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The Relationship Between Brain Injury and Behavioural Consequences of Thalamic Stroke

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Statement of Originality

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Signed _______________________________________


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Abstract

Scope

Stroke is a leading cause of death and disability in Australia and indeed the world. Research has consistently demonstrated that factors such as high cholesterol, hypertension, smoking, obesity, and diabetes increase the risk of stroke. These factors can also play a role in mortality and recovery from stroke.

Some recent studies have also begun investigating anatomical factors, and their role in stroke. Anatomical variances in major circulation pathways such as the circle of Willis have been linked with higher disability rates in stroke. Similarly, larger basilar artery measurements have been linked with poorer stroke outcomes.

Stroke generally leads to motor, cognitive and behavioural impairments. The motor and physical results of stroke are well reported and treated. However, post-stroke cognitive and behaviour changes receive much less attention in the literature. Furthermore, outcomes of cognitive and behavioural focused rehabilitation are sparsely reported.

Strokes affecting the thalamus have been given some attention in the literature due to their varied and extensive outcomes. Different outcomes have been reported based on both the specific location of the stroke lesion and the size or volume of the lesion. However, as with general stroke research, the outcomes investigated and reported are generally motor and physical changes. There is only minimal research into the cognitive and behavioural outcomes of thalamic stroke.

Purpose

This study aims to identify susceptibility factors in thalamic stroke including well-known risk factors and more newly identified factors such as anatomical variations. Furthermore, this study aims to examine outcomes in thalamic stroke, with a more detailed focus on cognitive and behavioural outcomes. It is hoped that this information may provide direction for rehabilitation and treatment in the future.
**Methods**

Ten patients with thalamic stroke were identified from the John Hunter Hospital Stroke Unit admission records. These patients participated in a demographic and behavioural data gathering interview. Nine of the 10 patients then completed the Audio Recorded Cognitive Screen (ARCS) to gain meaningful neuropsychological data. MRI scans for all 10 patients were examined to determine localisation and size of the lesion, as well as basilar artery size and anatomical variances in the circle of Willis.

**Results**

Consistent with previous data, risk factors such as high cholesterol, high blood pressure, and pre-existing heart conditions were identified in this small sample. In contrast to well-known risk factors, no participants reported being smokers prior to their stroke.

Circle of Willis variations were found in six of the 10 participants. Patient MRIs indicated that the posterior communication artery (PCOM) was absent or failed to join the posterior cerebral artery (PCA) in these six cases. However, basilar artery measurements were found to be no larger than would be expected in the general population.

Participants and their carers (where applicable) reported post-stroke changes such as decreased coordination, reduced mobility, poor balance, reduced energy, memory deficits, and mood changes. Participants’ overall scaled scores on the ARCS were significantly lower than same age peers.

More specifically, performance on the ARCS domains of memory, fluency, language and attention were all significantly below age norms. Interestingly, only three of the participants recalled having any form of psychological or neuropsychological interventions post-stroke.

**Conclusions**

The findings of this study are primarily consistent with previous research. However, the study’s very small sample size limits the significance and applicability of these findings. The risk factors identified in this study were primarily consistent with those previously identified in the literature. In addition to these, it is possible that variations in the circle of Willis may be an indicator of thalamic stroke susceptibility.
This study has identified cognitive deficits in areas such as memory and attention. Whilst this is consistent with previously reported observations, the present study has been able to provide more detailed cognitive data and age norm comparisons. Several participants also reported mood changes following their stroke. These cognitive and mood changes warrant investigation into the benefits of psychological and neuropsychological rehabilitation in thalamic stroke.
Critical Literature Review

The burden of stroke

Cerebrovascular accidents, more commonly known as a brain attacks or strokes, are the second leading cause of death worldwide (Moskowitz, Lo, & Iadecola, 2010). Stroke is also the leading cause of acquired disability in adults in most regions of the world (Addo et al., 2012; CDC, 2012; O'Donnell et al., 2010). In addition to this impact on health and mortality, the financial cost of stroke is considerable. Care for stroke survivors cost an estimated 18.8 billion dollars in the United States in 2008, plus an additional 15.5 billion dollars in lost productivity and premature mortality (CDC, 2012).

In Australia, stroke is estimated to affect approximately 45,000 people each year (March, 2011). Similar to worldwide statistics, stroke is the second leading cause of death in Australia. Of all Australians presenting with their first stroke, approximately 35 percent will die within 12 months of the stroke. Of those who survive, around 50 percent will become dependent on others for their care (Cadilhac, Dewey, Vos, Carter, & Thrift, 2010). Furthermore, the health cost of stroke is generally estimated to account for approximately two percent of health care expenditure by the Australian Government (Cadilhac, Carter, Thrift, & Dewey, 2009).

However, health expenditure data are likely to underestimate the true cost of stroke, as it accounts for direct costs to government only (Cadilhac, et al., 2009). Other estimates take into account loss of production due to inability to work or perform household tasks, informal care costs, out of pocket expenses incurred by stroke patients, and costs incurred by carers. With these factors considered, cost estimates nearly double to around two billion Australian dollars per year (Cadilhac, et al., 2009).

Outside of the financial impact, stroke heavily affects quality of life and life expectancy (Moskowitz, et al., 2010). Australian data estimates that a person presenting with a first stroke will lose five to six years of healthy and/or quality life when compared to the general population. Furthermore, health loss has been found to increase over time, indicating that secondary and non-stroke related disabilities further reduce health and quality of life following a first stroke (Cadilhac, et al., 2010).
**What is stroke?**

A stroke occurs when there is a disturbance in the blood supply to the brain (Stroke prevention, 2012). This can transpire in two ways and as such there are two types of stroke. Haemorrhagic stroke occurs when a blood vessel bursts and there is resultant bleeding into brain tissue (De Silva, Silva, Gunasekera, & Jayesekera, 2009; Stroke prevention, 2012). Ischaemic stroke is the converse, and occurs as a result of a blockage in the arteries. This blockage can be due to the formation of a blood clot at the site of the blockage, a mechanism known as thrombosis. Alternatively, a blood clot may form elsewhere in the body and travel to the blockage site, known as an embolism (Moskowitz, et al., 2010). This results in areas of the brain being starved of blood supply (Stroke prevention, 2012).

Ischaemic strokes are more common than haemorrhagic strokes, and account for approximately 85 percent of reported strokes (Stroke prevention, 2012). Whether a stroke is ischaemic or haemorrhagic, the result is an inability of the affected brain area to function. This can manifest itself in symptoms such as paralysis, impaired speech, loss of vision (Moskowitz, et al., 2010), and cognitive deficits (March, 2011).

There are few neurological conditions as multifaceted and devastating as stroke (Moskowitz, et al., 2010). Yet, it is a highly preventable condition, with both modifiable and non-modifiable risk factors well established and documented (March, 2011).

**Risk factors**

A stroke risk factor is a characteristic of an individual that increases their likelihood and risk for stroke when compared to someone without that characteristic (Moskowitz, et al., 2010). Some of these risk factors cannot be modified. Whilst other risk factors, such as lifestyle characteristics, can be modified to reduce the risk of stroke (Moskowitz, et al., 2010). It is estimated that modifiable risk factors account for 60 to 80 percent of stroke risk in the general population (Moskowitz, et al., 2010).

There is a significant amount of literature available in regards to modifiable stroke risk factors. This includes research papers and health authority issued educational material (March, 2011). Identified modifiable risk factors include smoking, weight range, hypertension, cholesterol, alcohol consumption, diet, exercise, and stress levels (O'Donnell, et al., 2010).
Smoking is perhaps one of the most publicised heart and cerebrovascular event risk factors (Bühler, Vesanan, Watters, & Bolli, 1988). Cigarette smoking is a well established risk factor for initial and recurrent stroke (Weng et al., 2011). This risk is independent of other risk factors, and the risk has been shown to increase with the number of cigarettes smoked (Hawkins, Brown, & Davis, 2002).

Smoking has been shown to increase the risk of stroke by as much as double (Bühler, et al., 1988). It is also estimated to be responsible for up to one quarter of all strokes (Hawkins, et al., 2002). However, smoking’s role in the severity of stroke is unclear. In some cases, smoking has been shown to exacerbate the severity of stroke, while in other cases it has no shown effect or may even reduce the initial severity of the stroke (Weng, et al., 2011).

Whilst the association between smoking and increased stroke risk has been demonstrated and reported (Moskowitz, et al., 2010), the mechanisms for this relationship are less reported. Some research indicates that smoking plays a role in the development of atherosclerosis, or hardening of the arteries, which can lead to the development of an embolism or thrombosis (Hawkins, et al., 2002). Chronic smoking is also linked with a reduction in cerebral blood flow, again related to atherosclerosis (Hawkins, et al., 2002) and vascular constriction (Bühler, et al., 1988).

Further research focuses on the hyperadrenergic state caused by smoking. This presents as increased heart rate and exaggerated release of adrenaline and noradrenaline. This state is said to lead to platelet aggregation and ultimately thromboembolic complications (Bühler, et al., 1988).

Whilst a causal link between cigarette smoking and stroke has been frequently reported, it is not the only risk factor. Hypertension, or high blood pressure, has also been consistently linked with stroke (E et al., 1997; Moskowitz, et al., 2010; O'Donnell, et al., 2010). It has, in some cases, been named as the single most important risk factor (Dubow & Fink, 2011; Johansson, 1999).

Hypertension can cause stroke through a number of mechanisms. High pressure in the arteries can lead to changes in the endothelium and smooth muscle function in these arteries (Johansson, 1999). This can increase permeability of the blood-brain barrier and hence
increase the potential for bleeding into brain tissue. Hypertension can also accelerate the process of arteriosclerosis, which can then lead to thrombus and clot formation (Johansson, 1999).

Increased blood pressure has been shown to increase the chance of stroke by up to 40 percent (Johansson, 1999). Studies have found that hypertension accounts for approximately 35 percent of population attributable risk (O'Donnell, et al., 2010). However, the direct link between hypertension and stroke is difficult to isolate as many people with high blood pressure also have other stroke risk factors present. These may include poor diet, lack of exercise and/or smoking. These are risk factors for stroke on their own, but are also contributors to hypertensive risk (March, 2011).

Poor diet, lack of exercise, and high body mass index (BMI) are risk factors that are often interlinked (O'Donnell, et al., 2010). High daily dietary intake of fat is associated with weight gain and higher BMI. Fat intake may act as an independent risk factor, or may affect other risk factors such as hypertension, diabetes, hyperlipidemia, and cardiac disease (Boden-Albala & Sacco, 2000). Obesity, or high BMI, is consistently linked with an increased risk of stroke independent of gender or ethnic background (Katsiki, Ntaios, & Vemmos, 2011).

Several research papers have reported a relationship between BMI and risk of stroke (Katsiki, et al., 2011; Rheaume, Leblanc, & Poirier, 2011; Vemmos et al., 2011). Waist to hip ratio, a measure of excess body fat, has been named as an independent risk factor for stroke (Katsiki, et al., 2011; Rheaume, et al., 2011). However, the mechanisms for this relationship are complex and not yet well defined. Secondary diseases such as hypertension, cholesterol and insulin resistance resulting from obesity are also risk factors in stroke (Towfighi, Zheng, & Ovbiagele, 2010). However, proteins and chemicals secreted by body fat may also affect changes in the vascular wall, inflammation and insulin resistance (Katsiki, et al., 2011).

However, the link between body fat and stroke is not straight forward. Although high BMI is likely related to increased risk, obesity has been linked to better outcomes following stroke (Vemmos, et al., 2011). Several studies have shown an inverse relationship between obesity and outcomes in stroke. Overweight and obese patients have lower early and long-term mortality compared with those in a normal weight range (Katsiki, et al., 2011; Vemmos, et al., 2011). The mechanisms for this relationship are still being investigated. However, factors
such as the increased use of hypertensive, anticoagulant, and lipid reduction medications in overweight and obese patients are hypothesised to play a role (Vemmos, et al., 2011).

Diet is also a key stroke risk factor. A diet high in sugar, fat, and nutrient-dense foods is linked with weight gain and obesity and hence with risk of stroke. However, a diet that is high in salt is linked with hypertension, and therefore increases risk of stroke. Hence, a diet that is high in whole grains, fruits and vegetables is likely to reduce the risk of stroke (Medeiros, Casanova Mde, Fraulob, & Trindade, 2012).

Similar to diet, exercise is a significant mediator in the risk of stroke. Aerobic exercise has been linked with weight reduction, blood pressure management, diabetes management, and increased overall health (Boden-Albala & Sacco, 2000; Kurl et al., 2001). As such, people who do not engage in regular exercise are at higher risk of obesity, hypertension, diabetes, and poor general health, and hence are at greater risk of stroke. Health campaigns focusing on stroke and heart disease prevention recommend 30 minutes of exercise per day (Boden-Albala & Sacco, 2000; March, 2011).

Other lifestyle factors also put an individual at risk of stroke. Heavy consumption of alcohol, that is more than 60 grams per day, can increase the relative risk of stroke (Hillbom, Saloheimo, & Juvela, 2011; Reynolds et al., 2003). Alcohol may contribute to the risk of stroke in several ways. Firstly, alcohol has been shown to increase hypertension and alcohol-induced peaks in blood pressure may predispose an individual to stroke (Gorelick, 1987; Hillbom, et al., 2011; Reynolds, et al., 2003).

Furthermore, alcohol has been linked to cardiac arrhythmias and cardiac wall motion abnormalities. Alcohol has also been linked with reduced cerebral blood flow and increased clotting in the blood (Gorelick, 1987). However, light consumption of alcohol may actually be a protective factor against stroke (Reynolds, et al., 2003).

