

The copyright of this thesis vests in the author. No quotation from it or information derived from it is to be published without full acknowledgement of the source. The thesis is to be used for private study or non-commercial research purposes only.

Published by the University of Cape Town (UCT) in terms of the non-exclusive license granted to UCT by the author.

**Cognitive outcome of aneurysmal subarachnoid
haemorrhage after clipping or coiling: A comparative post
intervention study in a hospital population.**

by

Eleni Pantelis (PNTELE001)

A minor dissertation in partial fulfilment of the requirements for the award

of

Degree of Master of Arts in Psychological Research

Department of Psychology

University of Cape Town

2005

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:

14/02/05

Acknowledgements

The following persons are sincerely thanked for their support and contribution.

Prof. Mark Solms

Dr. Allan Taylor

Dr. David Le Feuvre

Efstratios Pantelis

Ekaterina Fotopoulos

Daniella Mark

Helen Kinnear

Ross Balchin

Dimitri Koukoulis

University of Cape Town

Contents

	Page
1. Acknowledgements	2
2. Contents	3
3. List of tables	5
4. Abstract	6
5. Introduction	7
Treatment Options	7
Surgical Intervention: The risks and complications of clipping	8
Endovascular Intervention: The benefits and risks of coiling	12
Cognitive and Emotional Deficits: Limitations of gross measures of outcome	13
Comparative Studies that include neuropsychological assessment	16
Prognostic factors related to SAH that could effect neuropsychological outcome	17
6. Aim of the study	20
7. Method	21
Study Design	21
Sample – SAH Participants	24
Sample – Control Participants	29
Procedure	31
Neuropsychological Testing	31
Quality of Life Assessment	32
Comparability of participant characteristics	34
Comparability of treatment groups with respect to prognostic clinical variables	35
Data Analysis	37

8. Results	
Neuropsychological Data	37
Quality of Life Assessment Data	41
9. Discussion	43
10. Limitations	52
11. References	54
12. Appendix	
WFNS Grading of SAH	64
Glasgow Outcome Scale	64
Grading System of Fisher	64
Patient's Consent Form	65
Patient's Information Sheet	66
Neuropsychological Tests	67
Quality of Life Questionnaire	69

List of tables

	Page
Table 1 – Time from intervention to assessment	24
Table 2 – Exclusions from the study	26
Table 3 – Clinical data of patients	27
Table 4 – Treatment-related data of patients	28
Table 5 – Clinical data of control patients	30
Table 6 – ANOVA results for age, years of education and WART	35
Table 7 – Statistical results for prognostic clinical variables	36
Table 8 – Significant results for neuropsychological test variables	38
Table 9 – Post-hoc test results for significant test variables	39
Table 10 – Pre and post employment status of participants	41
Table 11 – Socioeconomic and psychosocial data	42

Abstract

Background: Subarachnoid haemorrhage secondary to ruptured cerebral aneurysm and clipping are associated with substantial morbidity and mortality. Despite favourable neurological outcomes, many patients report persistent cognitive and emotional deficits post intervention.

Objective: To compare cognitive and quality of life outcomes in patients with ruptured aneurysmal subarachnoid haemorrhage treated with surgical clipping or endovascular coiling.

Method: Twenty-four patients with aneurysmal subarachnoid haemorrhage treated by clipping or coiling were retrospectively assessed by use of a battery of cognitive tests and a quality of life questionnaire. All patients had favourable grades on admission, that is, WFNS ≤ 2 and favourable neurological grades on discharge, that is, GOS ≤ 2 . treated with surgical clipping or endovascular coiling. Patients in the two treatment groups were matched on age, years of education and on premorbid IQ. The two groups were further matched on time from intervention to assessment and number of treatments. The cognitive performance of the treatment groups was compared to hospitalised controls, matched for age, years of education and premorbid IQ.

Results: Comparison of cognitive outcome between the two groups indicated a trend towards poorer outcome in the surgical group which achieved significance on six test measures. There were no significant differences with respect to the quality of life measure.

Conclusion: Patients surviving aneurysmal subarachnoid haemorrhage are likely to suffer from a 'subarachnoid-induced encephalopathy' which appears to be more aggravated by the invasive nature of surgery, compared to endovascular coiling, as demonstrated by the poorer cognitive performance of the clipping patients.

Introduction

Subarachnoid haemorrhage (SAH) accounts for 5-10% of all strokes and affects most people in the fifth decade of their lives – at the peak of their productivity. Mild to moderate dysfunction across multiple cognitive domains is characteristic and is attributed to diffuse disruption of brain cortices caused by “ictal intracranial circulatory arrest and exposure of the brain to subarachnoid blood” (Kreiter et al., 2002, p.200). There may also be areas of localised dysfunction as a consequence of vasospasm (i.e. arterial narrowing) and ischemia (or infarction) that can develop following SAH.

Patients with ruptured aneurysm should be treated as soon as possible after their haemorrhage to prevent secondary complications such as rebleeding and secondary ischemia. The risk of second haemorrhage within the first three weeks is approximately 40% when the aneurysm has not been treated (Kahara, Seppanen, Kuurne, & Laasonen, 1999). The principal goal of treatment of cerebral aneurysms is thus prevention of further rupture by occlusion of the aneurysm from the arterial circulation.

Treatment Options

Since the 1960's, surgical clipping has been the predominant treatment of both ruptured and unruptured cerebral aneurysms (Brilstra, Algra, Rinkel, Tulleken & van Gijn, 2002). Clipping entails the direct exposure of the aneurysm, the parent vessel(s) and surrounding structures. The aneurysm is then secured by placing a metallic clip along the neck. Although occlusion is usually achieved, postoperative aneurysm remnants can occur in 4% to 8% of patients. These remnants can regrow and lead to rebleeding and compressive symptoms (Rabinstein & Nichols, 2002). Coiling or endovascular therapy (EVT) is increasingly gaining popularity as an alternative treatment for intracranial aneurysms as it offers the likelihood of reducing the risk of further rupture without the need for craniotomy. Access to the aneurysm is gained by using a microcatheter and the sac is filled with coils until the lumen has been totally occluded.

In terms of comparative long-term efficacy, the unequivocal dominance of one procedure over the other has not yet been established, evidenced by the variability of opinion prevalent in the literature. Some reports claim that both short and mid-term outcomes of the two procedures are comparable (Dovey et al., 2001; Koivisto et al., 2000; Kremer et al., 2002; Raymond & Roy, 1997 & Vanninen, Koivisto, Saari, Hernesniemi & Vapalahti, 1999). Others clearly delineate the comparative advantages of coiling over clipping (Brilstra et al., 2004; Chan, Ho & Poon, 2002; Hadjivassiliou et al., 2001 & Molyneux et al., 2002).

Surgical Intervention: The Risks and Complications of Clipping

SAH secondary to ruptured cerebral aneurysm and clipping are associated with substantial morbidity and mortality (Bornstein, Weir, Petruk & Disney, 1987; Bryan, Rigamonti & Mathis, 1997; Hadjivassiliou et al., 2001; Kreiter et al., 2002; Molyneux et al., 2002; Ogden, Mee & Henning, 1990; Ogungbo, Gregson, Blackburn & Mendelow, 2001; Rabinstein & Nichols, 2002 & Tateshima et al., 2000) with only 30% of patients regaining their pre-morbid neurological status following surgical treatment (Dovey et al., 2001). On the one hand, surgery reduces the risk of further rupture but on the other hand, some risks may be increased by procedural complications (Brilstra et al., 2002). Between 5 and 25% of the morbidity after SAH can be attributed to surgical complications such as intraoperative aneurysm rupture, occlusion of a major vessel that could lead to cerebral infarction and stroke, incompletely obliterated aneurysms, surgical contusion, intracerebral haemorrhage, meningitis and wound infection (Hutchinson, Power, Tripathi & Kirkpatrick, 2000 & Le Roux, Elliot, Newell, Grady & Winn, 1996). Factors that can influence the risk of procedure-related complications are inexperience or poor surgical technique (Brilstra et al., 2002; Le Roux et al., 1996 & Raftopoulos et al., 2003), aneurysms location and aneurysm size (Le Roux et al., 1996).

More specifically, surgery with its associated retraction, dissection and stretching accompanying clip placement can damage perforating arteries (Chiang, Gailloud, Murphy, Rigamonti & Tamargo, 2002 & Tateshima et al., 2000). Furthermore, oedema following

SAH can cause brain tissue to be more susceptible to damage through manipulation during acute surgery. MRI (Magnetic Resonance Imaging) investigations have shown lesions produced by retractor pressure to the basal areas of the frontal and temporal lobes (Kivisaari, Salonen & Ohman, 2000), and parenchymal damage in the region of the Sylvian fissure (Romner et al., 1989). The surgical procedures and events in surgery identified as having detrimental neuropsychological effects are damage to the small perforating arteries that originate from the anterior communicating artery (ACoA), resection of the gyrus rectus and the temporary clipping of vessels (Vilkkii, Holst, Ohman, Servo & Heiskanen, 1989). Furthermore, in patients with pathological SPECT (Single Photon Emission Computerised Tomography) findings following surgery, the location of reduced regional CBF (Cerebral Blood Flow) correlated with the location of the ruptured aneurysm and/or side of surgical approach. Various possible causes of reduced blood flow in these areas have been identified: (1) the SAH itself can cause decreased neuronal activity and disturbances in flow patterns, (2) during surgery, at least one retractor is used to facilitate access, and because of differences in the extent of brain oedema between patients, the applied forces of the retractors to the brain parenchyma may differ substantially, (3) temporary clipping of the feeding arteries to the aneurysm, and (4) vasospasm located in the vicinity of the ruptured aneurysm may result in some local tissue damage (Säveland, Uski, Sjöholm, Sonesson & Brandt, 1996).

When examining the outcomes of surgical intervention, many studies have attempted to limit the confounding effects of the SAH itself by investigating the impact of surgery on unruptured aneurysms. Ohue et al. (2003) found decreased neuropsychological function in 40% of patients who had undergone surgery for unruptured aneurysms, particularly in those patients with aneurysms of the anterior circulation. The most sensitive test was one of frontal lobe functioning, namely, a test of immediate memory, supporting their argument that excessive retraction during surgery may cause unilateral or bilateral injury to the frontal lobes. Furthermore, they found that CBF in patients with neuropsychological deterioration after surgery was significantly reduced compared to those patients without neuropsychological deterioration. Fukunaga, Uchida, Hashimoto and Kawase (1999) also found a possible relationship between neuropsychological deterioration and reduced CBF

in their series of patients who had surgery for unruptured aneurysms. Once again, deterioration was particularly evident in patients with aneurysms of the anterior circulation and the authors attributed this to cerebral ischemia possibly resulting from greater retraction of the frontal lobes during operation. Brilstra et al. (2004) compared the quality of life of patients who were either clipped or coiled for unruptured aneurysm. They found that at one year post-intervention, the recovery of function and quality of life had occurred fully for those patients who had been coiled but that recovery was not satisfactorily complete for those who had been clipped. Specifically, 12% of those clipped had a permanent neurological deficit and their quality of life had not returned to baseline levels. Johnston et al. (2000) found that following intervention for unruptured aneurysms, greater rates of early and persistent disability, more procedure-related complications and adverse events such as cranial neuropathy and cortical deficit were more common in clipping than coiling patients. The clipping patients experienced longer delays in return to function and were more likely to report persistent new symptoms such as changes in self- image, appearance, concentration and memory. Evidence of sub-optimal neurological grades experienced by surgical patients with unruptured aneurysms has also been proffered by Raaymakers (2000). Furthermore, the International Study of Unruptured Intracranial Aneurysms concluded that clipping was associated with greater immediate risks compared with coiling. Poorer outcomes were related to age, aneurysm diameter greater than 12mm, aneurysm location in the posterior circulation, previous ischemic cerebrovascular disease and aneurysm symptoms other than rupture (Wiebers, 2003).

On the other hand, however, Tuffiash, Tamargo and Hills (2003) found no significant change between preoperative and postoperative neuropsychological scores for patients clipped for unruptured aneurysms. In fact Raftopoulos et al. (2003) concluded that clipping may lead to better results than coiling in the case of unruptured intracranial aneurysms. Clipping resulted in total occlusion in 93% of cases versus 62% for coiling. Coiling was also associated with three times as many transient and asymptomatic events as clipping.

As previously stated, opinions on the relative pros and cons of clipping are diverse. There are those who conclude that there is reason to doubt the view that marked cognitive

impairment after clipping is common, unless there have been known complications associated with the surgery (Hillis, Anderson, Sampath & Rigamonti, 2000; Hutter & Gilsbach, 1993; Hutter, Gilsbach & Kreitschmann, 1995; Maurice-Williams, Willison & Hatfield, 1991, Ogden et al., 1990 & Tuffiash et al., 2003). There is evidence to suggest that excellent outcomes after surgery are achievable and that patients are able to recover fully both neuropsychologically and emotionally (Germano et al., 1997 & McKenna, Willison, Lowe & Neil-Dwyer, 1989). In this respect, Maurice-Williams et al. (1991) psychometrically assessed 27 patients undergoing surgery for ruptured aneurysms. At one year post surgery, only two of the 27 patients showed any psychological impairment on testing. They argued that these minor symptoms could have reflected minimal cerebral damage, too slight to be demonstrated even on full neuropsychological testing. Alternatively, they could have reflected a degree of “psychological destabilisation” caused by enduring a major life-threatening illness requiring intracranial surgery. Similar results have been reported by Richardson (1991) who found that although clipping patients may demonstrate a small number of relatively specific cognitive deficits in the short term, in the longer term they are not left with any generalised cognitive impairment. In this regard Hillis et al. (2000) and Kreiter et al. (2002) argue that where neuropsychological deficits are present, they usually reflect a few very poor scores that lower group means. Furthermore, Vilkki et al. (1989) found that the only surgery related variable that exerted persistent adverse effects on health related quality of life (QoL) was the duration of temporary vessel clipping. However, these effects were minimal and secondary to the effects of the bleeding itself. Ogden et al. (1990) compared two groups, that is, an “aneurysm” group (who underwent clipping) and a “no-aneurysm” group (who did not undergo surgery) and found that there were no significant differences between these groups in terms of the number of signs of cognitive dysfunction.

Endovascular Intervention: The Benefits and Risks of Coiling

Coiling has continued to evolve as a viable alternative to conventional microneurosurgery. Accounts are very favourable, claiming that there are no complications directly related to coiling, that a high total aneurysmal occlusion percentage exists and that there are excellent clinical outcomes (Rabinstein & Nichols, 2002 & Thornton et al., 2002). Coiling carries a

lower morbidity rate (Kremer et al., 2002), and significantly reduces the risk of rebleeding (Friedman et al., 2003 & Gruber, Zimmermann, Tomsick, Byrne & Battersby, 1999). In fact, Molyneux et al. (2002) found that when compared to clipping, coiling improved a patient's chances of independent survival with an absolute risk reduction of 6.9%.

At first coiling was limited to aneurysms that were surgically difficult to treat but its use has subsequently become more widespread (van den Berg, Rinkel & Vandertop, 2003). Coiling is now considered to be the first treatment option for ruptured aneurysms associated with severe vasospasm (Murayama et al., 2003) and in the elderly (Birchall, Khangure, McAuliffe, Apsimon & Knuckey, 2001). Coiling is moreover considered preferential for aneurysms of certain locations, the surgical management of which is considered technically difficult because of the exposure needed for clipping. In particular, basilar tip aneurysms (Gruber et al., 1999; Lusseveld et al., 2000 & Tateshima et al., 2000) and posterior circulation aneurysms (Johnston et al., 2000 & Lempert et al., 2000). Conversely, however, Ogilvy, Hoh, Singer and Putman (2002) compared outcomes in the treatment of posterior circulation aneurysms by use of clipping or coiling and found in favour of higher occlusion rates for clipping.

