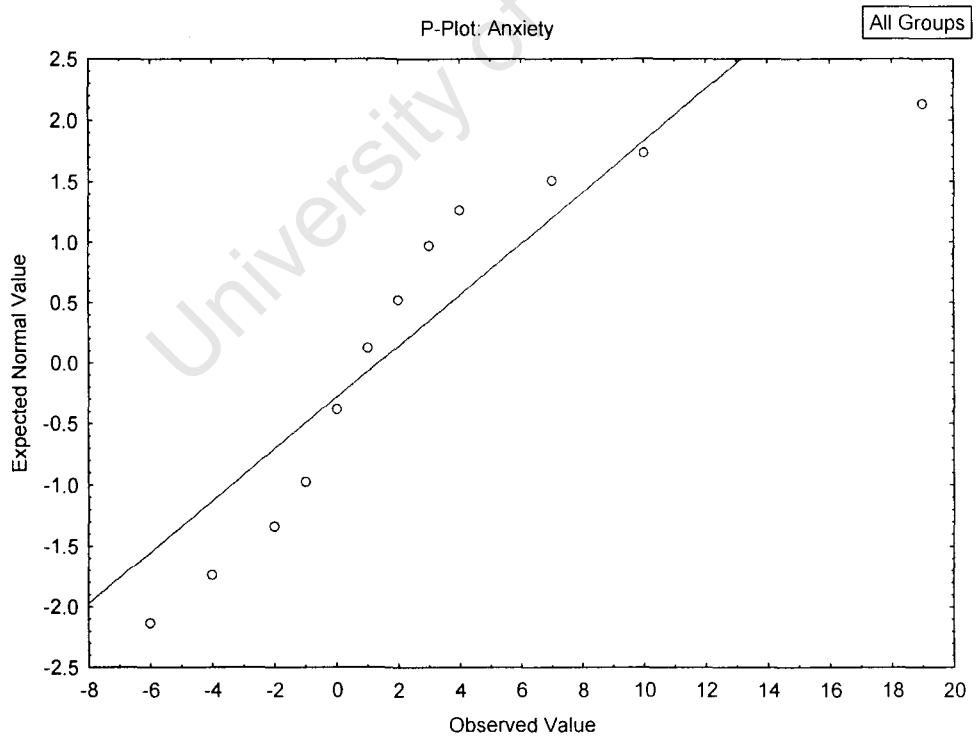
Note that the residuals are scattered closely around the regression line, indicating normality.

Figure 8



Note that the residuals are scattered closely around the regression line, indicating normality.

Figure 9



Note that the residuals are scattered closely around the regression line, indicating normality.