Lifestyle factors such as alcohol consumption, diet, exercise, and smoking can also lead to diseases such as diabetes and heart disease, both of which are risk factors for stroke (O'Donnell, et al., 2010). Cumulative data on diabetes and stroke indicates that around one in every eight or nine cases of stroke is attributable to diabetes (Luitse, Biessels, Rutten, & Kappelle, 2012). Moreover, individuals with diabetes are two to six times more susceptible to
stroke than those without the disease (Ergul, Kelly-Cobbs, Abdalla, & Fagan, 2012). Diabetes causes artherosclerotic changes in the heart and arteries. Furthermore, the risk of atrial fibrillation, a major cause of stroke, is increased by around 40 percent in individuals with diabetes (Luitse, et al., 2012).

Heart or cardiovascular diseases, such as coronary heart disease, are precursors to up to 20 percent of strokes (O'Donnell, et al., 2010). Coronary heart disease alone is responsible for about one in every six deaths in America. The mechanism of this disease is hardening and blocking of the arteries, also a mechanism of stroke. As such, it is no surprise that being diagnosed with one cardiovascular disease increases an individual’s chances of stroke (O'Donnell, et al., 2010; Roger et al., 2012).

There is also some evidence to indicate that psychosocial factors can play a role in stroke susceptibility (Boden-Albala & Sacco, 2000; Moskowitz, et al., 2010; O'Donnell, et al., 2010). High pre-morbid levels of anxiety have been found in up to 72 percent of stroke victims (Gafarov, Gromova, Gagulin, & Pilipenko, 2004). Furthermore, stress is known to activate the hypothalamic-pituitary-adrenal (HPA) axis. Extended activation of the HPA axis is associated with neurodegeneration, and further linked with increased risk of stroke (Stuller, Jarrett, & DeVries, 2012). Stress is also linked with decreased immune efficiency, and in some cases is linked with the onset of cardiovascular incidents such as stroke and heart attacks (O'Donnell, et al., 2010; Stuller, et al., 2012).

Stress, pre-existing heart disease, diabetes, alcohol intake, diet, exercise, body weight, hypertension and cigarette smoking are all risk factors for stroke. They are almost always interlinked, and are highly modifiable (Boden-Albala & Sacco, 2000; Heeley et al., 2011; O'Donnell, et al., 2010). However, there are some stroke risk factors that are not modifiable.

Socioeconomic status (SES) is perhaps one of the most widely researched non-modifiable risk factors. This is probably because SES itself does not cause stroke, and as such secondary factors that come alongside SES may be modifiable (Heeley, et al., 2011). The impact of stroke in low-income areas is approximately three fold when compared with middle and high-income areas (Addo, et al., 2012). This is primarily explained by the fact that people in more deprived areas are also more likely to smoke, consume alcohol, and have diabetes and hypertension, all risk factors for stroke (Heeley, et al., 2011). Higher incidence of stroke,
stroke risk factors, and rates of stroke mortality are observed in low SES areas when compared with high SES areas worldwide (Addo, et al., 2012).

Gender is another factor that has been reported to modify risk of stroke. Females have been reported to differ from males in stroke outcomes, stroke subtypes, and response to treatments (Leslie-Mazwi et al., 2007). Some research indicates that women experience different initial symptoms of stroke, and hence there can be a delay before presenting for treatment (Jerath, Reddy, Freeman, Jerath, & Brown, 2011). However, other studies have found no significant differences in initial presenting symptoms between the sexes (Beal, 2010). Research has indicated that women are more likely to seek treatment for somatic complaints than men, yet are less likely to receive MRI and echocardiography examinations (Giralt et al., 2012).

The prevalence of stroke had been significantly higher in men (Wyller, 1999) until recent years when male and female statistics became comparable (CDC, 2012). 2008 United States data reports a stroke prevalence rate of 2.7 percent amongst all males, compared with 3.3 percent for all females (Roger, et al., 2012). However, differences between the genders become apparent when age is accounted for.

Women have a lower risk of stroke than men when matched by age, up until approximately age 80 to 85 years when women’s risk is significantly higher than men’s (Giralt, et al., 2012; Sealy-Jefferson et al., 2012). Hormone differences, such as estrogen and progesterone levels, are thought to modify risk in women (Katsiki, et al., 2011). Women are likely to have poorer outcomes than men. Women are also generally more affected by stroke, given their stroke is likely to occur at an older age. (Katsiki, et al., 2011).

Age, therefore is also a risk factor for stroke. Risk of stroke increases with age, with the majority of strokes occurring in middle or old age, generally reported as over 49 (Delilovic-Vranic, Alajbegovic, Tiric-Campara, & Todorovic, 2011). The prevalence of modifiable risk factors is generally higher up until the age of about 70 to 80, when these factors decrease. The mean age of first presentation for stroke in women has been reported at around 73, versus 68 years for men (Andersen, Andersen, & Olsen, 2010).

Age and gender are both independent and interlinked risk factors. Race, or ethnicity, is also considered a risk factor. Hispanic or Black race is linked with increased risk of stroke and
poorer stroke outcomes (Moskowitz, et al., 2010). The 2010 United States statistics indicate a 5.9 percent prevalence of stroke amongst Native Americans, and a 3.9 percent prevalence amongst Black Americans. This is compared with a 2.2 and 1.5 percent prevalence amongst White and Asian/Pacific Islander Americans respectively (CDC, 2012).

In Australia, the incidence rate of stroke for Indigenous Australians is reported at around three times the incidence in the non-indigenous population. Furthermore, Aboriginal and Torres Strait Islander individuals are up to seven times more likely to have a stroke between the aged of 35 and 54 (Thrift, Cadilhac, & Eades, 2011). The reasons for these disparities are generally linked with higher rates of modifiable risk factors amongst non-white populations, as well as genetic factors in some races (CDC, 2012; Thrift, et al., 2011).

Genetic and familial factors therefore also play a role in risk of stroke. A family history of stroke or cardiovascular disease can more than double an individual’s likelihood of having a stroke (Liao et al., 1997). Furthermore, there are several single-gene disorders, and phenotypes that have been linked with an increased risk of stroke (Meschia, Worrall, & Rich, 2011). Genetic risk is complex, involving both gene-gene and gene-environment interactions (Hamzi, Tazzite, & Nadifi, 2011). There are also genetic determinants as to how individuals respond to medication treatments such as anticoagulants and cholesterol lowering drugs (Meschia, et al., 2011).

Genetic and familial factors are not the only biological risks. Anatomical features of the brain and circulatory system are gaining increasing interest in the stroke literature. The circle of Willis is a circle of arteries that supply blood to different parts of the brain, located near the base of the brain (Kapoor, Singh, & Dewan, 2008). The circle operates such that if one part of the circle or one of the arteries becomes blocked or narrowed, the other blood vessels in the circle can generally preserve blood flow (Egan, 2005).

The circle of Willis is composed of the anterior cerebral arteries, anterior communication artery, internal carotid arteries, posterior cerebral arteries, and posterior communication artery (PCOM) (Egan, 2005). There are numerous anatomical variants of the ‘typical’ or ‘textbook’ circle of Willis. Some investigations have found over 20 different variations on the typical pattern (De Silva, Silva, Amaratunga, Gunasekera, & Jayesekera, 2011).
However, there is little consensus in the literature as to the prevalence rates of normal or typical circle of Willis anatomy in the general population. Reported rates vary from as low as five percent to as high as around seventy percent (Alastruey, Parker, Peiro, Byrd, & Sherwin, 2007; De Silva, et al., 2011; El-Barhoun, Gledhill, & Pitman, 2009; Kapoor, et al., 2008; Li et al., 2011). Furthermore, there is some evidence to indicate that degeneration of the circle may occur, and as such the prevalence of atypical circles may increase with the age of the population (El-Barhoun, et al., 2009).

Variations in the circle of Willis have been linked with effects on the volume flow rate of blood in the circle of Willis arteries (Tanaka et al., 2006). As the circle of Willis is the main collateral pathway in the cerebral circulation, reduced blood flow means reduced collateral availability. Hence, variations in the circle of Willis have been linked with an increased risk of stroke and transient ischaemic attack (Alastruey, et al., 2007).

A deficient circle of Willis occurs when there is absence of a component vessel, or the underdevelopment of at least one artery, breaking or reducing the continuity of the circle (Alastruey, et al., 2007; Kapoor, et al., 2008). Any of the arteries may be absent or hypoplastic, and more than one artery or bilateral arteries may be affected (De Silva, et al., 2011). One such variation is the absence or hypoplasticity of one or both of the Posterior Communication Arteries (PCOMs). The PCOM connects the three cerebral arteries on each side of the circle of Willis (Egan, 2005).

Again, prevalence rates for this type of variation are inconsistently reported. Whilst absence of the PCOM has been more often reported at around one percent, and hypoplasticity at around 13 percent (Kapoor, et al., 2008), other studies have found absence rates as high as 30 percent (Li, et al., 2011). However, modeling indicates that an absent anterior communication artery is more problematic than an absent PCOM (Alastruey, et al., 2007).

Another part of the circle of Willis, the basilar artery, supplies blood to the posterior part of the circle (Egan, 2005). Recent literature has focused on the role of basilar artery size in risk and outcomes in stroke. Measured at the level of the pons, the mean basilar artery diameter amongst the normal population is approximately 3.2 millimetres (El-Barhoun, et al., 2009; Smoker, Price, Keyes, Corbett, & Gentry, 1986).
A basilar artery diameter greater than 4.3 millimetres has been linked with a higher risk of death from stroke amongst stroke victims (Pico, Labreuche, Gourfinkel-An, & Amarenco, 2006). Basilar artery diameter has also been highlighted as a possible marker or screening factor for diseases linked with stroke, such as Fabry disease (Fellgiebel et al., 2011). Basilar artery diameter has also been associated with degeneration and neurological deterioration both with age (El-Barhoun, et al., 2009), and post stroke (Aoki et al., 2010).

**Effects and Outcomes of Stroke**

Once an individual has had a stroke they are likely to experience cognitive, physical and emotional changes (March, 2011). The severity of these changes is dependent on a number of different factors. These include a person’s pre-morbid health, age, the location of the stroke and the size of the lesion, as well as their response to and participation in treatment (Langhorne, Bernhardt, & Kwakkel, 2011).

A common neurological consequence of stroke is loss or limitation of muscle function. This generally occurs unilaterally, corresponding to the side and part of the brain affected by stroke. The direct effects of this are limitation or loss of movement, mobility and functional ability (Brazzelli, Saunders David, Greig Carolyn, & Mead Gillian, 2011). This can mean changes such as reduced fine motor skills, through to inability to walk, experiencing involuntary movements, inability to use one side of the body, difficulties eating and speaking, and requiring assistance for everyday tasks such as toileting and dressing (Langhorne, et al., 2011; Moskowitz, et al., 2010).

Physical consequences of stroke also include the development of chronic pain, incontinence, impotence and sexual dysfunction, sight disturbances, changes in consciousness and alertness, sleep disturbances, and inability to lift or hold objects (Langhorne, et al., 2011). For example, chronic pain is estimated to effect up to 53 percent of stroke survivors (Klit, Finnerup, Overvad, Andersen, & Jensen, 2011). The rate of erectile dysfunction in male stroke survivors is also estimated at up to around 50 percent (Ossou-Nguiet et al., 2012; Schmitz & Finkelstein, 2010). Sleep disturbances such as sleep disordered breathing (Johnson & Johnson, 2010; Ramar & Surani, 2010), daytime sleepiness and narcolepsy are reportedly present in up to 78 percent of stroke survivors (Pasic, Smajlovic, Dostovic, Kojic, & Selmanovic, 2011). However, sleep disturbances can be both a pre-cursor to stroke and a consequence of stroke (Wallace, Ramos, & Rundek, 2012).
Emotional changes are a common occurrence in stroke survivors. Changes in emotions such as sadness, passivity, denial, disinterest and aggressiveness have been found (Aybek et al., 2005). Research indicates that emotional disorders such as depression and anxiety occur in at least one third of stroke patients in the first year after stroke (Hackett Maree, Anderson Craig, House, & Xia, 2008; Lincoln et al., 2012). Some studies report prevalence of over 50 percent (Khan et al., 2012). These emotional changes tend to be independent of stroke location or size of lesion (Aybek, et al., 2005).

Post stroke dementia (PSD) is a term used to describe global loss of cognitive ability in an individual who has had a stroke (Pasi, Poggesi, Salvadori, & Pantoni, 2012). The combination of PSD and the physical effects of stroke is associated with increased mortality and morbidity (Ankolekar, Geeganage, Anderton, Hogg, & Bath, 2010). The prevalence of PSD at one year following stroke is estimated to be anywhere between six and 40 percent of stroke victims (Ankolekar, et al., 2010; Pasi, et al., 2012). However, these figures do not include stroke victims with cognitive impairment that does not meet criteria for dementia (Ankolekar, et al., 2010).

Cognitive impairment in general is recognised as a frequent consequence of stroke. However, the true prevalence of cognitive impairment amongst stroke victims is difficult to ascertain due to differing definitions as to what is classified as cognitive impairment. Visuo-spatial perception and apraxia, a disorder of motor planning, are examples of specific cognitive domains or impairments that are classified differently in the literature (T. Hoffmann, S. Bennett, C. L. Koh, & K. T. McKenna, 2010b). However, recent reviews have estimated that up to 56 percent of stroke victims have cognitive impairment following their stroke (Hoffmann, et al., 2010b; Patel, Coshall, Rudd, & Wolfe, 2003; Rabadi, Rabadi, Edelstein, & Peterson, 2008).

Cognitive impairment following stroke has been associated with reduced functional performance. Hence, stroke victims with cognitive impairment are likely to be less independent and need more care and assistance with activities of daily living than those without impairment (Hoffmann, et al., 2010b).
Stroke Treatment

Despite the fact that cognitive impairment has been identified as a frequent outcome in stroke, and a significant predictor of mortality, morbidity and dependence on care, treatment for stroke tends to focus on the physical. Health professionals tend to focus on physical measures and outcomes, such as activities of daily living, rather than cognitive deficits and executive function. As such, treatments tend to focus on general physical competencies rather than on cognitive retraining, memory aids and suchlike (Korner-Bitensky, Barrett-Bernstein, Bibas, & Poulin, 2011).