It has further been reported that coiling is the preferred treatment option in patients whose neurological condition is impaired following SAH (Brilstra, Rinkel, van der Graaf, van Rooij & Algra, 1999; Dovey et al., 2001 & Tateshima et al., 2000). Surgery is often difficult in these cases because of cerebral oedema and the associated increased intracranial pressure (van Loon et al., 2002). It has been argued that coiling is beneficial in this instance because it allows for early occlusion of the aneurysm and does not cause any additional damage to the brain. Increased intracranial pressure and vasospasm can therefore be treated timeously (van Loon et al., 2002).

Hutchinson et al. (2000) and Le Roux et al. (1996), however, claim that surgery may no longer be associated with more complications in poor versus good grade patients. With the exception of severe oedema, the risk of surgical complication is similar for poor and good grade patients.

Important treatment related complications related to coiling are perforation of the aneurysm caused by the coils, partial revascularisation in the aneurysm (Cloft & Kallmes, 2002), ischemic stroke and thromboembolic events (Derdeyn et al., 2002).

What is apparent from the preceding account is confirmation of the variance of opinion that exists on the relative outcomes of clipping and coiling. In light of this, a closer investigation of the criteria used to determine relative effects is necessary.

Cognitive and Emotional Deficits: Limitations of Gross Measures of Outcome

When evaluating the relative benefits of each procedure, many studies make use of gross measures of assessing patient outcomes. Neurological outcome scales such as the Rankin (van Swieten, Koudstaal, Visser, Schouten & van Gijn, 1988) and Glasgow Outcome Scales (GOS) (Drake, 1988) are commonly used.

Formerly, preserved motor functioning was considered sufficient to attain independence in performing activities of daily living. Assessment has been focused mainly on survival and determining the presence of motor deficits (Berry, Jones, West & Brown, 1997 & Saciri & Kos, 2002). However, the fundamental limitations of a gross outcome scale as a global predictor of the effects of neurosurgical treatment have been clearly demonstrated (Beristain et al., 1989; Hutter & Gilsbach, 1993; Hutter et al., 1995 & Koivisto et al., 2000). Gross outcome scale such as the GOS do not measure the more subtle impairments in neurological functioning such as cognitive deficits, behavioural changes and social and emotional dysfunction (Beristain et al., 1996). These changes may often act as a hindrance to the resumption of normal life. Moreover, these changes often occur in patients with no noticeable neurological abnormalities and who are otherwise regarded as coping well after intervention (Maurice-Williams et al., 1991). Overall data suggests that 20% of patients have subtle cognitive impairment, even at nine months following surgery for aneurysmal SAH. Neuropsychological assessment has revealed that 62% of patients with a GOS scores of 1 (i.e. good recovery) may be left with cognitive impairment following surgical

intervention (Powell, Kitchen, Heslin & Greenwood, 2003). Ogden, Utley and Mee (1997) found that cognitive deficits were still present in patients one to seven years after surgery. A diffuse “SAH-induced encephalopathy”, has been described in patients following aneurysm surgery (Ljunggren, Sonesson, Säveland & Brandt, 1985). Verbal and nonverbal memory disturbances are the most sensitive (Ogden et al., 1990 & Sonesson, Ljunggren, Säveland & Brandt, 1987) and prevail among patients with slight or moderate motor impairment (Ljunggren et al., 1985). Patients with severe cognitive disturbances also present with memory impairments but additionally have difficulties with higher-order executive functions (Bornstein et al., 1987, Ljunggren et al., 1985 & Tidswell, Dias, Sagar, Mayes & Battersby, 1995) such as cognitive flexibility and verbal efficiency (Vilkki, Holst, Ohman, Servo & Heiskanen, 1990), planning, attention, concentration, cognitive speed (Hutter & Gilsbach, 1993) and concept formation (Ljunggren et al., 1985). Ogden, Mee and Henning (1993) report that the most persistent deficits are evident on tests that require sustained attention, psychomotor speed, mental flexibility and complex visuospatial planning and construction, that is, deficits consistent with diffuse brain damage.

Neuropsychological testing is therefore essential in providing an objective measure of cognitive outcome. However, if used alone, disabling behavioural changes in daily life, not gauged by formal standardised testing, can be underestimated. The mere presence or absence of cognitive deficits does not give insight into the patient’s subjective feelings of physical, emotional and social well-being (Berry et al., 1997). A more comprehensive approach is therefore necessary to adequately address the issue of outcome. In conjunction with neuropsychological testing, a patient’s quality of life (QoL) should be investigated. QoL is an important outcome variable because it is an indicator of the patient’s overall ability to cope with daily life which has often more significance than performance on a battery of neuropsychological tests (Hütter, Kreitschmann-Andermahr & Gilsbach, 2001). Post SAH patients frequently complain of lack of initiative (Hütter et al., 2001), fatigue (Buchanan, Elias & Goplen, 2000 & Hütter et al., 2001), irritability (Hütter et al., 2001), and personality changes (Buchanan et al., 2000 & Hütter et al., 2001), even in the absence of any neurological deficit. Other symptoms that have been reported are high rates of

anxiety and depression (Beristain et al., 1996), adverse changes in employment, energy levels, tolerance of mild stressors, pursuit of leisure activities and social and sexual relations (Buchanan et al., 2000).

In this regard, Säveland et al. (1986) neuropsychologically assessed 78 patients more than a year post SAH and found that when cognitive and psychosocial impairment were accounted for, those patients previously rated as having a 'good' outcome dropped from 41% to 33%. Similar findings were reported by Beristain et al. (1996). Thirteen of their 20 patients undergoing surgery for intracranial aneurysms were classified as having good recovery on discharge (i.e. GOS=1). However, at six month follow-up, comprehensive neuropsychiatric assessment revealed that the actual morbidity in their sample (n=18) was much higher. Hop, Rinkel, Algra and van Gijn (1998) found that only those patients who had no symptoms at all (i.e. Rankin grade = 0) reported no reduction in QoL. Patients who had symptoms, but were still functioning independently (i.e. Rankin grades 1 to 3) and who are usually regarded as having had a good outcome often reported reductions in QoL on both the physical and psychosocial domains. Likewise, Ropper and Zervas (1984) found that 25% of good neurological grade patients reported emotional or psychosocial disturbances that interfered with their daily lives.

Thus despite 'good' neurological recovery from SAH, many patients continue to display both personality changes and cognitive dysfunction (Berry et al., 1997; DeSantis et al., 1989; Germano et al., 1997; Hadjivassiliou et al., 2001; Maurice-Williams et al., 1991; Ogden et al., 1990; Powell, Kitchen, Heslin & Greenwood, 2002; Saciri & Kos, 2002; Säveland et al., 1986 & Stenhouse, Knight, Longmore & Bishara, 1991).

In light of the overwhelming evidence that cognitive and emotional impairments are manifested by a large proportion of patients following surgery for aneurysmal SAH, the emphasis of what constitutes a 'good' outcome must extend beyond the purely neurological conception of recovery.

Comparative Studies that Include Neuropsychological Assessment

Attempts to assess the cognitive effects of clipping have previously been hindered by the lack of an appropriate control group. Coiling now provides an opportunity to assess the relative contribution of either procedure towards cognitive outcome (Hadjivassiliou et al., 2001). A few studies have to date explored the relative effects of each treatment on cognition.

Koivisto et al. (2000) concluded that the endovascular treatment of ruptured aneurysms resulted in clinical and neuropsychological outcomes equivalent to that of surgical clipping; 79% of EVT versus 75% of surgical patients had good or moderate recovery (as measured by GOS). No significant neuropsychological differences were detected between the two treatment groups. The similarity in patterns of impairment between these groups was attributed to the severity of impairment caused by the SAH itself.

Kahara et al. (1999) compared outcomes of 44 coiled and 106 clipped patients, 1-4 years post intervention by means of a postal questionnaire that assessed post-procedural physical, mental and social recovery. They found a trend towards better outcome in the coiling group but the difference was not statistically significant.

In the Hadjivassiliou et al. (2001) study, preliminary evidence was put forward that clipping may result in more frontotemporal brain damage than coiling and that this could possibly account for the additional cognitive deficits apparent in the surgical group. There was a trend towards favourable cognitive outcome for the coiling group with statistical significance being achieved in four tests, namely: the vocabulary subtest of the WAIS-R (Wechsler Adult Intelligence Scale- Revised) - a measure of current IQ; recall of a drawing of a complex figure – a measure of visual memory; semantic (category) fluency – a test of executive function and the extradimensional shift stage of the intradimensional/extradimensional shift test of the CANTAB (Cambridge Automated Neuropsychological Test Battery) – also a test of executive function.

Chan, Ho and Poon (2002) compared neuropsychological outcome (at least 1 year post intervention) of a group of 18 patients who underwent clipping or coiling of ruptured ACoA (anterior communicating artery) aneurysms. The performance of the two groups was not significantly different from controls on visual memory, language and visual perception. However, performance between the groups was significantly different on verbal memory, executive function and motor control. Performance of the clipping group was significantly poorer than the coiling group on verbal memory and executive function. None of the coiling patients demonstrated both severe memory deficits and executive dysfunction while 33% of the clipping patients demonstrated both.

In light of the detrimental effects that a SAH itself can have on cognition, it is important to consider the potential impact that the initial bleed, its consequences and other related factors, other than physical intervention, can have on cognitive outcome.

Prognostic Factors Related to SAH that Could Effect Neuropsychological Outcome

It has not yet been possible to identify the prognostic features of SAH that consistently predict whether a patient will manifest cognitive impairments (Powell et al., 2002). Reports on the exact nature and effects of these features are varied (De Santis et al., 1998) and remain a controversial issue (Ljunggren et al., 1985). The following prognostic factors have been identified in the literature as potentially having an impact on cognitive performance:

Age of the Patient:

Several studies have found that age (usually over the age of 65) is a significant predictor of outcome (Bornstein et al., 1987; Brilstra et al., 2002; Hutter & Gilsbach, 1993 & Wiebers, 1998). Others however have found that advanced age is not associated with adverse outcomes (Bryan et al., 1997; Richardson, 1991; Tateshima et al., 2000 & Tidswell et al., 1995).

Location of Aneurysm:

There are reports that claim that there is no systematic relationship between location of the ruptured aneurysm and nature and severity of cognitive impairment (DeSantis et al., 1998; Hillis et al., 2000; Hutter & Gilsbach, 1993; Bornstein et al., 1987; Ogden, Mee & Henning, 1993; Richardson, 1991; Romner et al., 1998; Sonesson et al., 1987; Tateshima et al., 2000 & Tidswell et al., 1995). Others have found that cognitive outcome is directly related to site of aneurysm. In particular, patients with aneurysms of the left MCA (middle cerebral artery) fair worse cognitively (Fobe, Haddad & de Douza, 1999) and complain of significantly more impairments in social contact and communication (Vilkki et al., 1989). In addition, an “Anterior Communicating Artery Syndrome” has been described after rupture with symptoms of memory deficits, frontal lobe dysfunction, confabulation, decreased initiative, perseveration and personality change (Bornstein et al., 1997; Chan et al., 2002 & Stenhouse et al., 1991). Better cognitive outcomes have been described for patients with posterior circulation aneurysms possibly because of less SAH blood coming in contact with the cortical surface of the brain (Kreiter et al., 2000).

Gender:

It is generally well accepted that gender does not have any significant influence on post-operative levels of cognitive impairment (Hutter & Gilsbach, 1993 & Ogden et al., 1993).

Clinical Grade on Admission:

The general consensus is that although poor initial clinical grade predicts poor outcome, initial grading alone is insufficient to reliably predict outcome (Bryan et al., 1997; Hutter & Gilsbach, 1993; Tateshima et al., 2000 & Tidswell et al., 1995). However, there are some studies that ascribe post-operative cognitive outcome directly to clinical grade on admission (Fobe et al., 1999; Kreiter et al., 2002 & Richardson, 1991).

Impact of initial bleed:

Many studies maintain that the lasting disturbances in cognition are primarily due to the impact of the initial SAH (Berry et al., 1997; Bryan et al., 1997; Fobe et al., 1999; Hadjivassiliou et al., 2001; Hutter & Gilsbach, 1993; Koivisto et al., 2000; Ohman, Servo

& Heiskanen, 1991; Proust, Hannequin, Langlois, Freger & Creissard, 1995; Roos et al., 2000 & Sonesson et al., 1987). There are reports, however, that have shown that there is no evident correlation between the distribution of blood on CT and occurrence and severity of neuropsychological deficits (Germano et al., 1998; Ogden et al., 1993; Romner et al., 1989 & Tidswell et al., 1995).

Complications :

Approximately 25% of patients develop clinical evidence of ischemia/infarction, which can occur any time between 24 hours and several weeks either before or after operation (Lindsay, Bone & Callander, 1991). Cerebral ischemia has been shown to account for substantial permanent deficits following SAH (Hillis et al., 2000; Ohman et al., 1991; Proust et al., 1995 & Vilkki et al., 1989). Contributing factors are vasospasm (i.e. arterial narrowing) and hydrocephalus. Vasospasm is the most significant cause of mortality and morbidity in patients surviving SAH long enough to receive medical attention. Some reports claim that there is a relationship between vasospasm and post-operative cognitive outcome (Fobe et al., 1999 & Stenhouse et al., 1991). Others have failed to support this relationship (Hillis et al., 2002; Hutter & Gilsbach, 1993; Ogden et al., 1993 & Richardson, 1991). With respect to treatment-related incidence of symptomatic vasospasm and ischemic infarction, Dehdashti, Mermillod, Rufenacht, Reverdin & de Tribolet (2004) found comparable rates between groups of patients that were clipped or coiled. Hydrocephalus can occur in approximately 20% of patients (Lindsay et al., 1991) and has been related to post-operative memory deficits (Ogden et al., 1993 & Hillis et al., 2000). Kreiter et al. (2002), however, found that cognitive outcome at three months was unrelated to hydrocephalus. Sethi, Moore, Dervin, Clifton & MacSweeney (2000) found that the type of treatment, whether clipping or coiling, did not significantly affect the development of hydrocephalus.

Clinical Grade at Discharge:

Ogden et al. (1993) argue that clinical grade at discharge (GOS) is an effective predictor of impairment since it takes into account both the condition of the patient after recovery from “complications of SAH as well as the severity of the initial hemorrhage” (p.574).

Timing of Surgery:

The timing of surgery, that is, early (less than 72 hours) as opposed to late intervention is a particularly controversial issue. Early treatment is usually recommended because it reduces the risk of rebleeding but delayed surgery has also been found to be related to favourable outcomes especially in those patients with a very poor initial clinical grade (Bryan et al., 1997). DeSantis et al. (1989) and DeSantis et al. (1998) found that patients operated on later than ten days following SAH had a worse prognosis than early or intermediate intervention. Romner et al. (1989) and Ohman et al. (1991) however, found that patients who were operated on within less than 72 hours following rupture had more permanent deficits. Other studies again have reported no significant differences on cognitive impairment between patients subjected to early versus late intervention (Hadjivassiliou et al., 2001 & Sonesson et al., 1987).

Aim of the Study

There are clearly many facets to clinical outcome. It is apparent from the preceding account that gross physical measures cannot begin to delineate the difficulties and obstacles that lie beneath an outcome of slight, moderate or severe disability. When the possibility exists that a patient's working capacity will be reduced or quality of life compromised despite no obvious neurological deficits, then a neurological diagnosis of 'favourable' is essentially devoid of any true relevance beyond the physical. Any study that attempts to compare the outcomes of clipping and coiling needs to consider not only the functional (i.e. physical), but also the cognitive and emotional aspects of outcome.

As previously stated, it is well documented that aneurysm surgery is not benign in terms of producing cognitive deficits and that there are many studies that claim that when compared to clipping, coiling patients have good outcomes. However, while there is abundant evidence on the benefits of EVT, the question remains to what extent does EVT render surgery undesirable with respect to cognitive outcome. In light of such claims, in June 2003, the neuropsychology division of the UCT (University of Cape Town) Psychology and GSH (Groote Schuur Hospital) Neurology departments, was approached by the GSH

neurosurgeons to investigate the relative impact of both procedures on the cognitive and emotional sequelae of intervention.

Traditionally, a neurosurgeon's decision to clip or coil a ruptured intracranial aneurysm is primarily dictated by the clinical features of the aneurysm, namely, its size and location. The purpose of the present study is thus to give a neuropsychological perspective on a neurosurgical decision. In other words, we needed to answer a specific question about coiling which is: "Just how good is a good outcome and from whose perspective?"

Method

Study Design

This was a retrospective study of 24 patients with aneurysmal SAH, recruited on a voluntary basis from the neurosurgical unit of GSH. The presence of SAH was classified as 'definite' when there were positive findings on CT and lumbar puncture (LP), or 'probable' when patients presented only with symptoms, such as cranial nerve deficits (Wiebers, 2003). The following information was obtained from the patient's medical records: age, date of onset of SAH, clinical presentation, CT scan report, WFNS score, previous medical history, GOS score, treatment type and treatment complications. Twelve patients had their aneurysms repaired by clipping and 12 were treated with coiling. All 24 patients completed a range of neuropsychological assessments and semi-structured interviews were conducted with 21 patients in order to ascertain the level of psychosocial functioning post intervention.

A random trial study would have been the preferential experimental design to assess the effects of treatment but due to the ethical consideration of patient care, this was not possible. Thus a considerable effort was made to match the two existing treatment groups according to a predefined set of factors, related to pre-, and postoperative periods. The purpose of matching the groups was to minimise any potential differences in pre- and postoperative prognostic factors related to the SAH itself and in so doing isolating the effects of treatment modality. However, given the numerous clinical factors identified in

the literature that could potentially have a prognostic impact, it was not possible to match the groups on all these within the specified time period of this study. The extent of matching was further restricted by our limited sample population because all participants were recruited from a single neurosurgical unit. The reason for this was the requirement of standardisation with respect to uniformity of procedure and professional expertise.

The following prognostic factors were selected for matching the two groups:

- (i) World Federation of Neurologic Surgeons (WFNS) grading of SAH (Greenberg, 1994). (Please see Appendix 1).
- (ii) Age
- (iii) Years of education
- (iv) Estimated Premorbid IQ
- (v) Number of treatments (single or multiple)
- (vi) Time from intervention to assessment (months)
- (vii) Clinical grade at discharge – Glasgow Outcome Scale. (Please see Appendix 2).

WFNS grade on admission was selected because it is generally accepted that admission grade correlates well with final outcome (Fobe et al., 1999; Kreiter et al., 2002; Lindsay et al., 1991 & Richardson, 1991). GOS was selected because as previously stated it focuses on the condition of the patient after they have recovered from the complications of SAH and the severity of the initial bleed (Ogden et al., 1993). Age, years of education, estimated premorbid IQ, ‘number of treatments’ and ‘time from intervention to assessment’ were selected because of their potential impact on the cognitive performance of patients on formal neuropsychological testing. With respect to ‘time from intervention to assessment’, the average time lapse was 10.7 months for the clipping group and 9.3 months for the coiling group. Detailed investigation times are illustrated in Table 1. Five patients in total were tested less than six months following intervention and the possible interference of acute-phase changes could act as a potential confound on cognitive performance. However, given the small inter-group difference in terms of the number of patients tested in the acute phase (3 in the clipping vs. 2 in the coiling group), this should not adversely affect relative cognitive performance. Furthermore, the majority of patients in both groups were tested

more than six months following intervention and six months is generally considered a good indicator of the final outcome as most of spontaneous recovery has occurred by then (Beristain et al., 1996).

The groups were not matched according to 'site of aneurysm', 'time from rupture to intervention' and CT Fisher Grade (Please see Appendix 3). As previously mentioned, the decision to exclude certain prognostic factors from the matching process was primarily based on study design considerations, that is, limited sample size and time-constraints. Adding an additional three prognostic match criteria over and above the seven already chosen would further restrict the number of patients that we could successfully match within the given available sample. Specifically, 'site of aneurysm' was excluded as a match criteria in light of the overwhelming number of studies that have failed to show a relationship between location of aneurysm rupture and degree of cognitive deficits (Bornstein et al., 1987; DeSantis et al., 1998; Hillis et al., 2000; Hutter & Gilsbach, 1993; Ogden et al., 1993; Richardson, 1991; Romner et al., 1998; Sonesson et al., 1987; Tateshima et al., 2000 & Tidswell et al., 1995). Twelve clipping and ten coiling patients had ruptured aneurysms of the anterior circulation. Two coiling patients had ruptured aneurysms of the posterior circulation. With respect to 'time from rupture to intervention', as previously stated, opinion in the literature with respect to early versus late intervention remains debatable. On the one hand, early intervention greatly reduces the risk of rebleeding and allows for the timeous treatment of vasospasm. On the other hand, inflammation and brain oedema are most severe immediately after SAH and this invariably necessitates greater brain retraction during surgery (Greenberg, 1994). Hadjivassiliou et al. (2001) and Sonesson et al. (1987), however, found that time to intervention did not significantly influence differences in cognitive impairment. At GSH, the decision to delay intervention was guided by the clinical condition of the patient. The exclusion of CT Fisher Grades as prognostic measures of the severity of SAH was of concern in light of the generally well-accepted opinion that the greater the amount of blood on CT, the higher the incidence of vasospasm and associated ischaemic deficits (Greenberg, 1994 & Lindsay et al., 1991). However, Germano et al. (1998) specifically investigated the question of the effects of subarachnoid blood and found that subarachnoid blood extravasation was not

associated with long-term neuropsychological deficits that could interfere with a patient's daily life. Furthermore, the patients in the Germano study had clinical features similar to the present study, namely, grade on admission less than and equal to 2 and Fisher scores less than and equal to 3.

All surgical and embolization procedures were conducted by the same neurosurgical team.

Table 1: Time from Intervention to Assessment

Time to assessment	Clipping Group N=12	Coiling Group N=12
At 3 months	2	1
Between 3 and 6 months	1	1
Between 6 and 12 months	3	6
More than 12 months	6	4
Average (months)	10.7	9.3

Sample

SAH Participants

During the period January 2002 – January 2004, 82 patients in total received treatment for a ruptured aneurysm at the GSH neurosurgical unit. Within the context of our pre-selected prognostic framework, participants were recruited according to the following criteria:

- (1) Aged between 18 and 70 years at time of SAH
- (2) Able to speak English or Afrikaans
- (3) Living within a defined geographical area close to GSH
- (4) No previous head trauma
- (5) No known history of premorbid alcoholism or psychiatric disturbance
- (6) Neuropsychological investigation within 2 years of intervention
- (7) Neurological state on admission rated according to WFNS grading system less than or equal to 2
- (8) Outcome at time of assessment rated according to GOS less than or equal to 2

Patients over the age of 60 years are often not included in studies assessing cognition post SAH in order to exclude the potential effects of an early dementia or normal ageing on neuropsychological performance (Berry et al., 1997; Germano et al., 1997 & Hütter et al., 1995). In the present study, only one patient over the age of 60 (patient's age at time of assessment was 65) was included in the surgical group. In this respect, Richardson (1991), Ropper and Zervas (1984) and Stenhouse et al. (1991) included patients aged between 60 and 70 when assessing cognitive outcome post SAH surgery. Patients whose first language was either English or Afrikaans (two of the eleven official languages of South Africa) was a practical requirement given that only English and Afrikaans versions of neuropsychological tests were available. Similarly, for practical purposes, only patients who lived within travelling distance of GSH were considered as potential participants. Patients with a previous head trauma, a history of premorbid alcoholism and/or psychiatric disturbance were excluded in light of potential effects on neuropsychological performance (Berry et al., 1997; Chan et al., 2002; Germano et al., 1997; Hütter et al., 1995; Hütter & Gilsbach, 1994; McKenna et al., 1989 & Ogden et al., 1990). The criteria of follow-up neuropsychological investigation within two years of intervention was introduced in light of the fact that the endovascular management of ruptured aneurysms was only introduced to GSH in late 2001 (Taylor & Le Feuvre, 2004). There were therefore very few coiling patients who could be investigated beyond a two-year period. WFNS and GOS scores of less than or equal to 2 were chosen as these are generally reported in the literature as being the best predictors of favourable outcome (Germano et al., 1997). Limiting our sample to 'favourable' outcome patients was necessary because SAH can lead to diffuse and focal disruption of brain cortices and neuropsychological function can therefore vary quite drastically across patients. Thus cognitive testing should only be carried out on patients who have had a relatively favourable outcome (Ogden et al., 1993). In so doing, the confounding effects on cognition of focal damage secondary to the SAH, resulting from vasospasm and ischemia, are limited as far as possible. Another reason why patients were limited to those with 'favourable' outcome is limited resources on the part of the hospital. GSH adopts a policy of mostly admitting patients with good neurological status (WFNS less than or equal to 2) whose chances of a functional recovery are comparatively better (Taylor & Le Feuvre, 2004).

The participant selection process is detailed below in Table 2. Note that seven patients who received both clipping and coiling were excluded from the outset. Patients were not excluded because of perioperative complications such as vasospasm or hydrocephalus (Hillis et al., 2000).

Table 2: Exclusions from the Study

	Coiling	Clipping	Both
Period: Jan 2002 – Jan 2004	44	31	7
Exclusions:			
Deceased as a result of SAH	1	1	
WFNS > 2	7	5	
GOS > 2	1	3	
Age	6	0	
Language	6	3	
Upcountry patients	6	0	
Previous head trauma	0	0	
Premorbid alcoholism / psychiatric disturbance	0	0	
Unable to contact patient	1	0	
Patient refusal to participate	0	1	
Available SAH sample for testing	16	18	

Neuropsychological assessment commenced in February 2004 and continued until July 2004. In the beginning of February 2004, the number of months that had lapsed since receiving intervention (clipping or coiling) to the month of February 2004 was calculated for each patient in the available sample. Once this had been established, patients from each of the available sample groups were matched in such a manner that the group averages with respect to our final prognostic criteria, that is, time (number of months) from intervention to assessment would be satisfied. Once this process was completed, we were able to successfully match 12 patients from each group, resulting in the exclusion of four coiling and six clipping patients from the study. We were unable to match the excluded patients because of a significant discrepancy between these patients with respect to the number of months that had lapsed since they received treatment. As mentioned previously,

coiling is a fairly new procedure at GSH and as a result a significant number of the available coiling sample had received treatment in the latter part of our two-year investigation period. Furthermore, if a patient is a suitable candidate for either procedure with respect to aneurysm anatomy and age, there is a tendency to favour coiling because of positive benefits such as shorter hospital stays and faster recovery times. Within our retrospective two-year investigation period, this has resulted in a greater number of coiling than clipping patients in more recent months. That is, the six excluded clipping patients had received treatment very early in the investigation period and the four excluded coiling patients had only recently received treatment. Thus matching these patients with respect to ‘time from intervention to assessment’ was not possible.

The exclusion of these patients introduces a possibly bias in the study with respect to cognitive outcome given that they were not investigated for comparability with the present sample with respect to age, years of formal education and premorbid intelligence. However, we were able to establish that these patients satisfied the balance of our inclusion criteria, namely, they were all ‘good’ grade patients (WFNS and GOS less than and equal to 2), between the ages of 16 and 70, had no previous head trauma and no history of premorbid alcoholism or psychiatric disturbances. Furthermore, they were from a similar psychosocial background as the present sample. These common characteristics do, to some extent, moderate the risk that the exclusion of these patients would either over- or underemphasise the cognitive deficits associated with treated ruptured aneurysms.

The clinical and treatment-related data of participants is shown in Tables 3 and 4.

Table 3: Clinical Data of Patients

Pt	Treatment	Age	Education	WART score	Sex
NL	Co	48	10	24	M
BN	Co	49	10	31	F
PA	Co	57	7	32	M
HS	Co	48	5	7	M
JV	Co	26	15	31	M

MW	Co	49	13	41	F
JJ	Co	42	5	7	F
SS	Co	44	13	42	F
AF	Co	51	13	38	F
GB	Co	49	12	36	F
MN	Co	39	10	16	F
MT	Co	53	3	16	F
RC	Cl	39	10	6	M
JM	Cl	47	7	19	F
EB	Cl	42	6	12	M
SUS	Cl	38	9	7	F
PB	Cl	57	7	39	F
HA	Cl	51	7	21	F
MB	Cl	46	7	29	F
RT	Cl	65	8	23	F
SP	Cl	48	10	27	F
EF	Cl	47	10	36	F
JAV	Cl	43	8	17	M
MN	Cl	55	3	13	F

Table 4: Treatment-related Data of Patients

Pt	Trmt	WFNS	CT	Site	Days	Complications	Deficit	No	Time	GOS
NL	Co	1	2	ACoA	7	Sz; H	None	S	13	1
BN	Co	1	1	PCoA	8	ND	3 rd NP	S	6	2
PA	Co	1	3	BA	ND	VSP	None	S	6	1
HS	Co	1	3	PCoA	17	VSP	None	S	3	1
JV	Co	2	2	BA	7	VSP	None	S	13	1
MW	Co	1	1	PCoA	ND	None	None	S	10	1
JJ	Co	2	4	PCoA	16	None	None	S	5	1
SS	Co	1	ND	MCA	ND	None	None	S	6	1
AF	Co	1	3	MCA	6	None	None	S	6	1
GB	Co	1	1	PCoA	20	None	None	M	15	1
MN	Co	1	1	PCoA	15	None	None	S	19	1

MT	Co	2	2	PCoA	5	VSP	None	S	10	1
RC	Cl	2	4	ACoA	38	Sz; VSP; Rb, HTR	Hemi	S	3	2
JM	Cl	1	1	PCoA	12	None	None	S	16	1
EB	Cl	1	1	OA	12	H	None	S	6	1
SUS	Cl	1	2	PCoA	17	VSP; H	None	S	14	1
PB	Cl	1	3	ACoA	ND	None	None	S	4	1
HA	Cl	2	3	ACoA	27	VSP; HTR; H	None	S	10	1
MB	Cl	1	2	MCA	ND	None	None	M	13	1
RT	Cl	1	3	ACoA	7	H	None	S	3	1
SP	Cl	2	3	P	14	H	None	S	9	1
EF	Cl	2	3	PCoA	36	H	None	S	16	1
JAV	Cl	1	1	PCoA	3	None	None	S	15	1
MN	Cl	1	2	PCoA	8	None	None	S	19	1

Abbreviations: Trmt= treatment; WART (Wechsler Adult Reading Test; scored out of 50); Co=coil; Cl=clip; Site = site of ruptured aneurysm; ACoA = anterior communicating artery; PCoA = posterior communicating artery; MCA = middle cerebral artery; OA = ophthalmic artery; P = pericallosal artery; BA = basilar artery; Days = number of days from rupture to intervention; No.= number of treatments; S = single treatment, M = multiple treatments; Deficit = neurological deficit; hemi = hemiparesis; 3rd NP = 3rd nerve palsy; VSP = vasospasm, Sz = seizure, Rb = rebleed, H = hydrocephalus, HTR = hyponatremia; Time = time to assessment measured in months; CT = Fisher score; ND = no data available.