The literature reflects this tendency, but not without exception. A 2010 review of cognitive interventions in stroke survivors identified four randomised control, or quasi-randomised control studies evaluating cognitive retraining interventions (T. Hoffmann, S. Bennett, C. L. Koh, & K. McKenna, 2010a). Similarly, a 2007 Cochrane review identified 12 randomised control trials that examined the outcomes of cognitive rehabilitation for spatial neglect following stroke (Bowen & Lincoln, 2007). A 2008 Cochrane review identified just two randomised control trials examining the effect of cognitive rehabilitation for memory impairment following stroke (Nair & Lincoln, 2007). Finally, a 2011 Cochrane review identified one randomised control trial that examined the outcomes of occupational therapy as treatment for cognitive impairment following stroke (Hoffmann, Bennett, Koh, & McKenna, 2011). Unfortunately, such small numbers of research trials has lead to inconclusive evidence (Hoffmann, et al., 2010a).

Hoffmann et al. (Hoffmann, et al., 2010a) found that there were no statistically significant improvements in measures of activities of daily living for stroke survivors who received cognitive retraining treatment, as compared to those who did not. Similarly, evidence for the effectiveness of cognitive intervention for both spatial neglect and memory was inconclusive (Bowen & Lincoln, 2007; Nair & Lincoln, 2007). Furthermore, the effectiveness of the delivery of cognitive retraining as part of occupational therapy treatment following stroke was found to be unclear (Hoffmann, et al., 2010b). Overall, research and literature reviews indicate that cognitive interventions such as retraining may yield some benefits for stroke survivors with cognitive impairment (Langhorne, et al., 2011). However, larger and higher quality trials need to take place before any such conclusion can be made (Bowen & Lincoln, 2007; Hoffmann, et al., 2011; Hoffmann, et al., 2010b; Nair & Lincoln, 2007).
There have also been few investigations into the role of post-stroke cognitive deficits on physical rehabilitation and recovery. However, one study demonstrated that, despite mild to severe cognitive impairments, cognitively impaired stroke patients made significant physical improvements in rehabilitation. Most of the study’s 435 cognitively impaired patients were discharged home as a result of rehabilitation (Rabadi, et al., 2008).

As such, the findings recommended that all stroke patients should be given access to acute rehabilitation services, whether or not they are cognitively intact (Rabadi, et al., 2008). However, it is important to note that these findings are in contrast with others. Some research has indicated that cognitive and motor impairments can worsen the course of rehabilitation, have negative impacts on activities of daily living, independence and quality of life, and extend the duration of rehabilitation (Milinaviciene, Rastenyte, & Krisciunas, 2011).

There has also been some investigation into medical treatments for cognitive impairment following stroke. A review of 14 studies into the effectiveness of cytidinediphosphocholine (CDP-choline) found that there was some evidence that the drug has a positive effect on memory and behaviour, at least in the short to medium term (Fioravanti & Yanagi, 2005). However, it is important to note that this study investigated cerebral disorders in general and not just cognitive deficits as a result of stroke.

Still, a 2011 study examined the effect of CDP-choline on stroke survivors with cognitive impairments. This study demonstrated that a six month course of the drug showed improved orientation, attention and executive function as compared to placebo (Alvarez-Sabin & Roman, 2011). Furthermore, research has indicated that antidepressant medication may be of benefit in the treatment of mood disorders occurring post-stroke. Psychotherapy, on the other hand, was not found to be effective (Hackett Maree, et al., 2008).

Research into treatment for stroke has focused primarily on medication and physical therapies. A large portion of literature focuses on the use of thrombolytic drugs. These drugs break down blood clots, helping to restore blood flow to the affected brain region. Research indicates that these drugs should be administered within 4.5 hours of symptom onset to ensure maximum restoration of function (Alonso de Lecinana et al., 2011; Taussky, Tawk, Daugherty, & Hanel, 2011). Overall, research indicates that thrombolysis results in a significant reduction in the number of patients that die or need substantial activities of daily
living assistance (Mielke, Wardlaw, & Liu, 2004; Wardlaw, Zoppo, Yamaguchi, & Berge, 2003).

However, there is also evidence to indicate that higher doses of thrombolytic agents can increase bleeding into the affected brain area (Mielke, et al., 2004). Some research indicates that not only does the dose play a role in effectiveness, but the specific agent or drug used, as well as the route of administration (Mielke, et al., 2004). Specific thrombolytic drugs include urikonase (UK), pro-urikonase (PRO-UK), streptokinase (SK), tissue plasminogen activator (rt-PA), tenecteplase, retevase, and lumbrokinase (LK). These drugs can be administered intravenously, orally, or intra-arterially (Wardlaw, et al., 2003).

Intravenous administration of rt-PA has been labelled the ‘gold standard’, or feasible at the least, for the treatment of acute stroke in recent years (Baltacioglu et al., 2003; Taussky, et al., 2011). However, systematic reviews have indicated that there is insufficient evidence to conclude whether one thrombolytic agent is better than others. Likewise there is inadequate evidence to determine whether one route of administration is superior. Intra-arterial administration, for example, has been associated with fewer dose risks. Yet this is off-set by the speed with which intravenous administration can occur and take effect (Mielke, et al., 2004).

Anticoagulant agents are similar to thrombolytic agents, in that they prevent and reduce the clotting of blood. However, they are generally considered separately to thrombolytic and defibrinogenating agents in the literature. This literature generally indicates that anticoagulant therapy immediately after a stroke is not associated with benefit. However, anticoagulant treatment reportedly reduces the risk of further strokes, deep vein thrombosis, and additional clot formation. Conversely, these agents can increase the risk of further bleeding (Sandercock Peter, Counsell, & Kamal Ayeesha, 2008).

Neuroprotective agents, such as endaravone, reportedly act as free radical scavengers. Many studies have been conducted to assess the efficacy of endaravone for treatment of stroke. Some of these studies report significant improvements in functional outcome with use of endaravone. However, the risk of bias has been identified in such trials, and as such the available evidence is inconclusive (Feng et al., 2011).
Other drug therapies, including the use of antiplatelet medications, have also been used and researched for stroke treatment. Antiplatelet medication, for example, has been found effective in reducing the risk of further stroke. It is also reportedly helpful in optimising outcomes following stroke (Sandercock Peter, Counsell, Gubitz Gordon, & Tseng, 2008). However, another type of drug, calcium antagonists, have not been found to be effective in patients with acute stroke (J. Zhang et al., 2012).

Mechanical revascularisation involves the use of mechanical devices to recanalise or revascularise artery occlusions. This includes procedures such as mechanical embolus removal and devices such as aspiration and Penumbra devices which remove blockage through the use of suction. As is common throughout the literature, there is a paucity of adequate research into the effectiveness of these methods. However, the literature generally points to better outcomes with recanalisation as compared to suction based interventions (Meyers et al., 2011).

More commonly used are angioplasty procedures which may be followed be the insertion of a stent. Angioplasty involves the insertion of a deflated catheter balloon that is inflated to re-open the collapsed artery. A stent is essentially an artificial tube that sits inside the artery to keep it open. Recanalisation rates are reportedly high using these methods, as are good outcomes (Meyers, et al., 2011).

Once a patient has moved out of the acute phase of stroke, treatment should generally focus on rehabilitation. Research indicates that rehabilitation should start as soon as possible to maximise its benefits (Alonso de Lecinana, et al., 2011). Rehabilitation in stroke generally involves a process of assessment, goal setting, intervention and reassessment. The primary focus of stroke rehabilitation is generally the restoration of motor control and function (Langhorne, et al., 2011).

Several principles underpin stroke rehabilitation. The use of multidisciplinary teams has been supported by substantial evidence. Individual and family motivation plays a key role in outcomes, and as such goal setting is best done on an individual basis. The interventions themselves are best focused on context specific and task specific exercises (Langhorne, et al., 2011).
Physiotherapy is usually part of stroke rehabilitation. There are a number of different approaches to physiotherapy after stroke. These can be broadly categorised into neurophysiological, motor learning and orthopaedic principle based approaches (Pollock, Baer, Pomeroy Valerie, & Langhorne, 2009). Some research has indicated that one principle has benefits over others, such as the motor learning versus neurophsyiological (Langhammer & Stanghelle, 2001).

Overall the research does not show any clear benefits of one approach over the other. However, research does indicate that physiotherapy, particularly using a mixed approach, is more beneficial than no treatment or control. Physiotherapy has been shown to significantly increase functional independence following stroke (Pollock, et al., 2009).

Occupational therapy is another significant part of stroke rehabilitation (Langhorne, et al., 2011). The focus of occupational therapy is the restoration of independence in activities of daily living. This may be through teaching physical skills, or sourcing aids to assist with tasks (Krug & McCormack, 2009). Research indicates that stroke survivors who receive occupational therapy as part of stroke rehabilitation are less likely to deteriorate, and are more likely to be independent in activities of daily living. However, the best form of occupational therapy to use is still unclear (Legg, Drummond, & Langhorne, 2006).

Gym based fitness training is often incorporated into both inpatient and outpatient rehabilitation programs. Fitness regimes aim to improve or maintain cardiorespiratory fitness, strength, and muscular endurance (Langhorne, et al., 2011). Recent research has indicated that task-oriented circuit training can be as beneficial as physiotherapy in terms of self reported walking competency (van de Port, Wevers, Lindeman, & Kwakkel, 2012). Meta-analyses of similar trials have found support for the conclusion that fitness training after stroke can improve walking. However, the effect on death, disability and dependence are unclear and more research is required (Brazzelli, et al., 2011).

Electromyographic biofeedback (EMG-BFB) is another aspect of stroke rehabilitation, often incorporated as an addition to traditional physiotherapy treatment. EMG-BFB uses visual or auditory signals to monitor muscle activity. However, its impact on recovery after stroke is uncertain. While some research indicates good outcomes, the literature overall is inconclusive and lacks robust trials (Woodford Henry & Price Christopher, 2007).
More alternative therapies are also available for stroke. Acupuncture has reportedly been used in the treatment of stroke for hundreds of years, and Chinese doctors continue to use it routinely as stroke treatment. It is generally used to improve motor, speech, and other functions after stroke. However, systematic reviews of the literature indicate that there is no clear evidence for the benefit of acupuncture in the treatment or rehabilitation of stroke (Wu Hong et al., 2009; S. Zhang, Liu, Asplund, & Li, 2005).

There are also a number of novel therapies being developed and trialled. These include stem-cell therapies, motor imagery, virtual reality, novel robotic therapies, amphetamine use in conjunction with exercise, and drugs such as dopamine agonists and antidepressants. These novel therapies are not yet known to improve functional outcomes in stroke (Langhorne, et al., 2011).

Overall, there is mixed literature available reporting a number of potential treatments and rehabilitation therapies for stroke. However, the research is weak in terms of defining a clear ‘gold standard’ care pathway for the treatment and rehabilitation of stroke (Kwan & Sandercock Peter, 2004). The proportion of studies examining physical and drug based therapies versus cognitive and psychological treatments is indicative of the focus of treatment in real-world settings (Korner-Bitensky, et al., 2011).

**Cognitive Assessment**

There are a number of medical assessment tools used to determine the location and extent of stroke lesions, through to the extent of the physical deficits the survivor is experiencing. Magnetic resonance imaging (MRI) or computed tomography (CT) scans, for example, allow medical professionals to obtain pictures of the exact location and size of a stroke lesion (Kwan & Sandercock Peter, 2004). To assess post-stroke changes and deficits, as well as improvements, scales and assessment tools such as the motor assessment scale (Langhorne, et al., 2011; Poole & Whitney, 1988), Glasgow coma scale, the Barthel index for assessment of activities of daily living, and many more have been identified for use in post-stroke assessment (Langhorne, et al., 2011). Furthermore, these assessment tools are frequently used by medical professionals to determine the level of deficits, and assess improvements during rehabilitation (Langhorne, et al., 2011).
However, the use of cognitive assessment tools in assessing stroke survivors is sparse (Korner-Bitensky, et al., 2011). There are several brief cognitive screening tools identified for use within a stroke setting. The most frequently used and studied is the mini mental status examination (MMSE) (Langhorne, et al., 2011). The MMSE is comprised of 30 items assessing orientation, attention, learning, calculation, delayed recall, and construction (Bour, Rasquin, Boreas, Limburg, & Verhey, 2010).

Several studies report good validity of the MMSE as a screening tool for cognitive deficits amongst stroke survivors (Bour, et al., 2010). However, others have reported that the MMSE is not a sensitive enough screening tool for use in stroke patients, and is not sufficiently accurate when use in this population (Bour, et al., 2010; Dong et al., 2010; Pendlebury, Mariz, Bull, Mehta, & Rothwell, 2012). Nevertheless, the MMSE is brief and easily applicable and as such has become the standard in post-stroke cognitive assessment (Bour, et al., 2010).

Assessment of cognition should include the broad domains of memory, language, executive function and visuospatial at the least. Memory assessment should include both short-term or working memory, as well as delayed recall or long-term memory. Executive function should encompass aspects such as problem solving, planning, organisational skills, attention, inhibitory control, and some aspects of short term memory (Lezak, 2004).

There are several individual tests for each of these domains, as well as test batteries designed to assess all aspects of cognitive function. However, the majority of these are lengthy assessments, generally requiring pencil and paper testing and/or the use of test specific resources. The MMSE is one assessment that can be conducted with a minimum of resources, and taking approximately 10 minutes to administer (Lezak, 2004)). However, the limitations of the MMSE, particularly in elderly and stroke populations, have lead to the development of alternative screening tools.