Control Participants

Twelve control participants were selected from the same hospital population. Selecting controls that have also been hospitalised was considered important because of any potential psychological impact that an illness and a stay in hospital may have on cognitive performance. Ten patients were recruited from GSH's neurology ward and two from the orthopaedics ward. In all twelve cases, the cerebrum was not involved. Controls were matched for age, years of education and premorbid intelligence (as measured by an estimate of premorbid IQ, the WART test). In all twelve cases, there was no history of previous head trauma, premorbid alcoholism or psychiatric disturbance. All controls were given the same neuropsychological battery but did not participate in the QoL assessment. The purpose of introducing a QoL assessment was to ascertain, specifically, if type of

treatment resulted in any significant differential with respect to emotional outcome. It was thus not considered necessary to include controls in this part of the assessment. The neuropsychological assessment of control participants was undertaken during their respective hospitalisation periods.

A limitation of this control group is that it does not take into account the psychological and lifestyle changes that follow surviving a sudden and major life-threatening illness such as SAH. However, despite this limitation, a control group was essential for the purposes of this study given the lack of age-appropriate normative data for our sample population on formal neuropsychological testing. Published norms are plagued by problems of validity given that they are based on a variety of population groups. A further limitation is that the performance of a group of people on a large number of tests compared with standardised norms would invariably reveal some degree of relative poor performance by virtue of variability in individual competencies (Hillis et al., 2000). The clinical data of control participants is shown in Table 5.

Table 5: Clinical Data of Control Patients

Control	Age	Education	WART score	Diagnosis
K	26	11	33	Neurofibromatosis
O	50	8	32	Peripheral Neuropathy
AD	64	8	33	Peripheral Neuropathy
JO	20	11	23	Peripheral Neuropathy
PE	63	8	35	Cervical Spondylotic Myelopathy
CO	47	10	16	Motor Neurone Disease
BA	39	8	29	Motor Neurone Disease
MA	39	7	12	Rheumatoid Arthritis
LE	60	10	40	Chronic Osteitis
FI	41	3	7	Motor Neurone Disease
DU	60	12	46	Spinal Injury
CH	49	12	35	Spinal Injury

Procedure

Prior to commencement, the study was approved by UCT's Psychology Department and GSH's Ethics Board. Patients were initially approached telephonically by the neurosurgical team who had performed the procedure. They were informed of the nature of the study and were invited to participate. Upon giving consent, their contact details were forwarded to the neuropsychological assessor. The assessor then made contact with the patients to set up appointments at GSH for formal testing. Prior to testing, they were provided with a consent form and an information sheet informing them of the purpose and nature of the study. (Refer to appendices 4 and 5 respectively) The neuropsychological testing and QoL assessment took approximately three hours. Patients were tested individually in a quiet examination room at GSH and the neuropsychological battery was delivered in the same format to all patients. All tests were conducted according to standard published protocols and subjects were allowed to take a break or terminate session at any time. Not all participants were able to complete the full neuropsychological battery due to time constraints on the part of the patient. Patients were compensated for any travelling expenses that they incurred.

Neuropsychological Testing

The tests selected were those on which performance has previously been suggested to be impaired after SAH. Specifically, the following cognitive functions were assessed: verbal and nonverbal learning and memory, attention, psychomotor speed, accuracy, concept formation, abstraction, cognitive flexibility and visuospatial planning and construction. As with many retrospective studies, information regarding a patient's premorbid intelligence is almost never available. Therefore, premorbid intelligence had to be estimated using the Wechsler Adult Reading Test (WART), a widely used measure of estimated premorbid intellectual functioning (Berry et al., 1997; Hadjivassiliou et al., 2001; McKenna et al., 1989 & Ogden et al., 1993). In light of the wide range of neurocognitive functions reported in the literature to be impaired following SAH, the use of three standardised cognitive batteries was necessary in order to comprehensively assess such a diverse range of potential deficits. The Wechsler Adult Intelligence Scale (WAIS) - Third Edition, was used to measure general intellectual functioning, the Wechsler Memory Scale (WMS) - Third

Edition, was used to assess memory and executive functions were assessed with the Delis-Kaplan Executive Function System (D-KEFS). From these batteries, individual subtests were selected in such a manner that would enable multiple measures of a particular cognitive domain to be assessed. In this way, specific cognitive functions could be assessed using different formats thereby increasing the likelihood of eliciting a deficit in a particular cognitive domain.

Where available, South African versions of the tests were used. For instance, the South African adaptation of the WAIS was used in this study. Afrikaans versions of the Similarities and Comprehension subtests of the WAIS were administered to Afrikaans-speaking patients. Furthermore, verbally-loaded tasks in the WMS such as Logical Memory I and II and Verbal-Paired Associates I and II were translated by the assessor for Afrikaans-speaking patients. Similarly, in the word generation task (Verbal Fluency) of the D-KEFS, patients were permitted to generate words in Afrikaans. In fact, if patients preferred, the entire assessment, including the QoL, was administered in Afrikaans. It must be noted that using the translated versions of some tests naturally raises the question of validity as these tests have not been normed for the Afrikaans language. Afrikaans-speaking patients had to be included in this study because a significant proportion of patients who attend GSH are Afrikaans-speaking and excluding these patients as potential participants would further compromise our sample size. Details of all neuropsychological tests, the functions they assess and specific sub-scores selected are listed in Appendix 6.

Quality of Life Assessment

The QoL assessment was undertaken once formal neuropsychological testing was completed. The questionnaire was comprised of two sections. Section A consisted of a number of 'ask and answer' questions relating to the patient's pre-and post SAH employment status, psychosocial and socioeconomic circumstances. The purpose of these questions was firstly to establish if patients had experienced any adverse changes with respect to their employment following SAH, as is commonly reported in the literature (Buchanan et al., 2000). Secondly, we needed to control for factors unrelated to SAH that could potentially contribute to the quality of the patients lives. (McKenna et al., 1989). In

other words, it was essential to distinguish changes that result from damage to the brain, from those that reflect the psychological impact of the SAH, and to situate these in relation to the relative impact of psychological and economic stressors arising in everyday life.

As regards employment, we established whether patients were employed at the time of their SAH and whether they had returned to their same employment post intervention. We further established if they were satisfied in their work environment prior to SAH. Those patients who had returned to their previous employment were asked to describe if they were experiencing any increased difficulties with performing their normal duties. Those patients who had decided not to return to their previous employment were asked to explain the circumstances behind their decision. With respect to the psychosocial and socioeconomic aspects of QoL, it must be stressed that before asking patients any questions relating to these issues, we emphasised the personal nature of these questions and reassured each patient that should they feel uncomfortable with the content of any question, they were under absolutely no obligation to answer. We asked patients whether they were currently experiencing any marital, familial or socioeconomic difficulties, whether there had been a recent death of a family member or close relative, whether they had recently suffered from a serious medical condition independent of SAH and finally, whether they were feeling depressed.

Section B of the QoL assessment consisted of 17 questions assessing a range of current moods and behaviours relative to premorbid states that have previously been reported to be adversely affected following SAH. For each item, the patient was asked to respond according to a 4-point comparative scale. Specifically: “0 – better”, “1 – no change”, “2 – bit worse” and “3 – lot worse”. This questionnaire was adapted from that used by Tidswell et al. (1995) and was specifically modified for the purposes of this study. Tidswell used this questionnaire to assess patient’s moods and behaviour, at least six months following surgery for a ruptured aneurysm. The following modifications were made to the original questionnaire: Firstly, Tidswell had used a 5-point comparative scale, specifically, there was an option between “a bit worse” and “a lot worse”: “significantly worse”. We chose to discard this option as we considered it to be redundant. Secondly, the original

questionnaire had 20 rated questions. We only chose eleven of these as we felt a number of the questions were repetitive. We then added six questions regarding mood and behaviour that we felt were not adequately addressed by the existing questionnaire. In particular, questions relating to anxiety (Beristain et al., 1996), energy levels and social and family relations (Buchanan et al., 2000) and loss of interest (Hutter et al., 2001) were added. Although this questionnaire is not a standardised measure, it was included in order to assess aspects of behaviour and quality of life not covered by standard neuropsychological tests. (Please see Appendix 7).

The QoL assessment was undertaken by the same assessor who administered the formal neuropsychological battery. Ten patients in the clipping and eleven patients in the coiling group completed the questionnaire. Three patients in total did not participate in the QoL assessment due to time constraints on the part of the patients.

Comparability of the Groups

Campbell and Machin (1994) and Altman (1991) recommend matching controls to treatment patients on no more than two to three variables that are closely related to outcome. In this respect, we investigated the three groups for comparability on factors that would affect neuropsychological performance, namely, age, years of education and premorbid I.Q. It must be noted that matching did not entail a strict case-control match between patients and controls. Controls were selected and assessed once we had established our sample size for each treatment group and completed our neuropsychological assessment of all clipping and coiling patients. Control participants were then chosen in such a manner that the mean value with respect to age, education and WART score were comparable across both treatment groups.

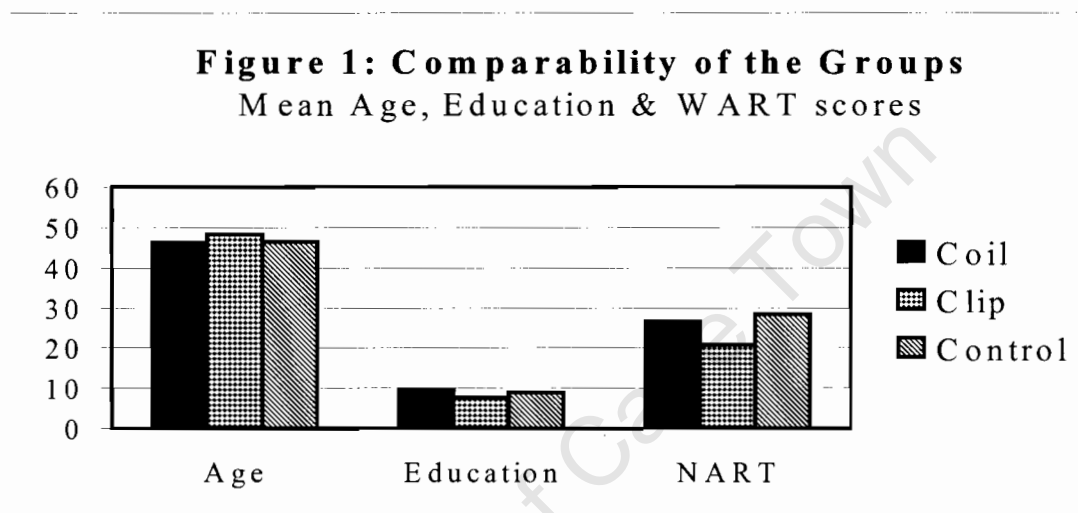
Comparability of Participant Characteristics

The three groups (coiling, clipping and control) were investigated for comparability with respect to age, years of education and premorbid IQ estimates by performing a one-way ANOVA with type of treatment as the predictor variable. Because of the matching process, there were no significant differences between the three groups (clipping, coiling and

control) with respect to age, years of education and on the estimate of premorbid intelligence. Univariate ANOVA results and comparative means for these 3 variables are illustrated in Table 6 and Figure 1 respectively.

Table 6: ANOVA results for Age, Years of Education and WART.

Dependent Variable	Degrees of Freedom	F value	p value
Age	(2,35)	0.119	0.888
Education	(2,35)	1.470	0.245
NART	(2,35)	1.442	0.251



Comparability of Treatment Groups with respect to Prognostic Clinical Variables

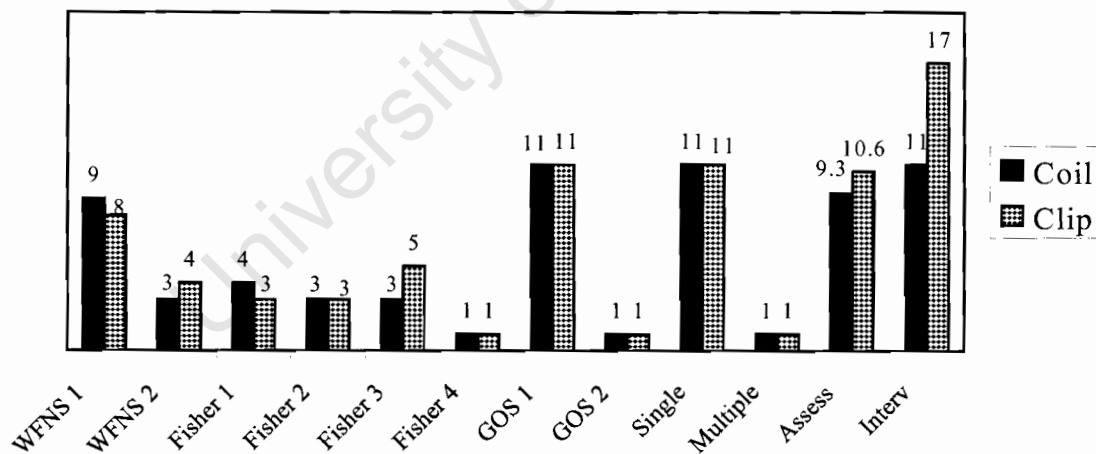
The data for four of the six prognostic variables was categorical in nature, namely, WFNS, GOS, CT Fisher Grade and number of treatments. In light of this, a discriminant analysis was performed to investigate any significant differences between the coiling and clipping groups with respect to the aforesaid prognostic variables. In this instance, mean substitution was used for missing data. The balance of prognostic criteria were continuous in nature and thus t-tests were performed for the variables: ‘time from intervention to assessment’ and ‘time from rupture to intervention’. There were no significant differences between the coiling and clipping groups on WFNS, GOS, ‘number of treatments’ and ‘time from intervention to assessment’. Furthermore, although we did not actively match the two

groups on CT Fisher Grade and ‘time from rupture to intervention’, there was no significant difference between the groups on these particular variables. Specifically, the discriminant function model for WFNS, GOS, CT Fisher Grade and ‘number of treatments’ was not significant, that is $F(4,19) = .23863$ $p < .913$. The results of the t-tests for ‘time from intervention to assessment’ and ‘time from rupture to intervention’ were also not significant. Individual discriminant analysis results for each clinical variable and t-test results for the variables ‘time from rupture to intervention’ and ‘time from intervention to assessment’, as well as comparative means, are illustrated in Table 7 and Figure 2 respectively.

Table 7: Statistical Results for Prognostic Clinical Variables

Clinical Variable	Degrees of Freedom	F value	p value
WFNS	(1,19)	0.106	0.749
CT Fisher Grade	(1,19)	0.069	0.796
GOS	(1,19)	0.013	0.909
Number of treatments	(1,19)	0.666503	0.424
		t-value	
Time from rupture to assessment	22	-0.623	0.539
Time from rupture to intervention	17	-1.388	0.183

Figure 2: **Comparative Clinical Match Variables**



Abbreviation list for Figure 2

Single = one clip or coil procedure; Multiple = more than one clip or coil procedure; Assess = time from rupture to neuropsychological assessment; Interv = time from rupture to intervention.