The Audio Recorded Cognitive Screen (ARCS) is an Australian developed cognitive screening tool that was designed to minimise the time required for the clinician to administer a cognitive screen. The ARCS has avoided the use of technologies such as computer based tests due to their limitations with elderly populations. The ARCS tests cover five domains; memory, verbal fluency, visuospatial functioning, language and attention/executive function, together with a speed of writing test (P.W. Schofield et al., 2010).
The ARCS includes a 12 word list learning task modelled on the Hopkins Verbal Learning Test. This test is known as the Newcastle Auditory Verbal Learning Test (NAVLT) and assesses verbal episodic memory including both immediate and delayed recall. Three verbal fluency tests are also included. These are category fluency, letter fluency, and action fluency (P.W. Schofield, et al., 2010).

A clock drawing task is used to assess visuospatial functioning. Language is assessed through picture naming tasks. For executive function, a new test known as the Hunter Attentional Task (HAT) has been created. The first part of this test presents participants with a task in which they are given a series of lower case letters. Beside each of these the participant must write the capital, or upper case version of the letter. The aim is to complete as many as possible in 30 seconds (P.W. Schofield, et al., 2010).

The second part of the HAT task is slightly different. The participants are again presented with an array of lower case letter. However, in this task, half of the letters are circled. The task is to write the capital form of the letter beside the non-circled letters, and the lower case beside those that are circled. Again participants have 30 seconds (P.W. Schofield, et al., 2010).

The final part of the ARCS is a speed of writing task, in which participants are required to write the same word over and over as many times as they can in 30 seconds (P.W. Schofield, et al., 2010). Testing lasts approximately 34 minutes. However, as the test involves participants listening to a compact disc (CD) and responding to the CDs tasks in a special booklet, the clinician is only required to be present for approximately two minutes of the testing (Peter W. Schofield, Lyall, & Lee, 2009).

The ARCS is a relatively new tool, first seen in the literature in 2009, taking over from its predecessor the Tape Administered Cognitive Screen (TACS) which used similar principles (P.W. Schofield, et al., 2010; Peter W. Schofield, Lyall, et al., 2009). Nevertheless, it has undergone comparison against the MMSE, as well as individual neuropsychological tests for each of the assessed domains (P.W. Schofield, et al., 2010; Peter W. Schofield, Lyall, et al., 2009).
The ARCS memory tests were statistically significantly correlated with ‘gold standard’ neuropsychological tests for memory such as the Rey Auditory Visual Learning Test (RAVLT). Fluency correlations were also statistically significant when compared to standard category and phonemic word fluency measures. The visuospatial task correlated significantly with the Rey Complex Figure task, the Wechsler Block Design task, and visual reproduction tasks. The language task was also statistically significantly correlated with its ‘gold standard’ version, the Boston naming task. Similarly the ARCS attention task correlated with Stroop, symbol digit and Trails tasks (P.W. Schofield, et al., 2010).

The ARCS has also been compared to the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), the Paced Auditory Serial Addition Test (PASAT), and of course the MMSE. Similar significant correlations have been found for the majority of these comparisons. This has included testing amongst populations such as patients with multiple sclerosis, psychosis and dementia (Lechner-Scott et al., 2010; Loughland et al., 2010).

The data has indicated that the ARCS is more sensitive to mild cognitive impairment than the MMSE, more in-depth, and more adaptable to different populations. This research has also reported that the ARCS has better psychometric properties than the MMSE (Peter W. Schofield, Lyall, et al., 2009). However, it is important to note that no independent studies of the psychometric properties of the ARCS have been reported. Furthermore, current research is restricted to Australian, and primarily Newcastle, population groups.

**Thalamic Stroke**

The thalamus is a small, symmetrical midline nuclear complex located between the cerebral cortex and the midbrain. The thalamus has multiple functions in the human brain and body. It acts as a relay and processing centre for sensory and motor signals. Sensory and motor data are received by the thalamus and then relayed to the appropriate primary cortical area. The thalamus also plays a role in regulating sleep and wakefulness (Herrero, Barcia, & Navarro, 2002).

The thalamus comprises four parts; the hypothalamus, epythalamus, ventral thalamus and dorsal thalamus (Herrero, et al., 2002). Different parts of the thalamus are linked to specific functions, as evidenced by deficits acquired by specific lesions in the thalamus (Schmahmann,
The regions of the thalamus in which these lesions can occur are classified variably within the literature (Schmahmann, 2003; Song, 2011).

Thalamic infarctions are generally classified based on topographic location, however the definition of locations and topographic boundaries are not consistent in the literature. Schmahmann (Schmahmann, 2003) describes four regions of the thalamus. These are the tuberothalamic, paramedian, inferolateral, and posterior choroidal regions, named for the primary artery from which they obtain their blood supply. Nakane et al. (Nakane, Tamura, Sasaki, & Teraoka, 2002) describe three regions; ventral, dorsomedial and pulvinar. While Carrera et al. (Carrera, Michel, & Bogousslavsky, 2004) describe four classic regions; anterior, paramedian, inferolateral, and posterior. They also describe three additional variant types; anteromedian, central and posterolateral.

Some of the described regions are consistent through some of the literature, such as the paramedian and anterior regions (Carrera, et al., 2004; Schmahmann, 2003). However, none of the described regions are consistent throughout the literature, nor are all boundaries consistent. Kumral et al. (Kumral, Kocaer, Ertubey, & Kumral, 1995) describe four thalamic regions, continuing on from thalamic syndromes reported by Fisher (Fisher, 1959) and earlier studies (De Smet, 1986). Other studies report similar regions, albeit with different names (Chung et al., 1996; Song, 2011).

A 2012 research paper has clarified these regions further, highlighting four regions and their various names. These are the medial, or thalamoperforate; posterolateral, or thalamogeniculate; dorsal, or posterior choroidal; and anterior, or anterolateral or tuberothalamic regions (Kumral, et al., 1995; Tokgoz et al., 2012). These areas are supplied by four main arteries, the polar, thalamoperforating, thalamogeniculate, and posterior choroidal arteries (Song, 2011).

Thalamic hemorrhage prevalence ranges between six and 25 percent of intracerebral hemorrhages reported in the literature (Tokgoz, et al., 2012). It is generally accepted that hypertension is the most significant risk factor for thalamic stroke (Bilen, Comoglu, Sahin, & Ozbakir, 2001; Kumral, et al., 1995; Tokgoz, et al., 2012). However, factors such diabetes, cardiac diseases and obesity are also highly prevalent in the thalamic stroke population (Bilen, et al., 2001).
**Effects and Outcomes in Thalamic Stroke**

Three types of clinical signs have traditionally been associated with thalamic infarctions. These are the predominance of sensory deficits over motor deficits, oculomotor signs such as vertical gaze abnormalities, and language disturbances (Chung, et al., 1996; Fisher, 1959; Tokgoz, et al., 2012). The extent and type of symptoms has been found to vary according to the location and size of the lesion (Chung, et al., 1996; Kumral, et al., 1995; Schmahmann, 2003).

Lesions in the anterior (anterolateral/tuberothalamic) region of the thalamus have been characterized by severe sensory and motor deficits, with language and oculomotor disturbances less frequent (Kumral, et al., 1995). Reported clinical features of this lesion include fluctuating arousal and orientation, impaired learning, memory, and autobiographical memory, personality changes, apathy, executive dysfunction, language and hemispatial neglect (Schmahmann, 2003).

Lesions in the medial (thalamoperforate/paramedian) region have been characterized by moderate to severe sensorimotor deficits, language deficits, or neglect (Kumral, et al., 1995). Clinical features include decreased arousal, impaired learning and memory, confabulation, disorientation, poor autobiographical memory, aphasia or spatial deficits, and altered social skills and personality including apathy, aggression and agitation (Schmahmann, 2003).

Posterolateral (Inferolateral/thalamogeniculate) lesions have been characterized by severe sensorimotor deficits and neuropsychological disturbances (Kumral, et al., 1995). Clinical features reportedly include sensory loss, hemiataxia, hemiparesis, pain, auditory and behavioural consequences (Schmahmann, 2003).

Finally, dorsal (posterior choroidal) lesions are characterized by mild and transient sensorimotor disturbances, with some oculomotor and neuropsychological disturbances in larger lesions (Kumral, et al., 1995). Clinical features such as visual field loss, variable sensory loss, weakness, aphasia, memory impairment, dystonia and hand tremor are reported in dorsal lesions (Schmahmann, 2003).

Clinical features of thalamic stroke in general have also been reported. These include neuropsychological disturbances such as transcortical aphasia, anosognosia, hemi-neglect,
visual or tactile extinction, memory disturbances, agitation and hallucinations (Kalefa, Hodorog, & Stefanache, 2008). It is important to note that data on neuropsychological changes are primarily based on observation rather than psychometric testing. Sensorimotor changes such as motor deficit, hemiparesis, hemiplegia, ataxia, and sensory deficits such as facial and limb sensory deficits have been reported. Ocular symptoms such gaze preference, gaze palsy, skew ocular deviation, fixed pupils, visual field disturbances and hemianopia in the contralateral space, have also been reported (Kumral, et al., 1995).

The size of the lesion affects the extent and severity of the clinical symptoms, and can also affect prognosis (Kumral, et al., 1995; Kwak, Kadoya, & Suzuki, 1983). Studies have found that larger lesions are associated with more severe symptoms, including sensorimotor, oculomotor and neurobehavioural symptoms (Kumral, et al., 1995; Kwak, et al., 1983). Lesions are typically classified as either small or large, based on their diameter or volume. Large lesions are typically more than two centimetres in diameter, or four millilitres in volume (Kumral, et al., 1995).

The maximum size, diameter or extension of the thalamic lesion has been found to be an independent predictor of outcomes (Kumral, et al., 1995). Some research has reported that patients with a lesion larger than 3.3 centimetres are likely to die (Barraquer-Bordas, Illa, Escartin, Ruscalleda, & Marti-Vilalta, 1981; Vereshchagin, Peresedov, Shirshov, & Kugoev, 1997). However, this is not consistently reported, with other studies finding that survival rates are reasonable with lesions of this size (Kumral, et al., 1995). Still, other data indicate that poorer outcomes and prognosis are associated with lesions larger than 10 millilitres in volume (Kwak, et al., 1983). Prognosis is also reported to be considerably worse when the lesion is global, or affects more than one region of the thalamus (Tokgoz, et al., 2012). Poor prognosis is also associated with initial loss of consciousness, age, previous cardiac or stroke events, and neurological signs (Bilen, et al., 2001; Kumral, et al., 1995; Kwak, et al., 1983).

**Prevention and Treatment in Thalamic Stroke**

The prevention and treatment of thalamic stroke is scarcely addressed in the literature. The focus is primarily on description of syndromes and prediction of outcomes. However, there has been some research into risk factors in thalamic stroke, and this information can form the basis of prevention. As previously stated, the single most significant risk factor for thalamic stroke is hypertension (Bilen, et al., 2001; Kumral, et al., 1995). However, obesity, cardiac
disease, and diabetes have also been identified. As such, regulation of these parameters should play a significant role in the prevention of thalamic stroke (Bilen, et al., 2001).

There has been some investigation into the effectiveness of surgery, such as endoscopic surgery in thalamic haemorrhage. Findings indicate that surgery is indicated in lesions greater than 30 millilitres in volume. Lesions under this size are to be given conservative treatment (Cho, Chen, Lee, Lee, & Lin, 2008). Unfortunately, the term ‘conservative treatment’ is ill defined.

There is little in the literature investigating the efficacy of types of rehabilitation in thalamic stroke. Given that the presentation of thalamic stroke has been identified, and specific syndromes and deficits identified (Fisher, 1959; Kumral, et al., 1995; Schmahmann, 2003), it is possible that thalamic stroke survivors may benefit from a specific, rather than generic, care pathway.

**Summary**

The functional integrity of the thalamus in stroke has been described by several researchers. However it remains poorly understood in comparison to strokes affecting other brain sites. Research has indicated that the consequences of injury to the thalamus are highly variable and are, again, poorly understood. Therefore, further understanding of thalamic stroke is of clinical significance in stroke research.

There is significant literature describing thalamic syndromes and predicting outcomes in thalamic stroke. The literature also indicates numerous risk factors for stroke. Likewise, it indicates a number of treatment and rehabilitation options, although there is a paucity of research into cognitive rehabilitation options. Given the gaps in the existing literature, the present study aimed to obtain information on risk factors, cognitive and behavioural changes in the context of the type and size of thalamic lesions as well as the treatment and rehabilitation completed. It was predicted that thalamic stroke survivors would perform poorly on cognitive testing as compared to same age peers.
Submitted Journal Article

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Abstract

Background and Purpose: The variable clinical and behavioural outcomes of thalamic stroke have been reported in several studies. Studies have also investigated anatomical variances in brain structures such as the circle of Willis and basilar artery in relationship to stroke. This study examines susceptibility factors in thalamic stroke, as well as outcomes in order to identify rehabilitation needs.

Methods: 10 patients with thalamic stroke were interviewed and administered the Audio Recorded Cognitive Screen (ARCS). MRI scans were examined to determine localization and size of the lesion, as well as basilar artery size and anatomical variances in the circle of Willis.

Results: Risk factors such as high cholesterol, high blood pressure, and pre-existing heart conditions were identified. Circle of Willis variations were found in six of the 10 participants, with MR angiography indicating that the posterior communication artery (PCOM) was absent or failed to join the posterior cerebral artery (PCA). Basilar artery diameter measurements were no larger than expected. All participants reported post-stroke changes including decreased coordination and mobility, poor balance, reduced energy, memory deficits, and mood changes. Participants’ overall scores on cognitive tests were significantly lower than age matched norms. Performance on the test domains of memory, fluency, language and attention were all significantly below age norms.

Conclusions: The variability of outcome measures demonstrates the difficulty of defining patterns of relationship between risk factors and severity of functional sequelae in thalamic stroke.
The pattern of arterial blood supply to the thalamus is arranged such that perfusion territories of the posterolateral choroidal artery; the posteromedial choroidal artery; the inferotemporal arteries; the paramedical thalamic artery and the tuberothalamic artery can be mapped [1-5]. The neuroanatomical description of the various thalamic nuclei and the thalamic fibre tracts, the thalamic peduncles, are equally well described [4-6]. Despite the anatomical clarity, the clinical sequelae of thalamic stroke offer a complex picture of both physical, neuropsychological and functional effects, which are difficult to separate out into syndrome groupings [7].