Data Analysis

All analyses were carried out using STATISTICA version 6.1. The raw scores of neuropsychological tests were used in all analyses. Levene's test was performed to ensure that the assumption of homogeneity of variance was satisfied for all dependent variables.. One-way ANOVAs were performed to analyse neuropsychological data. Twenty-seven separate ANOVAs were performed, one for each dependent variable. Post-hoc Tukeys analysis was performed to establish directional significance. No Bonferroni corrections were made for the original dependent variables. In light of multiple comparisons, post-hoc analyses were Bonferonni corrected (Howell, 1997). In this respect, Altman (1991) recommends Bonferroni corrections only for a small number of comparisons, generally not exceeding five. In this study, six post-hoc comparisons were made. For section B of the QoL assessment, a total score for each patient was obtained by summing up the individual scores for each answer and a t-test was then performed on these totals to analyse any statistical differences.

Results

Neuropsychological Data

The assumption of homogeneity of variance was fulfilled for all dependent variables. In terms of differences between the coiling, clipping and control groups on formal neuropsychological testing, at the 0.05 level of significance, significant results were achieved on six test measures, namely:

Logical Memory I: score for total recall

Logical Memory II: score for total recall

Tower Of London: score for completion time

Design fluency: score for total correct designs conditions 2 & 3 combined

Verbal fluency: score for total correct responses letter and category conditions combined

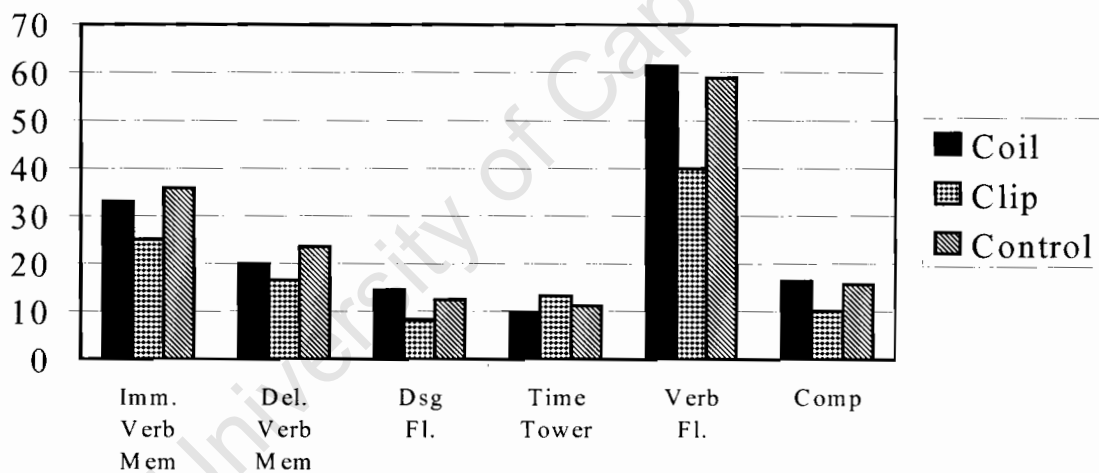
Comprehension: standard score

Univariate ANOVA results and comparative means of significant variables are illustrated in Table 8 and Figure 3 respectively.

Table 8: Significant Results of Neuropsychological Test Variables.

Neuropsychological Tests	Degrees of Freedom	F value	p value
Logical Memory I	(2,35)	4.068	0.026
Logical Memory II	(2,35)	3.721	0.035
Design Fluency	(2,30)	5.908	0.007
Verbal Fluency	(2,30)	4.944	0.014
Tower of London	(2,35)	5.849	0.007
Comprehension	(2,30)	5.412	0.010

Figure 3: Relative Means of Significant Tests



Abbreviation list for Figure 3

Imm. Verb Mem = Immediate Verbal Memory (Logical Memory I); Del. Verb Mem = Delayed Verbal Memory (Logical Memory II); Dsg Fl. = Design Fluency; Time Tower = Time on Tower test; Verb Fl. = Verbal Fluency; Comp = Comprehension

An obvious concern with respect to these results was the high rate of Type 1 error arising from the large number of test measures used. Post-hoc Bonferroni corrections were undertaken on significant variables. Directional and Bonferroni-corrected p values are shown in Table 9.

Table 9: Post-hoc Test Results for Significant Test Variables (Bonferroni-corrected)

Neuropsychological Tests	Degrees of Freedom	Clip vs. Coil	Clip vs. Control
Logical Memory I	33		0.028
Logical Memory II	33		0.030
Design Fluency	28	0.006	
Verbal Fluency	28	0.019	
Tower of London	33	0.006	
Comprehension	28	0.013	

On the test measures of Logical Memory I (total immediate verbal recall) and II (total delayed verbal recall), the clipping group but not the coiling group performed worse than the controls. On the test measures of Design Fluency, Verbal Fluency, Tower of London (completion time) and Comprehension, the clipping group performed worse than the coiling group.

The individual patient scores of the coiling and clipping groups on significant test measures are illustrated in Figures 4-9. (Please note that with respect to Figure 8, the time score on the Tower of London test, a higher score reflects a poorer performance).

Figure 4: Logical Memory I

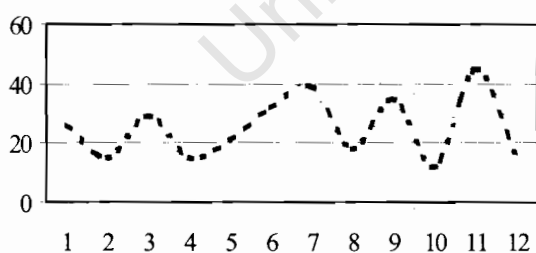
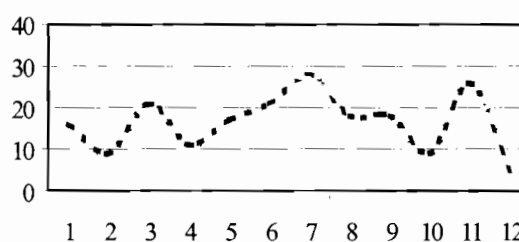
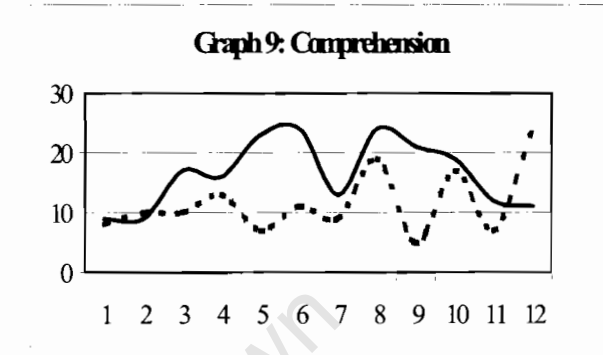
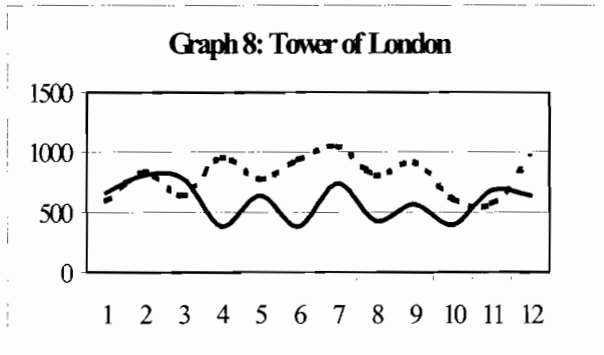
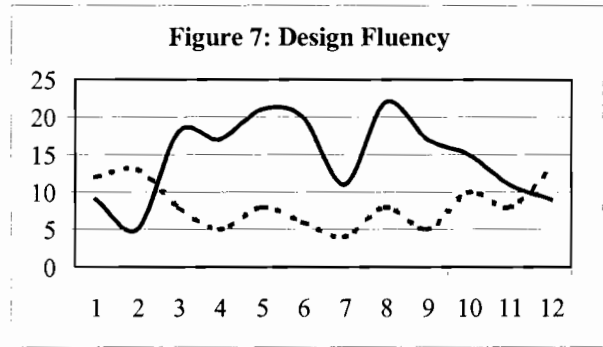
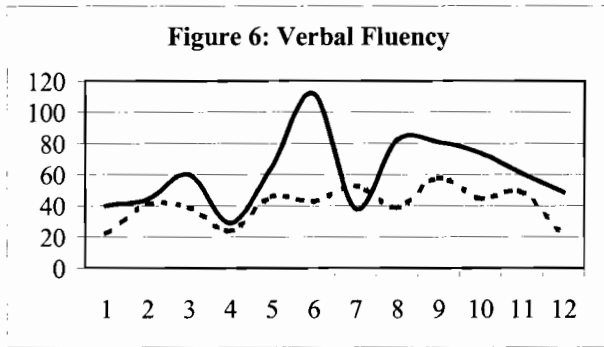


Figure 5: Logical Memory II





Coil	—————	Clip	-----	Control
-------------	-------	-------------	-------	----------------

Specifically, for Logical Memory 1, measuring immediate verbal recall, half (n=6) of the clipping patients scored less than 50% (scored out of 50) compared to the control patients. Only one control patient scored less than 50% on this test. On Logical Memory II, measuring delayed verbal memory, 17% (n=2) of the clipping versus 50% (n=6) of the control patients were able to retain more than 50% of the information from the first trial of this test (scored out of 50) to the second administration. Logical Memory II is administered half an hour following Logical Memory I. On the test of Comprehension, 83% (n=10) of the clipping group scored less than 50%, compared to 42% (n=5) for the coiling group. In Design Fluency, the coiling group was able to generate, on average, 15 correct designs in a minute compared to eight correct designs, on average, for patients in the clipping group. In Verbal Fluency, the coiling group was able to generate on average 61 correct responses in four minutes. The average number of correct responses in four minutes for the clipping

group was 40. On the Tower of London (completion time) test, the clipping group was, on average, four minutes slower in completing the task than the coiling group.

Quality of Life Assessment Data

Ten patients in the clipping and eleven patients in the coiling group completed the questionnaire. Seven patients in the clipping group were employed at the time of their SAH. All seven had returned to their previous employment at the time of assessment. Only one patient reported experiencing increased difficulties at work. In this instance, the patient felt more fatigued than usual. The balance of the group was unemployed at the time of the SAH and had remained so until the time of assessment. In the coiling group, eight patients were employed at time of the SAH. Of these, five had returned to their previous employment by the time of assessment. Only one patient reported increased difficulties at work, namely, problems with concentration and tolerance towards others. Of the three patients who had not returned to their previous level of employment, one had found alternate employment, one was unable to procure employment and the third chose not to return due to the fact that the SAH occurred at work and she thus felt traumatised in that context. The balance of the group was unemployed at the time of the SAH and had remained so until the time of assessment. Pre and post-SAH employment details of the coiling and clipping groups are shown in Table 10.

Table 10: Pre and Post-SAH Employment Status of Participants

	Clipping N=10	Coiling N=11
Employed at time of SAH	70%	73%
Unemployed at time of SAH	30%	27%
Returned to same employment post SAH	70%	45%
Employed elsewhere post SAH	0%	1%

Three patients in the clipping group reported that they were currently experiencing marital and/or familial tensions. Four patients described themselves as depressed. On further questioning as to the cause of their depression, reasons given were family, relationship and socioeconomic pressures and resultant feelings of anxiety and social withdrawal behaviour.

The extent of socioeconomic difficulties described by patients in this group was considerable and primarily financial (inadequate income, single-parent families, no financial support from spouse and sole responsibility for children). Two patients reported dissatisfaction with their current employment, specifically, tensions with colleagues and unhappiness due to uncompensated over-time work. In the coiling group, six patients described experiencing marital and/or familial tensions. Four patients described themselves as depressed and ascribed their depression to unhappiness in their intimate relationships as well as socioeconomic pressures. The majority of the patients reported that they were labouring under considerable socioeconomic difficulties and once again, the nature of these difficulties was primarily financial (inadequate income, single-parent families, no financial support from spouse and sole responsibility for children). Socioeconomic and psychosocial information is summarised in Table 11.

With respect to Section B of the QoL questionnaire measuring changes in behaviour and mood post intervention, there were no significant findings. Specifically, $df = 19$, t -value = 0.192 and $p = 0.849$.

Table 11: Socioeconomic and Psychosocial Data

	Clipping N=10	Coiling N=11
Marital or familial tensions post SAH	30%	55%
Death or serious physical illness of an intimate, post SAH	40%	1%
Serious medical conditions other than SAH	0%	0%
Feeling of being depressed	40%	36%
Socioeconomic difficulties (inadequate income, unemployment, poor living conditions)	50%	73%
Dissatisfaction with work preceding SAH	20%	0%

Discussion

In the present study, we compared cognitive and emotional outcome after aneurysmal SAH and treatment by two different procedures, clipping and coiling. Since its introduction, coiling has been gaining popularity because of the avoidance of craniotomy but its potential advantages over clipping in terms of better outcomes are only just beginning to be evaluated. In light of this favourable trend and the limitations of gross neurological scales as 'true' measures of outcome, we set out to answer a specific question concerning coiling, namely: "How good is a good outcome and from whose perspective?" To comprehensively answer this question, we chose to broaden the traditional concept of 'outcome' to include both the cognitive and emotional consequences of medical intervention following brain trauma.

It is evident from the preceding literature review that the question of cognitive performance following intervention for aneurysmal SAH is one composed of many potentially confounding factors. In order to isolate the effects of the treatment itself, we needed to control for the following effects: the SAH itself; neurological grades on admission (WFNS) and discharge (GOS), factors that could affect performance on cognitive testing (age, years of education and premorbid IQ) and number of treatments. We also limited participant selection to include only those patients with good neurological grades pre and post intervention (WFNS and GOS less than or equal to 2). The reason for this was twofold. Firstly, the expectation is that patients with good grades are less likely to suffer SAH-related complications. Secondly, these are the very patients considered by neurosurgeons as having had good outcomes. We did not actively match patients on amount of blood on CT (Fisher Grade) and 'time from rupture to intervention'. However, statistical analysis revealed no significant differences between the coiling and clipping groups on these clinical variables. Furthermore, the two groups were not matched on site of aneurysm. However, in light of the generally accepted opinion that site of aneurysm rupture does not account for significant differences in cognitive performance, we feel that the difference in cognitive performance between the clipping and coiling groups found in this study cannot be attributed to location.

Once we had matched the two treatment groups in terms of age, years of education, premorbid IQ, WFNS, GOS, time to assessment and number of treatments, we were able to show that despite the fact that all patients were rated as having a good neurological outcome, the clipping patients, compared to the coiling ones, performed worse on formal neuropsychological testing post intervention. Moreover, there were no significant differences between the coiling and clipping groups with respect to the severity of the bleed and 'time from rupture to intervention'. Performance of the clipping patients was assessed, on average, nine months following surgery. As previously mentioned, we included three clipping patients in our sample who were still in the acute phase (i.e. less than 6 months post intervention). In this respect, Hillis et al. (2000) and Kreiter et al. (2002) have argued that group means on neuropsychological performance post surgery can be lowered by the deviant scores of only a few patients. We were thus concerned about the effects of acute-phase changes on cognitive performance for these three clipping patients. These patients are identified as numbers 1,5 and 8, in Figures 4-8 and it is evident that they did not consistently score the lowest, confirming that their particular inclusion in the analysis did not skew our results.

In particular, we found significant differences in cognitive performance on six test measures (at the 0.05 level of significance, post Bonferroni adjustments), namely:

Logical Memory I – a test of immediate verbal memory recall; Logical Memory II – a test of delayed verbal memory recall; Comprehension – a test of common-sense judgement and practical reasoning; Verbal Fluency – a test of fluency in word generation, speed of mental processing, cognitive flexibility and initiation; Design Fluency – a test of fluency in nonverbal generation, visual-perceptual skills, initiation, cognitive shifting, motor speed and initiation; Tower of London – a test of spatial planning, rule-learning and ability to learn and maintain an instructional set. On the tests of immediate and delayed verbal memory recall, the clipping but not the coiling patients, performed worse than the controls. On the tests of comprehension, fluency in verbal and nonverbal generation and spatial planning, the clipping patients performed worse than the coiling patients.

In light of the large number of variables in SAH prognosis, the different results reported in the literature and small sample size, it is necessary to exercise caution in drawing specific conclusions from the present study. Our small sample size cannot provide a definitive basis for arguments about general patterns of neuropsychological impairment in patients after intervention for aneurysmal SAH. Furthermore, direct comparisons with other studies that have found similar results is difficult given different study designs, inclusion and or exclusion criteria, time to assessment and neuropsychological tests used. However, a more discrete comparison on points of commonality or discrepancy is worthwhile in this instance.

As previously mentioned, Chan et al. (2002) and Hadjivassiliou et al. (2001) found in favour of better cognitive outcomes for patients coiled for ruptured aneurysms compared to those who have been clipped. Chan et al. found that the performance of the coiling patients on memory and executive function tasks was better than that of the clipping patients. On the one hand, although these findings support those of the present study, it could be argued that a direct comparison is not entirely warranted given that Chan et al. focused entirely on anterior communicating aneurysms. On the other hand, the anterior communicating artery forms part of the anterior circulation and save for two coiling patients in our study who had posterior circulation ruptured aneurysms, the balance of our patients had ruptured aneurysms of the anterior circulation. It is well documented that there is not a well-established relationship between aneurysm location and severity of cognitive deficits (Bornstein et al., 1987; DeSantis et al., 1998; Hillis et al., 2000; Hutter & Gilsbach, 1993; Ogden et al., 1993; Richardson, 1991; Romner et al., 1998; Sonesson et al., 1987; Tateshima et al., 2000 and Tidswell et al., 1995). The patients in the Chan et al. study were also rated as having good or moderate neurological recovery (GOS less than or equal to 2), similar to our own.

In the Hadjivassiliou et al. study, the clipping and coiling patients were matched on WFNS, age and location of aneurysm. Although they included aneurysms of different locations, it should be mentioned that all ruptured aneurysms were located in the anterior circulation. Significant differences were found on four 'frontotemporal' tests measuring

memory and executive functions. They interpreted their findings to reflect that clipping may result in more frontotemporal damage, hence why these particular tests were more sensitive in differentiating between the groups. Their conclusions were supported by MRI investigations revealing more frontotemporal damage in patients following clipping.

Koivisto et al. (2000) also investigated the cognitive performance of clipping versus coiling patients and although they found no significant differences in cognitive performance between the groups, their results confirm those of the Hadjivassiliou study in that clipping is associated with more MRI-detectable injury than coiling. A possible reason for this is the degree of sensitivity of the test measures selected in adequately differentiating performance between the two groups. They also argued that clinical outcome could have been affected in a larger series of patients. The results of the Chan et al. study also appear to support those of Hadjivassiliou et al. to the extent that they argued that the greater cognitive deficits found in the clipping group are attributable to the more invasive nature of clipping and consequent increase in the likelihood of occluding the ACoA parent vessel and perforators. Thus Hadjivassiliou et al. concluded that the neurocognitive presentation of the deficits found in clipping patients is focal in nature, that is, 'frontotemporal'.

At first glance, it would seem that the results of the present study support Hadjivassiliou's 'frontotemporal' deficit conclusion. Specifically, Verbal, Design Fluency and the Tower of London are tests that originate from an exclusively frontal neuropsychological battery (D-KEFS). Comprehension, a subset of the WAIS, measures reasoning and judgement abilities and these cognitive functions are regarded as frontal. Logical Memory I and II measure immediate and delayed verbal memory recall and in the absence of a demonstrable working memory deficit, such memory deficits could be localised to the temporal region.

However, drawing such a definitive conclusion is problematic for a number of reasons. Firstly, we are unable to categorically attribute these deficits to more frontotemporal damage following surgery because we do not have any MRI data to support this view.

Secondly, and more importantly, a patient can fail on formal neuropsychological testing for a variety of reasons. Formal neurocognitive tests are only indirect measures of neuropsychological function and their localising value is uncertain (Mountain & Snow, 1993). In this respect Shapiro (1973) cited in Walsh & Darby (1999: 388) states that “most tests have only an indirect relationship with the variables they are supposed to measure”. Many formal neuropsychological tests are multifactorial in nature meaning that successful completion of a test inevitably requires the engagement of other cognitive abilities in addition to the ‘main’ cognitive function specified by the test. It is therefore hazardous to assume that when a subject fails on a particular test, the reason for their failure is a deficit in the cognitive function stipulated by the manual to be measured by this test. Failure on complex tasks could reflect a deficit in any of the functions involved or a combination thereof (Walsh & Darby, 1999). There are as such no direct measures of localising ‘frontal’ function (Morgan & Lilienfeld, 2000). To illustrate, our clipping patients performed worse than the coiling patients on the Design Fluency test. As previously mentioned, this test measures visual-perceptual skills, cognitive shifting, motor speed, problem-solving and initiation and is considered a test of frontal function. Why did the clipping patients perform so poorly compared to the coiling patients? Was it because they were experiencing difficulties with the visual-perceptual aspect of this task or the motor speed and problem-solving aspects of this task? Likewise for the Tower of London test. This test also has a spatial, a problem-solving and a psychomotor aspect. The multifactorial nature of formal neuropsychological tests is clearly demonstrated when one begins to delineate all of the cognitive functions required for successful completion. A single score, used in isolation, cannot tell us why these patients experienced difficulty with this task - a serious limitation of quantification.

A more sagacious interpretation of these results would be to focus rather on the common cognitive functions subserved by these tests. The Verbal Fluency, Design Fluency and Tower of London tests require the patient to initiate and maintain a set of responses; they require cognitive flexibility because the patient has to shift from one instructional set to another and finally, the patient has to process the above instructions and execute them within a given time frame. Thus the cognitive abilities of initiation, sustained generation,

cognitive flexibility and speed are requisites of all three tasks. In this respect, Hutter et al. (1995) describe that post SAH patients frequently perform poorly on tasks that rely on cognitive abilities such as reaction-time, attention, concentration and memory. They further report that SAH patients frequently experience loss of motivation and initiative and that the primary disturbance is one of cognitive speed. They describe a syndrome consisting of reduced speed of information processing, lack of motivation and initiative. It is evident that their description of cognitive deficits is very similar to the kind of deficits we found in our clipping patients. Added to this, our clipping patients showed concrete thinking and reduced insight, as demonstrated by their poor performance on the Comprehension test. This cluster of deficits adequately accounts for the clipping patient's poorer cognitive performance on the six significant test measures. Likewise, the same cognitive deficits could account for poor performance on many of the other tests used in this study. We would possibly have achieved significance in a greater number of tests with a larger sample.

We therefore choose to interpret our results as supporting evidence that patients surviving an aneurysmal rupture are more likely to suffer from a "SAH-induced encephalopathy", very much like that proposed by Llunggren et al. (1985). Furthermore and with specific reference to intervention, this encephalopathy could possibly be aggravated by the more invasive nature of surgery compared to endovascular management. The neurocognitive presentation of these patients is thus diffuse in nature, that is, mild to moderate impairment across multiple cognitive domains, specifically: memory and visuospatial abilities and higher order cognitive functions such as cognitive slowing, abstraction and cognitive flexibility. This is consistent with Ogden et al. (1993) view that the most persistent deficits following aneurysmal surgery are those associated with diffuse brain damage. To this end, Germano et al. (1998:805) explain that the presence of blood in the subarachnoid spaces "induces a global brain dysfunction by setting in motion a complex pathophysiological process, which results in focal and generalised disturbances of brain functions". Furthermore, the finding that clipping patients are more likely to experience more cognitive deficits post intervention correlates well with the clinical course of their treatment. That is, the nature and extent of recovery from surgery is more traumatic,

requiring intensive care, prolonged stays in hospital and longer delays in attaining functional independence, compared to endovascular treatment.

No patients, either spontaneously or on direct questioning, attributed any of the current psychosocial difficulties that they were experiencing to the SAH and/or the treatment they had received. An interesting and important clinical observation was that the majority of the clipping patients showed reduced insight into the fact that they had survived a major life-threatening stroke. When asked why they were hospitalised, a common answer was because of headache.

With respect to QoL assessment, we were unable to demonstrate significant differences in social and emotional outcome between the two procedures. The reason for this is that the clipping patients exhibited reduced insight, observed clinically during assessment, and demonstrated formally by their poor performance on the Comprehension test. This naturally accounts for the reduced insight these patients had into their deficits, both cognitively and behaviourally, post intervention. Buchanan et al. (2000) assessed the neurobehavioural changes of surgically-treated patients approximately 19 months after surgery by means of an Adjective Checklist rated questionnaire. They found that 30% of their patients were unable to complete the questionnaire due to reduced insight into personality and behavioural changes post surgery. Furthermore, patients significantly underestimated the extent of the burden that primary caregivers and relatives experienced as a consequence of these changes. A shortcoming of the present study is the sole reliance on patient's subjective accounts of social and emotional experiences post intervention. A more effective method to assess QoL changes post intervention would have been to have patients' relatives participate in the QoL assessment in order to provide a more objective account of the patient's deficit.

A criticism that has been lodged against studies that assess neuropsychological functioning post surgery are that they only include patients with aneurysmal SAH (Tuffiash et al., 2003). The presence of the SAH blood itself, irrespective of effects of intervention, can have many detrimental effects on the brain. This is a valid argument in light of the

difficulty in differentiating those deficits attributable to surgery from those caused by the SAH. However, the aim of the present study was to evaluate the efficacy of treatment options with respect to ruptured aneurysms and thus the presence of SAH blood was common to both groups. More importantly, there was no significant difference with respect to Fisher Grades (i.e. amount of blood) between our groups and thus the cognitive deficits we found in our clipping group cannot be attributed solely to the effects of SAH blood. Furthermore, Brilstra et al. (2004) compared the outcome of patients who had their unruptured aneurysms (i.e. no SAH blood) either coiled or clipped and found that the operated patients endured a considerable impact on their functional health and QoL. Coiling in turn did not have an effect on functional health and QoL. Similar results were found by Johnston et al. (2000) who concluded that surgical patients who had received treatment for unruptured aneurysms were more likely to report new symptoms and disabilities and reported longer periods of recovery compared to coiling patients.

In 2001, James Ausman, a neurosurgeon, wrote an article that predicted the “Death of Cerebral Aneurysm Surgery”. He stated that increasingly more studies would be published that employ neuropsychological testing to show that clipping patients are left with significantly more cognitive deficits than coiling patients. He further claimed that such studies would “mark the beginning of a new era for neurosurgeons” and would “show that the routine postoperative follow-up examinations that neurosurgeons perform in their offices are not adequate to reveal the functional deficits that can occur after surgery”. (p.348)

Within the confines of this study’s limitations, we were able to demonstrate better outcomes for coiling patients. We were able to show that good outcome translates into a relatively better cognitive performance and uncompromised QoL for the coiling patient. Our results complement those of Taylor and Le Feuvre (2004) who sought to examine whether the introduction of coiling to GSH in 2001 improved the overall outcome (GOS) of patients treated for ruptured cerebral aneurysms. They found that there was an absolute reduction in mortality and major morbidity of 16%. Moreover, patients were treated more

rapidly through coiling because of reduced waiting times since the procedure can proceed without anaesthesia or an operating list.

This study has illustrated the usefulness in employing neuropsychological testing to tease out more subtle but nonetheless important deficits that can contribute towards outcome. It is easy to forget that these tests do not merely assess the stipulated function they are designed to measure – they provide a sampling of cognitive deficits which, in the real world, can have devastating implications for functional outcome. Furthermore, our findings emphasise the need to redefine the current conceptualisation of morbidity beyond the neurological and provide neurosurgeons and patients with a better appreciation of the relative risks of intervention.

University of Cape Town

Limitations

(i) Size and Availability of Sample:

As previously mentioned, the small sample size of the present study limits our ability to draw definitive conclusions. Furthermore, the small sample size in relation to number of tests used increases our Type 1 error. Bonferroni corrections were performed on significant variables

(ii) Prognostic Factors:

We attempted to match the two treatment groups on as many prognostic factors as time and patient availability allowed. The exclusion of time from rupture to intervention, Fisher Grades and aneurysm location have been addressed.

(iii) Cultural Suitability of tests:

Except for the SA-WAIS, the other tests used have not been culturally adapted which raises the question of suitability for the current sample. We addressed this problem by not comparing the performance of our patients to standardised norms but to the performance of controls recruited from similar geographic, psychosocial and socioeconomic backgrounds. Furthermore, a limited number of substitutions were made in the Logical Memory and Verbal Paired Associates subtests of the WMS-R for terms not appropriate for use in the South African context. Specifically, in Logical Memory, the following words were replaced: “South London” with “East London”; “pounds” with “rand”; “Liverpool” with “Johannesburg” and “films” with “movies”. In Verbal Paired Associates, “badger” was replaced with “squirrel”. As previously mentioned, some tests that were translated into Afrikaans were not normed.

(iv) Formal Standardised Testing:

The limits of quantified standardised tests have been addressed.

(v) Retrospective Studies:

The problems with retrospective studies are significant subject selection and difficulty in assessing relative cognitive change in function since SAH. The preferred means by which to assess whether SAH intervention has caused cognitive impairment would be to carry out a longitudinal assessment of patients over time.

In the present study, significant subject selection was necessary in order to isolate the effects of treatment. As to the question of relative cognitive change since SAH, premorbid intelligence was estimated by administering a reading test to all adults which is generally well-accepted in the literature as a reliable estimate of premorbid intelligence. A further problem with retrospective studies is that data obtained from hospital records is invariably incomplete due to missing data and/or notes. The QoL assessment highlights a further problem with retrospective studies, which is recall bias of events and emotions on the part of the patients regarding their experience of SAH and intervention.

(vi) Lack of MRI investigations:

MRI investigations post intervention were not available due to cost considerations.

(vii) QoL Assessment:

As previously mentioned, the questionnaire used in the QoL assessment was not standardised. The problem with non-standardised format questionnaires is that it makes direct comparison with the results of other studies impossible. The reliability and validity of the current questionnaire has not been established. Moreover, the lack of collateral information from patients' relatives regarding changes in mood and behaviour post intervention is a limitation.

(viii) Group Means:

A problem with using group means as a basis for comparison is that the deviant scores of one or two patients can result in a bimodal distribution and thus skew results. As illustrated in Figures 4-9, this was not the case in the present study.