Thalamic hemorrhages are generally classified by their topographic location with a conventionally used differentiation into anterior, medial, posterolateral, and dorsal areas. However, the definition of location and the topographic boundaries are not identified consistently in the literature [3, 4, 8] and so this convention is not without problems. Nevertheless, it has been proposed that outcomes and deficits can be associated with these different lesion locations, together with the additional general rubric that ‘the larger the lesion the greater the deficit’ (especially if the lesion is greater than 4mL in volume) [3, 5, 9]. Anterior thalamic injury is associated with language and memory impairments together with cognitive deficits that have been identified with the neocortical frontal dysexecutive syndrome by some researchers [4, 6, 9]. Medial thalamic injury is associated in the longer-term with severe memory loss, disorientation, with motor dysfunction and some personality changes [3, 4, 10]. Posterolateral thalamic injury can lead to the effects of “sensorimotor stroke” with associated sensory loss (hemi-neglect), motor incapacity and associated cognitive deficits such as perceptual (‘Pusher syndrome’), language and memory problems [10, 11]. Anterior thalamic injury has been associated with cognitive and behavioural disturbances including memory, language deficit, acalculia, visual memory impairment and mild cognitive deficits [3, 4, 10]. Lastly, dorsal thalamic stroke has been associated with mild transient hemiparesis but also with longer-term language and memory deficits [3, 4, 10].

Risk factors associated with thalamic stroke include physical and environmental risks such as pre-existing heart conditions; hypertension; high cholesterol and smoking. Of particular interest here is the risk associated with the anatomical variables of the basilar artery diameter [12] and the structural variations in the circle of Willis [17]. The mean diameter of a normal basilar artery is approximately 3.2mm [13, 14]. Higher mortality is associated with larger basilar artery diameters [12]. Anatomical variances in the circle of Willis are also associated
with increased risk of thalamic stroke [17], although there is some lack of consensus in the literature as to the incidence of normal and abnormal patterns of the circle of Willis. Reported prevalence rates of abnormality range from five to over 70 percent [15-18]. Studies have identified over 20 variants in the circle of Willis, including variations in the posterior communicating artery (PCOM) [17], from which the thalamic perfusing arteries arise. The absence of the PCOM and hypoplasticity of the PCOM are both variants. Absence of the PCOM has been reported at about one percent of the population [15] although other studies have found absence rates as high as 30 percent [19]. Hypoplasticity of the PCOM is reported at rates of around 13 percent, but without consistency in reported incidence rates. The interest here is that evidence suggests that people with an incomplete circle of Willis may be at higher risk for stroke [7].

Here we report 10 cases of patients who sustained thalamic strokes and who were examined for risk factors and post-stroke changes in behaviour and cognitive function.

Method

Participants:

The participant sample comprised 10 patients having sustained thalamic strokes and referred to the John Hunter Hospital Stroke Unit. Patients were aged between 66 and 83 years (M = 75.67, SD = 5.7). Four of these participants were female and six were male. Participants were sourced from patient records for the two years preceding the commencement date of the study (November 2011). All Stroke Unit patient records were examined and those patients who had been admitted for a stroke affecting the thalamus were shortlisted. From this short list, patients who had subsequently died; had suffered further strokes affecting other parts of the brain; or who were so severely disabled as to make participation in testing impossible, were excluded from the study. Twenty patients were contacted by the Neurologist from the Stroke Unit (CL) and invited to participate. Ten patients declined to participate either at initial contact or when being contacted to make a testing appointment.

Instruments:

The ARCS is a cognitive test that is administered to participants by tape recorder or compact disc (CD). Participants write their responses in a booklet for later scoring [20]. Tests within
the ARCS cover the key domains of memory, verbal fluency, visuospatial functioning, language, attention/executive function, and speed of writing [21]. The ARCS includes a 12-word list learning task that assesses verbal episodic memory with both immediate and delayed recall. The ARCS has three verbal fluency tests; category fluency, letter fluency, and action fluency [21]. A clock-drawing task assesses visuospatial functioning and language is assessed through picture naming tasks. Executive function is assessed with an attention test. The first part of this test presents participants with a series of lower case letters. For each of these the participant must write the corresponding upper case version for as many letters as possible within a 30 second time limit [21]. In the second part of the task the letters are randomly circled or not, with participants being required to write lower case letters next to circled, and upper case letters next to non-circled stimulus letters during the 30 second time limit [21]. The final part of the ARCS is a speed of writing task, in which participants are required to write a given word repeatedly as many times as possible in 30 seconds [21].

The ARCS possesses a good psychometric profile when compared with other neuropsychological test batteries [21, 22]; and has been found to be sensitive to mild cognitive impairment in clinical samples [23, 24]. The test takes approximately 30 minutes to complete. It was designed to measure functional abilities in the elderly and normative data for elderly groups are available for comparison [21].

Procedure:

Ethical approval for the research was granted by the Hunter New England Human Research Ethics Committee (HNEHREC reference number: 10/09/15/4.02).

All patient diagnoses of thalamic stroke were confirmed by two independent neurologists on clinico-radiological criteria - sudden focal neurological deficit of vascular aetiology and MR brain imaging of thalamic stroke (either infarction or haemorrhage) consistent with the acute clinical presentation. Participants attended one testing session, which took 60 to 90 minutes to complete. The first part of the appointment consisted of an interview in which details of the patient’s medical history, and pre- and post-stroke functioning were elicited. Five of the participants attended this appointment with a partner or carer, and input from this support person was encouraged during the interview. In the second part of the session, participants completed the Audio Recorded Cognitive Screen (ARCS), administered by, and in the
presence of a researcher, (JF). Participants completed the ARCS by listening to instructions on a CD and completing their responses in a response booklet. Partners/carers were not present during testing. One participant was unable to complete any of the ARCS. With the participants’ consent, their patient records were also accessed in order to assess MRI images of the participants’ stroke lesions. These images were used to determine the location and size of the stroke lesion and any anatomical variations in the anatomy of the circle of Willis. The volume of the stroke lesion was estimated using the area measures from the MRI slices, multiplied by the thickness of the slices. Measurements of the basilar artery diameter at the level of the mid-pons, were also taken from the “time of flight” MR angiographic source image scans.

**Results**

The 10 patients involved in this study were all aged over 66 (mean age 75.67 years) and living in their own homes. One of the ten participants required a high level of care from their spouse, and one received regular community assistance for showering and shopping. The remaining participants all reported living relatively independently. The mean time between stroke and neuropsychological testing was 17.6 months.

[Table 1 here]

The results from the ARCS cognitive function tests for this sample of patients are presented in Table 1. ARCS scores are presented with the mean normed scores from an aged healthy population (bottom row) [21]. As can be seen from Table 1, patient ‘J’ was unable to perform any of the tasks. Of the nine patients with measurable performances, the individual profiles show mixed levels of cognitive function. Patients ‘A, D and H’ show memory deficit; patients ‘D and H’ performed poorly on the fluency tests; patients ‘C, E, F and G’ all performed poorly on the visuospatial task; patients ‘C, D and H’ showed language deficits; patients ‘B, D and H’ exhibited attention deficits; and patient ‘A’ was particularly slow in the speed of writing task.

[Table 2 here]

Overall the participants exhibit a range of cognitive deficits and, as a group, this performance shows clear impairment when compared with age-matched healthy control ability scores
taken from the published ARCS standardized scores. Table 2 shows the means of the ARCS subscale scores and the normed scores from a healthy older population. Single sample t-tests were conducted comparing the scores of this sample with reported population norms. There were statistically significant differences between the thalamic stroke patients and the normed healthy elderly for memory, fluency, language, attention and for overall ARCS scores (domain comparisons: memory \(t(8) = -3.396, \ p = .009\); fluency \(t(8) = -3.082, \ p = .015\); language \(t(8) = -2.691, \ p = .027\); attention \(t(8) = 7.959, \ p = .000\); and overall ARCS scaled score \(t(8) = 5.476, \ p = .001\)).

[Table 3 here]

Measurements of the basilar artery diameter (in mm); hemisphere (right or left) of lesion; abnormality of circle of Willis (normal or abnormal); volume of lesion (in ml); lesion location (left versus right + anterior, medial, dorsal or posterolateral); pre-stroke risk factors; together with age and gender of participant, are all shown in Table 3. The mean basilar artery measurement taken from this sample (M=2.9mm) was compared with the average diameter taken from published data [14] (M= 3.17mm) with no statistical difference being found \(t(9) = 1.504, \ p=.167\). The lesion volumes reported here ranged from 0.01ml to 1.11ml (M=0.43ml) - all less than 4mL [3] and so all considered to be of small size. Nonetheless, there is no evidence in this sample that a larger lesion leads to greater deficit. Taking the overall ARCS score as a measure of overall cognitive functioning, the three patients with the largest lesions (patients ‘A’, ‘F’ and ‘I’) had three of the four highest ARCS overall scores. Taken overall there was no statistical difference shown in ARCS scores when patients were grouped according to lesion volume, based on a median split of volumes.

However, lesion volume was associated with abnormalities of the circle of Willis such that the lesion volume for participants with a circle of Willis abnormality (M= 0.63ml) was greater than that for those patients with a normal appearing circle of Willis (M= 0.125ml) \(z=2.558, \ p=0.011\). Non-parametric tests were also used to compare ARCS domain and overall scores for participants with or without circle of Willis variations and no statistically significant differences were found. Likewise, no statistically significant differences were found when ARCS domain scores were used to compare the hemisphere (left or right) of the thalamic lesion location. The small sample size prevented statistical comparison of the sub-areas (1 posterolateral; 2 anterior; 3 dorsal and 4 medial lesions) of the thalamic lesion location.
Discussion

Despite showing clear impairment, the test outcomes for this group provide very little in terms of interpretable patterns of deficit. Inspection of the best and worst overall performance shows that patient ‘I’ with the best overall performance was assessed with absence of the PCOM, a relatively large volume lesion (0.88ml) and a basilar artery diameter of 2.5mm, whereas patient ‘D’ with the worst overall performance also had an absent PCOM, a lesion volume of 0.33ml and a basilar artery of 3.5mm diameter. Even so, it might be argued that some elements of a pattern can be elicited. For example, of the 3 participants with left dorsal lesions, one could not perform any of the tasks and the other two performed very poorly on the language sub-scale. Indeed, one of the two tested (patient ‘D’) performed poorest overall and the other (patient ‘C’) had the fourth poorest overall ARCS score yet with the smallest lesion. Generally, the patients with dorsal lesions showed deficit on all but the Speed of Writing task. Patient ‘A’, with a left posterolateral lesion, showed most impairment on the Speed of Writing task, in line with a ‘sensorimotor stroke’, but also showed impaired memory function. Indeed, he was below average on all but the language scale. The two participants with right anterior thalamic lesions showed a very mixed pattern of responding, with one (patient ‘F’), showing deficit in visuospatial functioning, whereas the other (patient ‘I’) performed the best ARCS overall score even with a lesion which was the third largest in volume. The four patients with right (patient ‘B’), and left (patients ‘E’, ‘G’, and ‘H’) medial lesions also showed a very mixed pattern, but with a particular deficit in memory and language in one participant (patient ‘H’) and a deficit in visuospatial function in two (patients ‘E’ and ‘G’). In short, these data provide little in terms of the identification of patterns of cognitive deficit following thalamic stroke, either in terms of the size or the site of the lesion. And yet the performance scores demonstrate that, compared with appropriately matched normed scores, the patients are functionally very disabled.

The results of this study are clearly affected by the low statistical power offered by a small and, in terms of their thalamic lesion types, quite heterogeneous sample. The only inference that can be drawn concerns the general cognitive dysfunction shown by these patients post-stroke. Yet inspection of their rehabilitation program shows that their physical deficits have tended to be catered for, whereas their cognitive deficits have not. Table 3 illustrates that problems with coordination, with balance and with mobility quite appropriately receive physiotherapy in their rehabilitation program. The availability of rehabilitation for cognitive dysfunction is significant by its absence and yet these same cognitive deficits are the cause
major functional difficulties for these patients. Further research aimed at disentangling the complex nature of relationship between various thalamic strokes and functional outcomes needs to be matched by efforts to provide cognitive rehabilitation programs that will help patients adapt and overcome these consequent difficulties.

Acknowledgments

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Conflict(s)-of-Interest/Disclosure(s)

There are no conflicts of interest to disclose.
References


Table 1

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<th>Attention</th>
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Elderly normed mean 100 100 100 100 100 100 100
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<th>Attention</th>
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<td>83.67 (SD = 15.898)</td>
<td>81.44 (SD = 24.996)</td>
<td>68.11 (SD = 35.547)</td>
<td>77.33 (SD = 8.544)</td>
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<td>100</td>
<td>100</td>
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<td>Mean Difference (95% confidence interval of the difference)</td>
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<td>-16.333 (-28.55 - 4.11)</td>
<td>-18.556 (-37.77 - .66)</td>
<td>-31.889 (-59.21 - .56)</td>
<td>-22.667 (-29.23 - 16.10)</td>
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<td>6</td>
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<td>7</td>
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<td>Age</td>
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<td>Lesion volume</td>
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<td>Basilar artery</td>
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Legends

Table 1

Scaled ARCS domain and overall scores for each participant.

Table 2

Mean ARCS scores and comparative age norms.

Table 3

Participant data summary.


**Extended Discussion**

The present research has reported a number of general findings consistent with previously reported information. Risk factors such as high cholesterol, high blood pressure, and pre-existing heart conditions were identified in the small sample of thalamic stroke survivors. These findings are consistent with the literature; however the prevalence rate of smoking as a risk factor was inconsistent. The findings in relation to specific neuropsychological deficits, as measured by the ARCS and participant self-report, are also relatively consistent with existing literature.

However, the present research has been able to provide significantly more in-depth information on cognitive function. Participants’ overall scores on the ARCS were significantly lower than age norms. Performance on the ARCS domains of memory, fluency, language and attention were all significantly below age norms. This indicates specific deficits associated with thalamic lesions.

The present research also identified structural variations in brain anatomy, namely in the circle of Willis configuration, were highly prevalent in this small sample. However, the structure of the basilar artery, measured by its diameter, was not of significance in this sample. Participants reported post-stroke changes including decreased coordination and mobility, poor balance, reduced energy, memory deficits, and mood changes, all of which are relatively consistent with existing literature.

This research presents a number of interesting and potentially valuable findings. However, it needs to be highlighted that the validity and reliability of any of the study’s findings is limited. This is due to the very small sample size obtained for this study, with only 10 participants in total, and only nine of these able to complete ARCS testing. The small sample size, and hence low power of the study, means that any of the results may have occurred simply due to chance, and therefore hold little statistical significance.

Furthermore, the sample is comprised of thalamic stroke survivors with a low level of disability to ensure ability to complete ARCS testing. As such, the results are likely to provide an inaccurate snap-shot of thalamic stroke survivors as a whole. The data obtained likely do not cover the full extent of disability that would be found in this population. With the bias and
low power of the sample included in this study in mind, it is important to highlight that any findings of this study need to be interpreted with extreme caution.

The initial prediction of this research was that thalamic stroke survivors would perform poorly on cognitive measures, as compared to same age peers. The data obtained support this prediction. However, there are a number of other findings that are also of interest.

**Risk factors**

The risk factors identified in this small sample are primarily consistent with stroke risk factors reported throughout the literature (Bühler, et al., 1988; Castelli, 1984; De Caterina et al., 2010; E, et al., 1997; Larsson, Virtamo, & Wolk, 2012; Luitse, et al., 2012; O'Donnell, et al., 2010; Shaper, Wannamethee, & Whincup, 2004; Wy et al., 2007). The most obvious of these being pre-existing heart conditions, cholesterol issues, high blood pressure, and diabetes. Fifty percent of this small sample identified hypertension as an issue prior to the onset of stroke. This is consistent with other studies reporting an average 55 to 60 percent prevalence of hypertension amongst stroke victims (O'Donnell, et al., 2010; Wy, et al., 2007).

Hypertension has previously been identified as one of, if not the most significant risk factor for stroke (Dubow & Fink, 2011; Johansson, 1999; Kurl, et al., 2001; O'Donnell, et al., 2010) and thalamic stroke (Bilen, et al., 2001; Kumral, et al., 1995). As such, the findings of the present research provide additional support for the significant link between hypertension and stroke, as well as hypertension and thalamic stroke.

One participant reported a diagnosis of diabetes prior to their stroke. This is consistent with reported prevalence rates (Luitse, et al., 2012) and provides further support for the link between diabetes and stroke. Likewise, one participant reported possible high alcohol consumption as a pre-cursor to their stroke. However, a comprehensive assessment of the amount of alcohol consumed, and the frequency of consumption was not completed. It is therefore unclear whether or not these data support existing findings of a link between high alcohol consumption and stroke (Gorelick, 1987; Reynolds, et al., 2003).

The relationship between high cholesterol levels and stroke has been thoroughly investigated and consistently reported (Cui et al., 2012; De Caterina, et al., 2010; Larsson, et al., 2012; Lewington et al., 2007). However, prevalence rates and population attributable risk is difficult
to ascertain as other confounding factors such as hypertension and obesity modify this risk (Cui, et al., 2012). The prevalence of pre-existing cholesterol issues amongst the small sample in this study was 40 percent.

Amongst the four participants in this study who reported cholesterol as a pre-stroke factor, three also had hypertension, and one had diabetes (see table 1, Appendix B). These data provide further support for the association between cholesterol and stroke. However, it also highlights that cholesterol is an inter-linked risk factor, with three of the four participants with cholesterol as a risk factor also reporting confounding risk factors.

Fifty percent of this small sample reported having a pre-existing heart condition prior to their stroke. Current data indicate that an estimated one in 15 people with heart disease will eventually have a stroke (Castelli, 1984). The prevalence rate of pre-existing heart conditions amongst stroke victims is reported to be between four and 14 percent amongst stroke survivors. (O'Donnell, et al., 2010).

In comparison to previously reported prevalence rates, the incidence of heart conditions in this small sample appears to be higher than expected. This may be indicative of a stronger association between heart conditions and thalamic stroke, as compared to stroke in general. However, previous research that is more in-depth and robust than the present findings has not reported this association (Bilen, et al., 2001; Kumral, et al., 1995; Kwak, et al., 1983). As such these findings are more likely a result of the low reliability and power of the dataset obtained in this research.

There is a significant amount of research that focuses on the role of nicotine and cigarette smoking in the incidence of stroke. Likewise, there is a considerable amount of health promotion expenditure by governments and health organizations aimed at reducing smoking for the purpose of reducing the incidence of stroke (Boden-Albala & Sacco, 2000; Bühler, et al., 1988; Hawkins, et al., 2002; Moskowitz, et al., 2010; Shaper, et al., 2004). It is of interest then that none of the 10 participants in this study reported a history of smoking.

Previous studies have reported prevalence rates for smoking amongst stroke victims to be over 30 percent (O'Donnell, et al., 2010). Hypertension has already been highlighted as the most significant risk factor in thalamic stroke (Bilen, et al., 2001). Given that cigarette
smoking increases the risk of hypertension, and worsens existing hypertension (Bowman, Gaziano, Buring, & Sesso, 2007; Sleight, 1993), it is reasonable to expect that a strong association between smoking and thalamic stroke would exist.

Given the existing data on smoking and stroke, it would be fair to expect that some of the participants in this study would report current or previous smoking. The fact that this was not the case raises a number of possibilities. These data may point to a different relationship between cigarette smoking and thalamic stroke risk, as compared to the relationship with stroke risk as a whole.

However, it is also important to note that this study has excluded patients with a higher level of disability and of course those who had died. This is significant in the context of findings in relation to smoking and stroke outcomes. Smoking has been associated with higher mortality rates amongst stroke victims (Myint et al., 2006). Furthermore, smoking has been linked with the reduced efficacy of medications used in stroke treatment and prevention (Bühler, et al., 1988), higher severity of symptoms upon presentation in some types of stroke (Weng, et al., 2011), and poorer post-stroke quality of life (Bühler, et al., 1988). As such, it may be the case that this study has unintentionally excluded smokers from the sample, by excluding patients with high levels of disability.

Another risk factor that is emerging in the literature is variations in the circle of Willis anatomy. There is evidence to suggest that people with an incomplete circle of Willis, or significant variations in circle of Willis anatomy, may be at higher risk of stroke (Alastruey, et al., 2007; El-Barhoun, et al., 2009; Songsaeng et al., 2010). There is an apparent lack of consensus as to what a ‘normal’ circle of Willis looks like (El-Barhoun, et al., 2009; Songsaeng, et al., 2010). However, one anatomical variation identified in the literature is the absence or hypoplasticity of the PCOM (Kapoor, et al., 2008).

Sixty percent of the participants in this study showed variations in the PCOM on MRI images. These variations included the absence of one or more PCOM arteries, as well as the underdevelopment or hypoplasticity of one or more of these arteries. The incidence of this type of anatomical variation has been inconsistently reported. However, examination of the literature would indicate an expected prevalence of between one and 30 percent. (Kapoor, et al., 2008; Li, et al., 2011).
The prevalence of PCOM variations in this small sample is much higher than expected. It is also of interest to note that no other overt circle of Willis variations were observed in this small sample. These data may indicate that anatomical variations in the PCOM in the circle of Willis may be linked with a higher risk of thalamic stroke. The thalamus is supplied blood by the PCOM both directly, and indirectly from arteries and vessels that arise from the PCOM (Schmahmann, 2003). As such, there may be a biological explanation for the possible link observed in this study.

Data from this sample do not indicate that PCOM variation increases the chance of stroke in a particular part of the thalamus. The six participants with PCOM variances exhibited lesions in all of the four identified regions of the thalamus (see table 2, Appendix B). However, participants who exhibited PCOM variations had significantly larger stroke lesions than those exhibiting a ‘normal’ circle of Willis.

The circle of Willis operates such that if a blockage or failure of one part of the circle occurs, blood flow from the other vessels in the circle can preserve circulation. This can reduce or eliminate the symptoms of infarction in this area of the brain (Egan, 2005). As such, an absent or hypoplastic PCOM may reduce the circle’s ability to perform in this way. This may provide an explanation for the larger stroke lesions found in participants with PCOM variations.

This study has highlighted the possibility that PCOM variances may be a risk factor in thalamic stroke. Furthermore, there may be a link between PCOM variances and lesion volume in thalamic stroke. However, it is important to consider other factors when interpreting the data from this small study. Previous research has indicated that the circle of Willis is prone to deterioration over the lifespan (El-Barhoun, et al., 2009).

As such, it may be the case that the high prevalence of variances seen in this small sample may be reflective of the age range of participants, with the youngest participant being 66. Further investigation into these findings is warranted. Such investigations should examine MRI data across a broad cohort of thalamic stroke victims of all ages, genders, levels of disability, and including patients already deceased.
Basilar artery diameter is also emerging as a risk factor for stroke and stroke related diseases (Fellgiebel, et al., 2011; Pico, et al., 2006). Research indicates that the mean basilar artery diameter in the normal population is approximately 3.2 millimeters. This is true for both Australian and international population data (El-Barhoun, et al., 2009; Smoker, et al., 1986). The mean basilar artery diameter in this small group was 2.9 millimeters. Analysis found that this was not significantly different to that of the normal population (El-Barhoun, et al., 2009; Pico, et al., 2006). This finding may indicate that basilar artery diameter is not associated with higher risk of thalamic stroke.

However, it is more likely that this finding is a reflection of the screening process for the study. This study has excluded potential participants with higher levels of disability, such as those incapable of independent living and those unable to write. This exclusion criterion was intended to ensure participants’ capacity to complete the ARCS. However, it may well have also excluded potential participants with larger basilar artery diameters.

None on the 10 participants had a basilar artery measurement larger than 4.3 millimeters. Literature indicates that a basilar artery diameter greater than 4.3 millimeters is associated with higher stroke mortality rates (Pico, et al., 2006). As such, patients who had died, and hence were excluded from the study, may have also exhibited larger basilar artery measurements. Any research aiming to investigate this finding further would need to include a representative sample. This should include examining MRI scans for patients with all levels of disability, as well as those who have since deceased.

Other risk factors identified in the literature include BMI, psychosocial factors, diet, exercise, socio-economic status, genetic pre-disposition and familial history, and race or ethnic background (Addo, et al., 2012; Gafarov, et al., 2004; Heeley, et al., 2011; Katsiki, et al., 2011; Liao, et al., 1997; March, 2011; Meschia, et al., 2011; Moskowitz, et al., 2010; Roger, et al., 2012; Stuller, et al., 2012; Thrift, et al., 2011; Towfighi, et al., 2010). None of these factors were explored in the presented research. Further investigations into the risk factors associated with thalamic stroke, as compared with stroke in general, should encompass all identified risk factors to ensure a comprehensive and accurate assessment of this relationship.

However, data for the risk factors of age and gender were collected through patient demographic information (see table 3 and 4, Appendix B). The youngest participant in this
study was 66 years old. Given that only patients who had suffered a stroke in the preceding two years were included in this study, all the participants would have been over 49 years of age at the time of their stroke. This indicates that all participants were in a high risk age category at the time of their stroke (Delilovic-Vranic, et al., 2011).

Statistical analysis of mean ages for both males and females indicated that there was no significant difference in age between the two groups. The mean age for females was 75, and 77.17 for males. Women are reportedly at higher risk of stroke when they are over the age of 80, at which time men’s risk decreases (Giralt, et al., 2012; Sealy-Jefferson, et al., 2012). As such, the mean age for female participants may be expected to be higher than that of the males. However, that this is not the case is likely a reflection of the very small sample size.

**Outcomes**

Thalamic stroke can lead to cognitive, physical, and/or emotional changes (March, 2011). Previous literature has highlighted the fact that cognitive changes occur post thalamic stroke (Schmahmann, 2003). However, these cognitive changes have not received significant attention in the literature.

The general changes reported by the participants in this study (see Table 5, Appendix C) are relatively consistent with previously reported clinical features of thalamic infarction (Schmahmann, 2003). For example, eight of the 10 participants reported noticing changes in their memory. This is consistent with previous findings of impaired memory, and poor autobiographical memory in thalamic stroke survivors (Schmahmann, 2003). Participants also reported reduced grip strength, low energy and tiredness, reduced mobility, and concentration deficits. Again, these are consistent with previously reported outcomes such as hand tremors, motor weakness, impaired learning and concentration (Schmahmann, 2003) and lethargy (Tokgoz, et al., 2012).

This study has classified the thalamic lesions into four regions. These are the anterior, medial, posterolateral and dorsal regions as previously described (Chung, et al., 1996; Kawahara et al., 1986; Kumral, et al., 1995; Steinke et al., 1992).

As the thalamus essentially acts as a relay station for sensory and motor data (Herrero, et al., 2002), it is logical to assume that lesions in specific areas of the thalamus would produce
consistent deficits. Furthermore, these deficits should indicate what specific information that part of the thalamus receives and hence what primary cortical area the information is projected to. For example, a deficit in language may indicate a lesion in the area that projects to the language centers of the brain, such as Broca’s or Wernicke’s regions. Unfortunately, the very small sample size obtained in the present study does not allow for statistical analysis of outcome differences in the four different lesion locations. However, descriptive analysis of the data indicates that memory deficits were reported across all groups, and balance and energy loss/tiredness was reported in three of the four groups (see Table 5 Appendix C).