References

- Altman, D.G. (1991). *Practical statistics for medical research*. London: Chapman and Hall.
- Ausman, J.I. (2001). The death of cerebral aneurysm surgery. *Surgical Neurology*, 56, 348.
- Beristain, X., Gaviria, M., Dujovny, M., El-Bary, T.H.A., Stark, J. & Ausman, J.I. (1996). Evaluation of outcome after intracranial aneurysm surgery: The neuropsychiatric approach. *Surgical Neurology*, 45, 422-429.
- Berry, E., Jones, R.A.C., West, C.G.H. & Brown, J.D.K. (1997). Outcome of subarachnoid haemorrhage. An analysis of surgical variables, cognitive and emotional sequelae related to SPECT scanning. *British Journal of Neurosurgery*, 11, 378-387.
- Birchall, D., Khangure, M., McAuliffe, H., Apsimon, H. & Knuckey, N. (2001). Endovascular management of acute subarachnoid haemorrhage in the elderly. *British Journal of Neurosurgery*, 15, 35-38.
- Bornstein, R.A., Weir, B.K.A., Petruk, K.C. & Disney, L.B. (1987). Neuropsychological function in patients after subarachnoid hemorrhage. *Neurosurgery*, 21, 651-654.
- Brilstra, E.V., Algra, A., Rinkel, G.J.E., Tulleken, C.A.F., & van Gijn, J. (2002). Effectiveness of neurosurgical clip application in patients with aneurysmal subarachnoid haemorrhage. *Journal of Neurosurgery*, 97, 1036-1041.
- Brilstra, E.V., Rinkel, G.J.E., van der Graaf, Y., Sluzewski, M., Groen, R.J., Lo, R.T.H., & Tulleken, C.A.F. (2004). Quality of life after treatment of unruptured intracranial aneurysms by neurosurgical clipping or by embolization with coils. *Cerebrovascular Diseases*, 17, 44-52.
- Brilstra, E.V., Rinkel, G.J.E., van der Graaf, Y., van Rooij, W.J.J., & Algra, A. (1999). Treatment of intracranial aneurysms by embolization with coils. A systematic review. *Stroke*, 30, 470-476.
- Bryan, R.N., Rigamonti, D. & Mathis, J.M. (1997). The treatment of acutely ruptured cerebral aneurysms: Endovascular therapy versus surgery. *American Journal of Neuroradiology*, 18, 1826-1830.
- Buchanan, K.M., Elias, L.J., & Goplen, G.B. (2000). Differing perspectives on outcome after subarachnoid hemorrhage: The patient, the relative, the neurosurgeon.

Neurosurgery, 46, 831-840.

- Campbell, M.J. & Machin, D. (1994). *Medical Statistics: A commonsense approach*. 2nd Ed. Chichester: John Wiley & Sons Ltd.
- Chan, A., Ho, S., & Poon, W.S. (2002). Neuropsychological sequelae of patients treated with microsurgical clipping or endovascular embolization for anterior communicating artery aneurysm. *European Neurology*, 47, 37-44.
- Chiang, V.L., Gailloud, P., Murphy, K.J., Rigamonti, D. & Tamargo, R. J. (2002). Routine intraoperative angiography during aneurysm surgery. *Journal of Neurosurgery*, 96, 988-992.
- Cloft, H.J. & Kallmes, D.F. (2002). Cerebral aneurysm perforations complicating therapy with Guglielmi detachable coils: A meta-analysis. *American Journal of Neuroradiology*, 23, 1706-1709.
- Dehdashti, A.R., Mermillod, B., Rufenacht, D.A., Reverdin, A., & de Tribolet, N. (2004). Does treatment modality of intracranial ruptured aneurysms influence the incidence of cerebral vasospasm and clinical outcome? *Cerebrovascular Diseases*, 17, 53-60.
- Delis C.D., Kaplan, E. & Kramer, J.H. (1995). *Delis-Kaplan executive function system: Examiners manual*. London: The Psychological Corporation.
- DeSantis, A., Laiacona, M., Barbarotto, R., Basso, A., Villani, R., Stagnoli, D., & Capitani, E. (1989). Neuropsychological outcome of patients operated for an intracranial aneurysm: analysis of general prognostic factors and of the effects of the location of the aneurysm. *Journal of Neurology, Neurosurgery and Psychiatry*, 52, 1135-1140.
- DeSantis, A., Laiacona, M., Barbarotto, R., De Divitis, O., Migliore, M., & Capitani, E. (1998). Neuropsychological outcome of operated cerebral aneurysms: prognostic factors on 148 patients. *Acta Neurol Scand*, 97, 393-397.
- Derdeyn, C.P., Cross, D.T., Moran, C.J., Brown, G.W., Pilgram, T.K., Diringer, M.N., Grubb, R.J., Rich, K.M., Chicoine, M.R. & Dacey, R.G. (2002). Postprocedure ischemic events after treatment of intracranial aneurysms with Guglielmi detachable coils. *Journal of Neurosurgery*, 96, 837-843.
- Dovey, Z., Misra, M., Thornton, J., Charbel, F.T., Debrun, G.M. & Ausman, J.I. (2001).

- Guglielmi detachable coiling for intracranial aneurysms. *Archives of Neurology*, 58, 559-564.
- Drake, C.G. (1988). Neurosurgical Forum. *Journal of Neurosurgery*, 68, 986-987.
- Fobe, J.L., Haddad, L. & de Souza, A.M. (1999). Cognitive performance in patients with surgically treated aneurysms. *Arq Neuropsiquiatr*, 57, 233-242.
- Friedman, J.A., Nichols, D.A., Meyer, F.B., Pichelmann, M.A., McIver, J.I., Toussaint, G., Axley, P.L. & Brown, R.D. (2003). Guglielmi detachable coil treatment of ruptured saccular cerebral aneurysms: retrospective review of a 10-year single-center experience. *American Journal Of Neuroradiology*, 24, 526-533.
- Fukunaga, A., Uchida, K., Hashimoto, J. & Kawase, T. (1999). Neuropsychological evaluation and cerebral blood flow study of 30 patients with unruptured cerebral aneurysms before and after surgery. *Surgical Neurology*, 51, 132-139.
- Germano, A., Tisano, A., Raffaele, M., Munao, F., Cacciola, F., La Rosa, G., & Tomasello, F. (1997). Is there a group of early aneurysmal SAH patients who can expect to achieve a complete long-term neuropsychological recovery? *Acta Neurochir (Wien)*, 139, 507-514.
- Germano, A., Caruso, G., Caffo, M., Cacciola, F., Belvedere, M., Tisano, A., Raffaele, M., & Tomasello, F. (1998). Does subarachnoid blood extravasation per se induce long-term neuropsychological and cognitive alterations? *Acta Neurochir (Wien)*, 140, 805-812.
- Greenberg, M.S. (1994). *Handbook of neurosurgery* (3rd ed.). Greenberg Graphics
- Gruber, D.P., Zimmerman, G.A., Tomsick, T.A., van Loveren, H.R., Link, M.J. & Tew, J.M. (1999). A comparison between endovascular and surgical management of basilar artery apex aneurysms. *Journal of Neurosurgery*, 90, 898-874.
- Hadjivassiliou, M., Tooth, C.L., Romanowski, C.A.J., Byrne, J., Battersby, R.D E., Oxbury, S., Crewswell, C.S., Burkitt, E., Stokes, N.A., Paul, C., Mayes, A.R., & Sagar, H.J. (2001). Aneurysmal SAH: Cognitive outcome and structural damage after clipping or coiling. *Neurology*, 56, 1672 – 1677.
- Hillis, A.E., Anderson, A., Sampath, P., & Rigamonti, D. (2000). Cognitive impairment after surgical repair of ruptured and unruptured aneurysms. *Journal of Neurology, Neurosurgery and Psychiatry*, 69, 608-615.

- Hop, J.W., Rinkel, G.J.E., Algra, A. & van Gijn, J. (1998). Quality of life in patients and partners after aneurysmal subarachnoid haemorrhage. *Stroke*, 29, 798-804.
- Howell, D.C. (1997). *Statistical Methods for Psychology* (4th ed.). New York: Duxbury Press.
- Hutchinson, P.J.A., Power, D.M., Tripathi, P. & Kirkpatrick, P.J. (2000). Outcome from poor grade aneurysmal subarachnoid haemorrhage – which poor grade subarachnoid haemorrhage patients benefit from aneurysm clipping? *British Journal of Neurosurgery*, 14, 105-109.
- Hütter, B.O. & Gilsbach, J.M. (1993). Which neuropsychological deficits are hidden behind a good outcome (Glasgow=1) after aneurysmal subarachnoid hemorrhage? *Neurosurgery*, 33, 999-1006.
- Hütter, B.O., Gilsbach, J.M. & Kreitschmann, I. (1995). Quality of life and cognitive deficits after subarachnoid haemorrhage. *British Journal of Neurosurgery*, 9, 465-475.
- Hütter, B.O., Kreitschmann-Andermahr, I., & Gilsbach, J.M. (2001). Health-related quality of life after aneurysmal subarachnoid hemorrhage: impacts of bleeding severity, computerised tomography findings, surgery, vasospasm, and neurological grade. *Journal of Neurosurgery*, 94, 241-251.
- Johnston, S.C., Wilson, C.B., Halbach, V.V., Higashida, R.T., Dowd, C.E., McDermott, M.W., Applebury, C.B., Farley, T.L. & Gress, D.R. (2000). Endovascular and surgical treatment of unruptured aneurysms: comparison of risks. *Annals of Neurology*, 48, 11-19.
- Kahara, V.J., Seppanen, S.K., Kuurne, T. & Laasonen, E.M. (1999). Patient outcome after endovascular treatment of intracranial aneurysms with reference to microsurgical clipping. *Acta Neurol Scand*, 99, 284-290.
- Kivisaari, R.P., Salonen, O., & Ohman, J. (2000). Basal brain injury in aneurysm surgery. *Neurosurgery*, 46, 1070-1076.
- Koivisto, T., Vanninen, R., Hurskainen, H., Saari, T., Hernesniemi, J. & Vapalahti, M. (2000). Outcomes of early endovascular versus surgical treatment of ruptured cerebral aneurysms. A prospective randomised study. *Stroke*, 31, 2369-2377.
- Kreiter, K.T., Copeland, D., Bernardini, G.L., Bates, J.E., Peery, S., Claassen, J., Du, E.,

- Stern, Y., Connolly, E.S. & Mayer, S.A. (2002). Predictors of cognitive dysfunction after subarachnoid hemorrhage. *Stroke*, 33, 200-209.
- Kremer, C., Groden, C., Lammers, G., Weinech, G., Zeumer, H., & Hansen, H.C. (2002). Outcome after endovascular therapy of ruptured intracranial aneurysms: morbidity and impact of rebleeding. *Neuroradiology*, 44, 942-945.
- Le Roux, P.D., Elliot, J.P., Newell, D.W., Grady, M.S., & Winn, H.R. (1996). The incidence of surgical complications is similar in good and poor grade patients undergoing repair of ruptured anterior circulation aneurysms: A retrospective review of 355 patients. *Neurosurgery*, 38, 887-895.
- Lempert, T. E., Malek, A.M., Halbach, V.V., Phatouros, C.C., Meyers, P.M., Dowd, C.F. & Higashida, R.T. (2000). Endovascular treatment of ruptured posterior circulation cerebral aneurysms. Clinical and angiographic outcomes. *Stroke*, 31, 100-110.
- Lezak, M.D. (1995). *Neuropsychological Assessment* (3rd ed.). New York: Oxford University Press
- Lindsay, K.W., Bone, I., Callander, R. (1991). *Neurology and neurosurgery illustrated* (2nd ed.). London: Churchill Livingstone.
- Ljunggren, B.; Sonesson, B., Säveland, H. & Brandt, L. (1985). Cognitive impairment and adjustment in patients without neurological deficits after aneurysmal SAH and early operation. *Journal of Neurosurgery*, 62, 673-679.
- Lusseveld, E., Brilstra, E.H. Nijssen, P.C.G., van Rooij, W.J.J., Sluzewski, M., Tullek, C.A.F., Wijnalda, D., Schellens, R.L.L.A., van der Graaf, Y. & Rinkel, G.J.E. (2002). Endovascular coiling versus neurosurgical clipping in patients with a ruptured basilar tip aneurysm. *Journal of Neurology, Neurosurgery and Psychiatry*, 73, 591-591.
- Maurice-Williams, R.S., Willison, J.R. & Hatfield, R. (1991). The cognitive and psychological sequelae of uncomplicated aneurysm surgery. *Journal of Neurology, Neurosurgery and Psychiatry*, 54, 335-340.
- McKenna, P., Willison, J.R., Lowe, D. & Neil-Dwyer, G. (1989). Cognitive outcome and quality of life one year after subarachnoid haemorrhage. *Neurosurgery*, 24, 361-367.

- Molyneux, A., Kerr, R., Stratton, I., Sandercock, P., Clarke, M., Shrimpton, J. & Holman, R. (2002). International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *Lancet*, 360, 1267 – 1274.
- Mountain, M.A. & Snow, W.G. (1993). Wisconsin Card Sorting test as a measure of frontal pathology: A review. *Clinical Neuropsychologist*, 7, 108 – 118.
- Morgan, A.B. & Lilienfeld, S.O. (2000). A meta-analytic review of the relation between antisocial behaviour and neuropsychological measures of executive function. *Clinical Psychology Review*, 20, 113 – 156.
- Murayama, Y., Song, J.K., Uda, K., Gobin, P., Duckwiler, G.R., Tateshima, S., Patel, A.B., Martin, N.A., & Vinuela, F. (2003). Combined endovascular treatment for both intracranial aneurysm and symptomatic vasospasm. *American Journal of Neuroradiology*, 24, 133-139.
- Ogden, J.A., Levin, P.L. & Mee, E.W. (1990). Long-term neuropsychological and psychosocial effects of subarachnoid haemorrhage. *Neuropsychiatry, Neuropsychology and Behavioural Neurology*, 3, 260-274.
- Ogden, J.A., Mee, E.W., & Henning, M. (1993). A Prospective study of impairment of cognition and memory and recovery after subarachnoid haemorrhage. *Neurosurgery*, 33, 572-587.
- Ogden, J.A., Utley, T., & Mee, E.W. (1997). Neurological and psychosocial outcome 4 to 7 years after subarachnoid hemorrhage. *Neurosurgery*, 41, 25-34.
- Ogungbo, B., Gregson, B.A., Blackburn, A. & Mendelow, A.D. (2001). Trends over time in the management of subarachnoid haemorrhage in Newcastle: review of 1609 patients. *British Journal of Neurosurgery*, 15, 388-395.
- Ohman, J., Servo, A., & Heiskanen, O. (1991). Risk factors for cerebral infarction in good-grade patients after aneurysmal subarachnoid hemorrhage and surgery: a prospective study. *Journal of Neurosurgery*, 74, 14-20.
- Ohue, S., Oka, Y., Kumon, Y., Ohta, S., Sakaki, S., Hatakeyama, T., Shiraishi, T., Takeda, S., & Ohnishi, T. (2003). Importance of neuropsychological evaluation after surgery in patients with unruptured cerebral aneurysms. *Surgical Neurology*, 59, 269-276.