Reduced coordination was reported by two participants with medial lesions. No participants with other types of lesions reported coordination as an issue. Likewise anxiety and mood issues were recalled by participants with dorsal lesions only. This descriptive data may indicate that the medial region of the thalamus feeds forward coordination data, projecting to the motor cortex, while the dorsal region deals with emotional data. The notion of different outcomes based on the location of the stroke lesion has been previously reported (Kumral, et al., 1995; Schmahmann, 2003). However, the limited data set in this study limits conclusions that can be drawn.

Cognitive deficits were apparent in patients with all four types of lesions in this small group. Overall performance on the ARCS indicates that these thalamic stroke survivors scored significantly below their same aged peers on the domains of memory, fluency, language, attention, and for the overall ARCS scaled score. Again, these data are consistent with previously reported memory deficits, language disturbances, aphasia, executive failure and impaired learning (Amici, 2012; Kumral, et al., 1995; Schmahmann, 2003). The findings of this study add to the existing literature by providing measurable and quantifiable data on these deficits in the form of ARCS scores.

The very small sample size also makes it ineffectual to compare the prevalence of each of the four lesion types with prevalence rates elsewhere reported. However, some comparisons can be made in relation to cognitive performance and lesion location. While no statistically significant correlation was found between ARCS scores and location of the lesion (see Table 6, Appendix C), some comparison between lesion types can be made.
There were three participants in this study with lesions in the dorsal region of the thalamus. Only two of these participants were able to complete cognitive testing. In general, these two participants performed poorly on each of the ARCS domains and overall ARCS score, with the exception of the speed of writing domain. At the time of writing, there was no published neuropsychological test data from other thalamic stroke samples with which to compare these findings. However, the present study’s results do correspond with previous findings of language disturbances including aphasia (Kumral, et al., 1995; Schmahmann, 2003) and memory impairment (Chung, et al., 1996; Schmahmann, 2003) in patients with dorsal thalamic lesions.

Looking more closely at the participants with dorsal lesions, patient ‘D’ in this group had the poorest overall ARCS performance for the whole group. Patient ‘C’ from this group had the lowest overall lesion volume, and was also the only dorsal lesion with a ‘normal’ PCOM. Nevertheless, this individual had the fourth lowest ARCS overall score. As such, looking at individual cases, it is difficult to elicit specific patterns of deficit. Interestingly, all of the dorsal lesions in this sample were on the left side.

Thalamic stroke lesions in the anterior, anterolateral, or tuberopontine region are characterized by their principal manifestation being severe and wide ranging neuropsychological deficits (Schmahmann, 2003). The two participants with lesions in the anterolateral region of the thalamus generally performed below age norms on each of the ARCS domains of fluency, visuospatial, and attention, and on the overall ARCS scaled score. Previous literature has reported deficits such as language disturbances (Kumral, et al., 1995), executive function (Carrera, et al., 2004) and learning and memory deficits (Amici, 2012; Chung, et al., 1996; Schmahmann, 2003). The ARCS attention domain is considered a measure of executive function and has been significantly correlated with well-known neuropsychological tests of executive function such as symbol digit, stroop and trails tasks (P.W. Schofield, et al., 2010). As such, poor performance on the attention domain of the ARCS is consistent with previous findings of executive dysfunction (Carrera, et al., 2004).

Furthermore, the ARCS fluency domain is an indicator of semantic memory (P.W. Schofield, et al., 2010). Previous research has reported memory deficits in patients with anterolateral lesions (Schmahmann, 2003). However, this literature has primarily described such memory deficits to encompass primarily recent memory, memory recall and new learning or memory
acquisition (Amici, 2012; Schmahmann, 2003). As such, it appears that the present study’s findings are inconsistent with previous findings in this area. Moreover, this group’s language scores were not below expected norms. This finding is inconsistent with previously reported language deficits in this group (Amici, 2012; Kumral, et al., 1995; Schmahmann, 2003). Language deficits previously found have included lack of meaningful content, impaired comprehension and fluency, and semantic errors (Amici, 2012; Schmahmann, 2003).

At the individual level, the participants with anterior lesions showed varied patterns of impairment. Whilst both participants had lesions on the right side, patient ‘F’ underperformed on the ARCS domains of fluency, visuospatial, language, and attention, as well as being the third lowest performer on the overall ARCS scaled score. In contrast, patient ‘I’ scored in the range expected for his age on all domains, with the exception of a slight underperformance on the attention task. This is despite patient ‘I’ having the second largest lesion of the entire group. Again, examination of individual cases demonstrates the difficulty in eliciting a specific pattern of deficit for this group. Both these participants had an absent or hypoplastic PCOM.

The mean scaled ARCS scores for the four participants with medial thalamic lesions were below those expected for same aged peers on the domains of memory, visuospatial, language, attention, and on the overall ARCS scaled score. These findings provide more detailed data in support of previously reported deficits for this group. Language and visuospatial disturbances (Kumral, et al., 1995), memory impairment (Chung, et al., 1996), and disorientation (Amici, 2012) are characteristics previously observed in patients with medial thalamic lesions. Impaired learning has also been reportedly observed in this group (Amici, 2012; Schmahmann, 2003). This may correlate with the present attention deficits, or executive dysfunction. However, as detailed descriptions of previous findings are not available, it is difficult to confirm this possible correlation.

Of the participants with medial lesions, three were located on the left side, and the other on the right. The individual participants all performed poorly on the speed of writing and overall ARCS scores. Performances were also below age norms on the language tasks, with the exception of patient ‘G’, who had the highest overall language score. Memory performance was at, or close to, the level expected for age in all but patient ‘H’. Other scores were mixed across this group. Fluency was below expected for patients ‘G’ and ‘H’, but not for patients
‘B’ and ‘E’. Whereas visuospatial performance was at the expected age level for patients ‘B’ and ‘H’ but not for ‘G’ and ‘E’. As with other types of lesions, examination of the data at the level of individual cases indicates that there is not a consistent pattern of deficit that can be elicited from the data obtained for this group.

The one participant with a posterolateral lesion performed below average on all ARCS domains with the exception of language. Poor performance on the visuospatial domain is consistent with previously reported visuospatial disturbances (Kumral, et al., 1995). Likewise, poor performance on the memory and attention tasks is consistent with previous reports of memory impairment and executive dysfunction in patients with posterolateral lesions (Amici, 2012; Carrera, et al., 2004).

Language disturbances have also previously been reported for this group (Chung, et al., 1996; Kumral, et al., 1995). However, the participant with a posterolateral lesion in the present study did not perform below age norms on the ARCS language domain. This inconsistency is not likely to be of statistical significance. However, it is worthy to note that Schmahmann (Schmahmann, 2003) reported that language is only occasionally impaired in lesions of this type. This is hypothesized to be due to the number of vessels that supply this part of the thalamus, and the resultant number of different nuclei that may be impacted by interrupted blood supply (Schmahmann, 2003).

The cognitive function data found in this study was, at a general level, consistent with previously reported findings and observations. However, at the individual case level, it is difficult to ascertain any true patterns. Hence further studies looking at cognitive measures in thalamic stroke would need to include a much larger sample size that is more likely to representative of the population, and of each of the lesion types.

No significant correlations were found between performance on cognitive tasks and the side (left or right) of the brain the lesion was on. Previous literature has highlighted different presentations of thalamic stroke, dependent on which side of the brain the stroke occurred. For example, medial lesions have been associated with language disturbances when the lesion is left sided. However right sided lesions are instead associated with spatial deficits (Schmahmann, 2003).
Likewise, there were no significant findings in relation to cognitive outcomes based on the size or volume of thalamic lesion. Previous literature has found differences in clinical presentations of thalamic stroke based on the size or volume of the lesion (Amici, 2012; Kumral, et al., 1995). However, the participants in this study had a mean lesion volume of 0.43 milliliters, with the largest lesion only 1.11 milliliters. Therefore, all the lesions in this group would be classified as small according to the parameters of previous research (Kumral, et al., 1995; Kwak, et al., 1983). Hence, this would explain why no meaningful results were found in relation to cognitive outcomes and size of lesion.

However, even when these data are examined at the level of individual cases, no specific pattern can be ascertained with respect to lesion volume and cognitive deficits. For example, patient ‘D’ has the lowest overall ARCS score, but the fourth largest lesion volume. Whereas patient ‘I’, who had the highest overall ARCS score, had the third largest lesion volume.

The lack of meaningful results for cognitive changes in relation to both location and size of the lesion is again a reflection of the inadequate sample size obtained in this study. There is simply not enough data with which to make comparison. Furthermore, lesion size has been associated with higher levels of disability and poorer outcomes in thalamic stroke (Kumral, et al., 1995; Kwak, et al., 1983). Therefore, the exclusion of patients with higher levels of disability has potentially also excluded patients with larger lesions.

Mood, personality and emotional changes have been identified relatively consistently throughout the literature, in both thalamic stroke and stroke in general (Aybek, et al., 2005; Chung, et al., 1996; Hackett Maree, et al., 2008; Kumral, et al., 1995; Lincoln, et al., 2012; Schmahmann, 2003). Mood disorders are estimated to occur in at least one third of patients in the first year after a stroke (Hackett Maree, et al., 2008). No prevalence rates have been reported specific to thalamic stroke. However the prevalence of mood changes including anxiety in the present sample was consistent with estimated stroke population prevalence rates. This may indicate that the prevalence of mood disorders in thalamic stroke is comparable to that of stroke in general. However, again the present data need to be interpreted with extreme caution due to the size of the sample.
Treatment and rehabilitation

Six of the 10 participants in this study recalled having physical rehabilitation such as physiotherapy, occupational therapy and speech therapy, and participating in physical exercise programs. One of the ten participants, patient ‘A’, recalled having counselling intervention. One of the participants, patient ‘C’, also reported undergoing cognitive testing but did not report any neuropsychological rehabilitation or follow-up testing. This finding is consistent with previous research indicating that stroke assessment, treatment and rehabilitation tends to focus primarily on physical symptoms and interventions, and neglect cognitive and psychological symptoms and interventions (Korner-Bitensky, et al., 2011).

Previous research has identified that stroke generally leads to motor, cognitive and behavioural impairments (Khan, et al., 2012). The current study has shown that all of these types of impairments were present in this small sample of thalamic stroke survivors. However, where other studies have focused primarily on sensory and motor deficits, the present study has focused on cognitive changes.

This study has highlighted that thalamic stroke has a likely association with general cognitive deficits, as well as possible specific deficits in areas such as memory, language and executive function. In fact, only one of the nine participants who were able to complete ARCS testing scored within the normal range for their age. Furthermore, eight of the 10 participants self-reported memory to be an outcome or side-effect of their stroke. Whilst the low power of the study is acknowledged, the data reported here are not inconsistent with previous research (Chung, et al., 1996; Kumral, et al., 1995; Schmahmann, 2003) indicating a strong association between thalamic stroke and cognitive deficits. As such, it is reasonable to question whether this population would benefit from access to cognitive rehabilitation.

Rehabilitation regimes that include both physical therapy and psychological and social work assistance have been associated with better cognitive, behavioural, and motor outcomes in some studies (Milinaviciene, et al., 2011). However, there is a limited amount of research into the effectiveness and usefulness of psychological and neuropsychological interventions with stroke survivors (Hoffmann, et al., 2011). Furthermore, the existing research generally focuses on cognitive interventions delivered by occupational therapists or similar (Bowen & Lincoln, 2007; Nair & Lincoln, 2007), rather than specialists such as neuropsychologists. As
such, the benefits of cognitive rehabilitation for thalamic stroke survivors cannot be accurately extrapolated from the existing literature.

However, given that the participants in this study performed significantly below average on five of the seven ARCS domains, including the overall ARCS score, there is cause to suggest that cognitive rehabilitation may in fact be of benefit for this population. It is also of interest to note that research has found that patients exhibiting cognitive impairment are less likely to be provided with physical rehabilitation. This is hypothesized to be due to cognitive impairments negatively affecting outcomes in physical therapy. This notion has been somewhat supported by the literature (Milinaviciene, et al., 2011). However, other literature indicates that cognitively impaired patients still benefit from rehabilitation (Rabadi, et al., 2008). As such, the benefits of both physical and cognitive rehabilitation are worthy of further investigation.

Furthermore, mood changes were also reported post-stroke in this small sample. Again, this is consistent with previous findings of mood and behavioural changes as a result of thalamic stroke. These observed changes reportedly include increased aggression, agitation, emotional blunting and loss of initiative (Schmahmann, 2003).

There is limited available literature investigating the effectiveness of psychological interventions for mood disorders occurring post-stroke. However, the existing literature suggests that there are some efficacious interventions available. These are primarily psychotropic medications, such as antidepressants. No evidence has been found for the overall efficacy of psychotherapy in post-stroke depression treatment. However, again there are a limited number of trials to draw this conclusion from (Hackett Maree, et al., 2008).

The mood changes highlighted by this and previous research detail post-stroke symptoms that may benefit from intervention. At the time of writing, the most efficacious option for treating such changes was antidepressant medication. However, this medication often causes an array of side effects that may be worsened in patients with stroke (Hackett Maree, et al., 2008). As such, further research needs to be conducted into the many possible mood interventions available, and their efficacy in stroke and thalamic stroke. This should include different medications, as well as looking at different modalities of psychological counselling and
psychotherapy, as well as alternative treatments commonly used in the treatment of mood disorders.

**Strengths and limitations**

This study has a number of limitations. The most overt and significant of these is the very small sample size, and the resultant low power of any findings. The study had intended to include a sample of at least 30 thalamic stroke patients. However, a highly exclusive screening process reduced the number of possible participants to around 20. Unfortunately, only half of these possible participants agreed to attend an interview and testing session.

The reasons for such a low consent rate are unclear. However, it is possible that patients felt a sense of obligation when initially contacted by their doctor that was no longer present when contacted by the researcher to obtain consent. It is also possible that potential participants were not provided with sufficient information on the nature of the research and what was required of them, prior to contact from the researcher.