- Ogilvy, C.S., Hoh, B.L., Singer, R.J. & Putman, C.M. (2002). Clinical and Radiographic Outcome in the management of posterior circulation aneurysms use of direct surgical or endovascular techniques. *Neurosurgery*, 51, 14-22.
- Powell, J., Kitchen, N., Heslin, J. & Greenwood, R. (2002). Psychosocial outcomes at three and nine months after good neurological recovery from aneurysmal subarachnoid haemorrhage: predictors and prognosis. *Journal of Neurology Neurosurgery Psychiatry*, 72, 772-781.
- Proust, F., Hannequin, D., Langlois, O., Freger, P. & Creissard, P. (1995). Causes of morbidity and mortality after ruptured aneurysm surgery in a series of 230 patients. The importance of control angiography. *Stroke*, 26, 1553-1557.
- Rabinstein, A.A. & Nichols, D. A. (2002). Endovascular coil embolization of cerebral aneurysm remnants after incomplete surgical obliteration. *Stroke*, 33, 1809 – 1815.
- Raaymakers, T.W.M. (2000). Functional outcome and quality of life after angiography and operation for unruptured intracranial aneurysms. *Journal of Neurology, Neurosurgery and Psychiatry*, 68, 571-576.
- Raftopoulos, C., Goffette, P., Vaz, G., Ramzi, N., Scholtes, J., Wittebole, X. & Mathurin, P. (2003). Surgical clipping may lead to better results than coil embolization: Results from a series of 101 consecutive unruptured intracranial aneurysms. *Neurosurgery*, 52, 1280-1290.
- Raymond, J. & Roy, D. (1997). Safety and efficacy of endovascular treatment of acutely ruptured aneurysms. *Neurosurgery*, 41, 1235-1246.
- Richardson, J.T.E. (1991). Cognitive performance following rupture and repair of intracranial aneurysm. *Acta Neurol. Scand*, 83, 110-122.
- Romner, B., Sonesson, B., Ljunggren, B., Brandt, L., Saveland, H., & Holtas, S. (1989). Late magnetic resonance imaging related to neurobehavioral functioning after aneurysmal subarachnoid haemorrhage. *Neurosurgery*, 25, 390-397.
- Roos, Y.B.W.E.M., de Haan, R.J., Beebe, L.F.M., Groen, R.J.M, Altrecht, K.W. & Vermeulen, M. (2000). Complications and outcome in patients with aneurysmal subarachnoid haemorrhage: a prospective hospital based cohort study in The Netherlands. *Journal of Neurology Neurosurgery and Psychiatry*, 68, 337-341.
- Ropper, A.H. & Zervas, N.T. (1984). Outcome 1 year after SAH from cerebral aneurysm.

- Management morbidity, mortality and functional status in 112 consecutive good risk patients. *Journal of Neurosurgery*, 60, 909-915.
- Saciri, B.M., & Kos, N. (2002). Aneurysmal subarachnoid haemorrhage: outcomes of early rehabilitation after surgical repair of ruptured intracranial aneurysms. *Journal of Neurology Neurosurgery Psychiatry*, 72, 334-337.
- Säveland, H., Sonesson, B., Ljunggren, B., Brandt, L., Uski, T., Zygmunt, S., & Hindfelt, B. (1986). Outcome evaluation following subarachnoid haemorrhage. *Journal of Neurosurgery*, 64, 191-196.
- Säveland, H., Uski, T., Sjöholm, H., Sonesson, B., & Brandt, L. (1996). SPECT with Technetium-99m-HMPAO in relation to late cognitive outcome after surgery for ruptured cerebral aneurysms. *Acta Neurochir (Wien)*, 138, 301-307.
- Sethi, H., Moore, A., Dervin, J., Clifton, A. & MacSweeney, J.E. (2000). Hydrocephalus: comparison of clipping and embolization in aneurysm treatment. *Journal of Neurosurgery*, 92, 991-994.
- Sonesson, B., Ljunggren, B., Säveland, H. & Brandt, L. (1987). Cognition and adjustment after late and early operation for ruptured aneurysm. *Neurosurgery*, 21, 279-287.
- Stenhouse, L.M., Knight, R.G., Longmore, B.E. & Bishara, S.N. (1991). Long-term cognitive deficits in patients after surgery on aneurysms of the anterior communicating artery. *Journal of Neurology, Neurosurgery and Psychiatry*, 54, 909-914.
- Tateshima, S., Murayama, Y., Gobin, Y.P., Duckwiler, G.R., Guglielmi, G & Vinuela, F. (2000). Endovascular treatment of basilar tip aneurysms using Guglielmi detachable coils: Anatomic and clinical outcomes in 73 Patients from a single institution. *Neurosurgery*, 47, 1332-1342.
- Taylor, A. & Le Feuvre, D. (2004). The impact of endovascular treatment on cerebral aneurysm outcome at Groote Schuur Hospital. *South African Medical Journal*, 94, 977-980.
- Thornton, J., Debrun, G.M., Aletich, V.A., Bashir, Q., Charbel, F.T. & Ausman, J. (2002). Follow-up angiography of intracranial aneurysms treated with endovascular placement of Guglielmi detachable coils. *Neurosurgery*, 50, 239-250.
- Tidswell, P., Dias, P.S., Sagar, H.J., Mayes, A.R. & Battersby, R.D.E. (1995). Cognitive

- outcome after aneurysm rupture: Relationship to aneurysm site and perioperative complications. *Neurology*, 45, 875-882.
- Tuffiash, E., Tamargo, R.J., & Hillis, A.E. (2003). Craniotomy for treatment of unruptured aneurysms is not associated with long-term cognitive dysfunction. *Stroke*, 34, 2195-2199.
- Van den Berg, R., Rinkel, G.J.E., & Vandertop, W.P. (2003). Treatment of ruptured intracranial aneurysms: implications of the ISAT on clipping versus coiling. *European Journal of Radiology*, 46, 172-177.
- Van Loon, J., Waerzeggers, Y., Wilms, G., van Calenbergh, F., Goffin, J., & Plets, C. (2002). Early endovascular treatment of ruptured cerebral aneurysms in patients in very poor neurological condition. *Neurosurgery*, 50, 457-465.
- Van Swieten, J.C., Koudstaal, P.J., Visser, M.C., Schouten, H.J.A. & van Gijn, J. (1988). Interobserver agreement for the assessment of handicap in stroke patients. *Stroke*, 19, 604-607.
- Vanninen, R., Koivisto, T., Saari, T., Hernesniemi, J. & Vapalahti, M. (1999). Ruptured intracranial aneurysms: acute endovascular treatment with electrolytically detachable coils – A prospective randomised study. *Radiology*, 211, 325-336.
- Vilkki, J., Holst, P., Ohman, J., Servo, A., & Heiskanen, O. (1989). Cognitive deficits related to computed tomographic findings after surgery for a ruptured intracranial aneurysm. *Neurosurgery*, 25, 166-172.
- Vilkki, J., Holst, P., Ohman, J., Servo, A., & Heiskanen, O. (1990). Social outcome related to cognitive performance and computed tomographic findings after surgery for a ruptured intracranial aneurysm. *Neurosurgery*, 26, 579-585.
- Walsh, K. & Darby, D. (1999). *Neuropsychology: a clinical approach* (4th ed.). Edinburgh: Churchill Livingstone.
- Wechsler, D. (1998). *Wechsler Adult Intelligence Scale: Administration and Scoring Manual* (3rd ed.). London: The Psychological Corporation
- Wechsler, D. (1998). *Wechsler Memory Scale: Administration and Scoring Manual* (3rd ed.). London: The Psychological Corporation
- Wiebers, D.O. (1998). Unruptured intracranial aneurysms- risk of rupture and risks of surgical intervention. *The New England Journal of Medicine*, 339, 1725-1733.

Wiebers, D.O. (2003). Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet*, 362, 103-110.

University of Cape Town

Appendices

Appendix 1 - WFNS Grading of SAH

WFNS grade	Glasgow Coma Scale	Major focal deficit +
0#	-	-
1	15	Absent
2	13-14	Absent
3	13-14	Present
4	7-12	Absent or present
5	3-6	Absent or present

intact aneurysm + aphasia and/or hemiparesis or hemiplegia

Appendix 2 - Glasgow Outcome Scale (GOS)

Grade	Description
Grade 1	Good recovery; patient can lead a full and independent life with or without minimal neurological deficit
Grade 2	Moderately disabled; patient has neurological or intellectual impairment but is independent
Grade 3	Severely disabled; patient conscious but totally dependent on others to get through daily activities
Grade 4	Vegetative survival
Grade 5	Dead

Appendix 3 - Grading system of Fisher

Fisher Group	Blood on CT
1	No subarachnoid blood detected
2	A diffuse disposition or thin layer with all vertical layers of blood (interhemispheric fissure, insular cistern, ambient cistern) less than 1 mm thick
3	Localised clots and/or vertical layers of blood 1 mm or greater in thickness
4	Diffuse or no subarachnoid blood, but with intracerebral or intraventricular blood

Appendix 4 - Patients Consent Form

TITLE OF PROJECT: Cognitive outcome of aneurysmal subarachnoid haemorrhage after clipping or coiling: A comparative post-intervention study in a hospital population

Have you read the information sheet? YES/NO

Have you had the opportunity to ask any questions you might have regarding the study? YES/NO

Have you received satisfactory answers to 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
 - Without affecting your future treatment
- YES/NO

Have you been given a copy of the information sheet and this consent form? YES/NO

Signed _____ Date _____

(NAME IN BLOCK LETTERS) _____

Appendix 5 - Patients Information Sheet

TITLE OF PROJECT:

Cognitive outcome of aneurysmal subarachnoid haemorrhage after clipping or coiling: A comparative post-intervention study in a hospital population

- You are invited to participate in a neuropsychological study conducted at Groote Schuur Hospital. Please read this information sheet carefully and do not hesitate to ask the researcher for any additional information.
- The overall purpose of this study is to test your mental functioning after you have received treatment for your aneurysm.
- You will be asked to participate in a number of different mental tasks. These tasks will basically test your memory, comprehension, verbal and attention abilities.
-
- You will also be asked to complete a questionnaire regarding personal issues and circumstances.
- 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 should inform the investigator immediately.
- It is up to you to decide whether or not to 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 in this study, 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 identity will be protected.
-
- The study has been reviewed by the Groote Schuur Hospital Ethics Committee.
- If you have any questions regarding this study or the way it was carried out or would like to know what the results of the study were, please feel free to contact the researcher. Contact details of the researcher are given at the bottom of this page.

Eleni Pantelis, Psychology Department, University of Cape Town; Tel: 021 – 975 3411 (h)
(cell) 082 775 2081

Appendix 6 - Neuropsychological Tests

Test	Cognitive Function Assessed	Specific sub-score selected
WART	Estimate of premorbid IQ	Standard score
Digit Symbol subtest of WAIS	Test of psychomotor performance, motor persistence, sustained attention, response speed and visuomotor co-ordination (Wechsler, 1998)	Standard score
Similarities subtest of WAIS	Test of verbal concept formation and general mental ability (Wechsler, 1998)	Standard score
Block Design subtest of WAIS	Test of construction, visuospatial conceptualisation, planning and ability to perceive errors and correct them (Wechsler, 1998).	Standard score
Digit Span subtest of WAIS	Test of span of immediate verbal recall, mental tracking and attentional capacity (Wechsler, 1998)	Standard score
Comprehension subtest of WAIS	Test of common-sense judgement and practical reasoning (Wechsler, 1998)	Standard score
Logical Memory I subtest of WMS	Test of immediate verbal memory (Wechsler, 1998)	Score for Total Recall
Logical Memory II subtest of WMS	Test of delayed verbal memory (Wechsler, 1998)	Score for Total Recall Score for Recognition Recall
Faces I subtest of WMS	Test of immediate visual memory (Wechsler, 1998)	Recognition Total Score
Faces II subtest of WMS	Test of delayed visual memory (Wechsler, 1998)	Recognition Total Score
Verbal Paired Associates I subtest of WMS	Test of word learning with built in cueing (Wechsler, 1998)	Score for Total Recall
Verbal Paired Associates II subtest of WMS	Test of delayed word learning with built-in cueing (Wechsler, 1998)	Score for Total Recall
Rey Complex Figure – Copy trial	Test of visuospatial construction and perceptual organisation. Also tests ability to program and plan approach to copy	Standard score

	task (Lezak, 1995)	
Rey Complex Figure – Immediate Recall	Test of immediate visual recall (Lezak, 1995)	Standard score
Rey Complex Figure – Delayed Recall	Test of delayed visual recall (Lezak, 1995)	Standard score
Trail Making Condition 4 subtest of D-KEFS	Test of cognitive flexibility on visual-motor sequencing task. Primary executive function task (Delis et al., 1995)	Completion time for Condition 4
Verbal Fluency (Conditions 1, 2 and 3) subtest of D-KEFS	Test of initiation, simultaneous processing (i.e. observing multiple rules), systematic retrieval of phonetically similar lexical items, speed of processing and cognitive flexibility (Delis et al, 1995).	Score for Total correct responses for conditions 1 and 2 Score for Total correct responses for condition 3 Score for Total errors for conditions 1, 2 & 3
Design Fluency (Conditions 2 and 3) subtest of D-KEFS	Test of fluency in generating visual patterns, basic visual attention, visual-perceptual skills, constructional skills, motor speed, problem-solving behaviour, cognitive shifting and inhibition (Delis et al, 1995)	Score for Total correct designs for conditions 2 & 3.
Sorting subtest of D-KEFS	Test of concept formation, problem-solving and ability to inhibit previous sorting responses in order to engage in flexibility of thinking (Delis et al., 1995)	Score for Total correct sorts on free-sort condition Score for Total correct on recognition condition
20 Questions subtest of D-KEFS	Test of categorisation, ability to form higher- level conception and ability to use feedback to guide problem-solving behaviour (Delis et al., 1995)	Score for initial abstraction
Tower of London subtest of D-KEFS	Test of spatial planning, rule-learning, inhibition of impulsive and perseverative responding and ability to establish and maintain instructional set.	Score for Total Achievement Score for Total Completion Time Score for Total number of rule violations

Appendix 7 – Quality of Life Questionnaire

Section A:

1. Were you working at the time when you had your stroke?
2. Are you currently back at your old work? If no, why?
3. Are you having more difficulties at work?
4. If yes, what kind of difficulties?
5. Were you unhappy in your job prior to your stroke?
6. Are you currently experiencing any marital or family problems? If yes, please describe.
7. Are you currently experiencing any socioeconomic difficulties such as unemployment, inadequate income or poor living conditions?
8. Has there recently been a death or serious physical illness of someone close?
9. Have there been other serious medical conditions other than your stroke?
10. Are you feeling depressed? If yes, please explain why?

Section B:

1. Have you been more irritable since your stroke?
“0” better “1” no change “2” bit worse “3” lot worse”
2. Have you felt more anxious since your stroke?
“0” better “1” no change “2” bit worse “3” lot worse”
3. Have you noticed a change in your desire to pursue activities of self-interest such as hobbies?
“0” better “1” no change “2” bit worse “3” lot worse”
4. Have you noticed a change in your willingness to spontaneously initiate things at home?
“0” better “1” no change “2” bit worse “3” lot worse”
5. Have you noticed a difference in your mood swings?
“0” better “1” no change “2” bit worse “3” lot worse”
6. Have you noticed any change in your ability to concentrate?
“0” better “1” no change “2” bit worse “3” lot worse”
7. Do you find that you are more absentminded than before?
“0” better “1” no change “2” bit worse “3” lot worse”
8. Do you find that you forget people’s names more than before?
“0” better “1” no change “2” bit worse “3” lot worse”
9. Do you find that you are more distractible than before?

“0” better “1” no change “2” bit worse “3” lot worse”

10. Have you noticed a change in your memory?

“0” better “1” no change “2” bit worse “3” lot worse”

11. Do you speak as fluently as before?

“0” better “1” no change “2” bit worse “3” lot worse”

12. Do you find that you are having more trouble understanding what other people say?

“0” better “1” no change “2” bit worse “3” lot worse”

13. Have you noticed if other people struggle to understand what you are trying to say ?

“0” better “1” no change “2” bit worse “3” lot worse”

14. Have you noticed a change in your willingness to socialise with friends and family?

“0” better “1” no change “2” bit worse “3” lot worse”

15. Have you noticed a change in your relationships with those close to you?

“0” better “1” no change “2” bit worse “3” lot worse”

16. Have you noticed a change in your levels of energy?

“0” better “1” no change “2” bit worse “3” lot worse”

17. Do you feel more dependent on those around you to get through the day

“0” better “1” no change “2” bit worse “3” lot worse”

University of Cape Town