The sample size is also quite small as the research has only accessed the patient population of one hospital, the John Hunter Hospital located in Newcastle. Furthermore, the study has included patients who presented within a two year time frame. Had the research not been limited by time constraints, patients who suffered a thalamic stroke after the commencement of the research could have been followed up at a later date. However, as time was a constraining factor, a number of potential participants with more recent strokes may have been missed.

Furthermore, the exclusion of patients who had higher levels of disability has impacted the study in many ways. Not only has this excluded a number of potential participants, it has also potentially skewed the response data obtained in this study. A comparison between data found in the present study, and those of previous research, highlights several disparities. However, it is more than likely that this is a reflection of the screening process. Including patients of all levels of disability would have both increased the sample size, and it would also have provided a more representative sample.

However, a strength of the present research is that it is potentially the first to provide measurable and comparable data on cognitive outcomes in thalamic stroke. Where previous
studies have reported specific cognitive outcomes, no measurable data such as cognitive or neuropsychological testing have been reported. The data in the present study allows comparison with other populations, as well as within the thalamic stroke population.

This being said, the cognitive test used in this study comes with its own limitations. The ARCS is a relatively new tool that is not likely to be known by a number of clinicians. This reduces the ability of other clinicians and researchers to replicate the research. However, the ARCS has demonstrated strong correlations with well-known cognitive tests (P.W. Schofield, et al., 2010; Peter W. Schofield, Lee, Lyall, Zunong, & Kwan, 2008). As such, the present research could be replicated using known tests and the data would still be comparable.

As previously highlighted, the ARCS has primarily been tested and used in the Newcastle area of New South Wales, and independent data on its validity and reliability has not yet been published. Furthermore, while the ARCS’ validity and reliability has been tested on patients with dementia, the elderly, depressed and psychotic patients, it has not been tested in a stroke population (Loughland, et al., 2010; P.W. Schofield, et al., 2010; Peter W. Schofield, Lee, & Lyall, 2009; Peter W. Schofield, et al., 2008)

The limitations of the ARCS being a pen and paper style test are also acknowledged. Given that thalamic stroke can produce motor dysfunction, it is important to acknowledge and control for the possibility that the physical effects of stroke may impact a participant’s ability to complete testing. In the present sample this was controlled for by the close observation of the researcher. All testing was administered by the researcher who closely monitored participant performance. Hence, the reported ARCS results can be confirmed as an accurate measure of the cognitive abilities of the participants and are not subject to the confound of physical dysfunction.

The ARCS was chosen due to its brevity and simplicity. As such, the fatigue often associated with stroke will have had minimal impact on testing. Although there are a number of well validated neuropsychological measures that could have been used, the length of time required to complete a battery of such tests would have been considerable. The scope, brevity and ease of administration of the ARCS were judged to be most appropriate for this sample.
Finally, it is acknowledged that information such as participant education levels and socio-economic status was not collected in this study and it is possible, therefore, that some of the variability in the present data set may be due to factors such as these. Nonetheless, the fact that the participant performance was so clearly and dramatically inferior to the aged matched normed sample taken from various social backgrounds, suggests that any such influence was minimal compared with the effects of the stroke.

**Future Research**

The limitations of the present study make it difficult to ascertain the significance and validity of the results obtained. Nevertheless, a number of these results are worthy of further investigation. First and foremost, the present study needs to be replicated with a larger and more representative sample. Ideally, this should include patients from more than one hospital, and patients with all levels of disability. Where examination of circle of Willis and basilar artery anatomy is concerned, MRI images from deceased patients should also be examined. A larger sample size should hopefully also allow comparison of cognitive outcomes based on the size of the thalamic lesion, as well as the location.

This study has also raised a number of questions that require further investigation. The results of this study are suggestive of a relationship between circle of Willis anatomy variations and thalamic stroke. Specifically, there may be a relationship between an absent or hypoplastic PCOM and thalamic stroke. Further research is needed to explore this finding. This research should include a larger sample size. Ideally, such research would examine the MRI images of patients with thalamic stroke. This should include patients with all levels of disability, stroke lesions additional to the thalamus, and deceased patients. The aim of such research would be to investigate the possibility that thalamic stroke victims have a higher prevalence of circle of Willis variations than expected in the general and stroke population. Furthermore, that there is a relationship between such variances and the size of the thalamic stroke lesion should be investigated.

The present study found no significant relationship between basilar artery diameter and thalamic stroke outcomes. However, this is likely due to the fact that the present sample is not representative of the population. It is recommended that this finding be further examined by including thalamic stroke victims of all levels of disability.
The cognitive outcomes measured by the ARCS in the present study indicate cognitive deficits in the thalamic stroke population. Whilst a more robust study needs to be conducted to confirm the findings of this study, this finding is not the first of its kind. However, it has been highlighted that little if any cognitive rehabilitation has been provided to this cohort, or to stroke patients in general. Further research should investigate the efficacy and usefulness of different types of cognitive rehabilitation with post-stroke cognitive deficits, as compared to placebo or no intervention.

Likewise, further investigation into the efficacy and usefulness of psychological and psychiatric intervention for post-stroke mood, personality and behavioural changes is warranted. Consistent with previous research, this study found mood and behavioural changes present in its small sample. However, the majority of the sample reported no psychological or psychiatric, or mood interventions post-stroke.

The benefits of different types of psychological, pharmacological, and alternate treatments for mood disorders in stroke and thalamic stroke needs further investigation. This would help to determine whether the low referral rate to such services is warranted, or whether such referrals would be beneficial to patients with stroke and thalamic stroke. However, it may also be of interest and benefit to determine the reasons behind these low referral rates. Such research should investigate the possibilities that mood assessment tools are underutilized in hospital settings; that medical staff are under-skilled in the identification and assessment of mood disorders; and that medical staff are of the belief that mood intervention would not be of assistance to stroke patients.

**Summary/Conclusion**

Due to a number of factors, this study has only obtained a very small sample. Due to this, the results of the study have limited statistical significance, validity and reliability. However, a number of the findings of this study are of clinical interest. These include the high proportion of PCOM circle of Willis variances, and possible link to lesion size; the underperformance on cognitive tasks across all types of thalamic stroke, and the variations based on specific location of the lesion; and the identification of mood and psychological changes, in addition to cognitive changes, in the context of minimal psychological and neuropsychological treatment and rehabilitation.
The low statistical power of these findings means that they are, on their own, of minimal clinical significance. However, these results are indicative of areas needing further exploration. Replication of the present study with a larger and more representative sample, further investigation of the presence of PCOM variances in thalamic stroke, and investigation into the benefit of psychological and/or neuropsychological treatment and rehabilitation in thalamic stroke, are future directions indicated by the limited results of this study.
References


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Appendices

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Appendix A

Journal Scope and Notes for Authors
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Instructions for Authors

Stroke: A Journal of Cerebral Circulation publishes reports of clinical and basic investigation of any aspect of the cerebral circulation and its diseases from many disciplines, including neurology, internal medicine, radiology, nuclear medicine, neuropathology, neurosurgery, epidemiology, vascular surgery, rehabilitation, anesthesiology, critical care medicine, vascular physiology, neuropsychology, speech pathology, and neuro-ophthalmology.

Original Contributions. For preparation, see "Instructions for New Submissions." Maximum length for manuscripts is 4,500 words. Please note that the 4,500-word limit includes title page, abstract, main body of text, acknowledgments, sources of funding, disclosures, references, figure legends, tables, and appendices intended for print publication. Please note the publication fees in the Costs to Authors section. Authors should eliminate redundancy, emphasize the central message, and provide only the data necessary to convey that message. The total number of figures and/or tables is limited to 6. Each figure may contain up to 4 panels (i.e., parts A to D) and must conform to the requirements for figures described in that section of the instructions to authors. Additional figures and tables up to a combined total of 4 may be submitted for publication but will appear as an online data supplement. The use of the online data supplement is strongly encouraged not only for additional tables and figures but for complex methodology, large tables, and complex figures. They must be clearly labeled as data supplement on the title page and in references throughout the paper and should be placed at the very end of the manuscript.

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• We recommend using Times New Roman 12-point font.

• Leave 1-inch margins on all sides. Number every page, beginning with the abstract page, including tables, figure legends, and figures.

• Cite each figure and table in text in numerical order.

• Manuscripts should be presented in the following sequence:

  1. **Title page**
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  7. **References**
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• Cite each reference in text in numerical order and list in the References section. In text, reference numbers may be repeated but not omitted. Do not duplicate references either in text or in the reference list.

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• 3 to 7 key words for use as indexing terms
• Subject Codes for use as search terms across Highwire Press online journals Article Collections database. Please select from the Journal Subject Codes List.
• Specify the number of words on your title page. Word count should include all parts of the manuscript (i.e., title page, abstract, main body of text, acknowledgments, sources of funding, disclosures, references, figure legends, tables, and appendices intended for print publication). Over-length manuscripts will NOT be accepted for publication without an additional page charge. See the Costs to Authors below.

**Abstract**
• Do not cite references in the abstract.
• Limit use of acronyms and abbreviations.
• Be concise (250 words, maximum).
• The abstract should have the following headings:
• Background and Purpose (description of rationale for study)
• Methods (brief description of methods)
• Results (presentation of significant results)
• Conclusions (succinct statement of data interpretation)
• When applicable, include a fifth heading: "Clinical Trial Registration Information." Please list the URL, as well as the Unique Identifier, for the publicly accessible website.
on which the trial is registered. If the trial is not registered, please indicate the reason in the heading.

Example 1: Clinical Trial Registration-URL: http://www.clinicaltrials.gov. Unique identifier: NCT00123456.
Example 2: Clinical Trial Registration-This trial was not registered because enrollment began prior to July 1, 2005.

Text

- Follow the instructions in “Manuscript Formatting.”
- The following are typical main headings: Materials and Methods, Results, Discussion, and Summary.
- Abbreviations must be defined at first mention in the text, tables, and figures.
- Introduction: This section should briefly introduce the context of the results to be presented and should duplicate what is contained elsewhere in the manuscript
- Methods:
  - For any apparatuses used in Methods, the complete names of manufacturers must be supplied.
  - For human subjects or patients, describe their characteristics.
  - For animals used in experiments, state the species, strain, number used, and other pertinent descriptive characteristics.
  - When describing surgical procedures on animals, identify the preanesthetic and anesthetic agents used, and state the amount or concentration and the route and frequency of administration for each. The use of paralytic agents, such as curare or succinylcholine, is not an acceptable substitute for anesthetics.
  - For other invasive procedures on animals, report the analgesic or tranquilizing drugs used. If none were used, provide justification for such exclusion.
  - Manuscripts that describe studies on humans must indicate that the study was approved by an institutional review committee and that the subjects gave informed consent.
  - Manuscripts involving animals must indicate that the study was approved by an institutional animal care and use committee.
  - Reports of studies on both animals and humans must indicate that the procedures followed were in accordance with institutional guidelines.
  - All drugs should be referred to by their generic names rather than trade names. The generic chemical identification of all investigational drugs must be provided.
  - A statistical subsection must be provided at the end of the Methods section describing the statistical methodology employed for the data presented in the manuscript.
  - The Methods section should provide essential information related to the conduct of the study presented in the manuscript. For methodology previously published
by the authors, the prior publication should be referenced and a copy of the paper provided to the reviewers, if necessary.

– The Methods section should only contain material that is absolutely necessary for comprehension of the results section. Additional (more detailed) methods can be provided as a data supplement.

– Prevention of bias is important for experimental stroke research (see Macleod et al, Stroke. 2009;40:e50–e52). For studies where the primary objective is the preclinical testing of therapies, the following checklist items must be adhered to:

1 Animals: Species, strains and sources must be defined. For genetically modified animals, wildtype controls including background and back-crossing must be defined.
2 Statistics and sample size: Specific statistical methods must be defined, including parametric versus nonparametric and multigroup analyses, and sample size powering based on expected variances and differences between groups.
3 Inclusions and exclusions: Specific criteria for inclusions and exclusions must be specified. For example, only animals where blood flow reductions fall below a certain threshold are included. Or only animals with a certain degree of neurological deficits are included. Once animals are randomized (see below), all excluded animals must be reported, including explicit presentation of mortality rates.
4 Randomization, allocation concealment and blinding: All animals must be randomized. Investigators responsible for surgical procedures or drug treatments must be blinded. End point assessments must be performed by investigators blinded to the groups for which each animal is assigned.

• Results: This section should succinctly report the results of experimental studies and clinical research or clinical series/observations.

• Guidelines for Human Phenotype–Genotype Association or Linkage Studies:
  A. Reporting issues
  1 Report process for selecting genes and SNPs.
  2 Report Hardy-Weinberg statistics or P values and method of calculating same.
  3 Refer to existing public domain websites for the Human Gene Ontology name and the rs number for SNPs.
     http://www.gene.ucl.ac.uk/nomenclature/
  4 Describe genotyping methods. If numerous primers have been used, please include them in an online supplement.
B. False-positive and false-negative concerns. Given well-described problems with both false-positive and false-negative associations, phenotype–genotype association studies should meet some or all of the criteria below:

1. Phenotype is clearly defined, is heritable, and if a quantitative phenotype is reported, reproducibility data are provided.

2. The sample size is adequate to detect a SNP or haplotype with a modest effect. For genotype-trait associations, provide an estimate of the effect size that could be detected with power 0.80 or higher with the allele frequency and sample size reported.

3. Since multiple statistical testing methods are frequently used in genotyping-phenotyping studies, please include specifics of the primary model(s) tested. Nonessential secondary models may be published as electronic data supplements. Clinically relevant confounders should be included in multivariable models or residuals.

C. Review criteria for human linkage studies. Manuscripts should include the following:

1. Identifying plausible candidate genes under the linkage peak.

2. Follow-up fine mapping to narrow the region of linkage, and/or genotyping some of the candidate genes under the linkage peak.

3. Replication data from another sample.

• Guidelines for Genomic and Proteomic Studies:

- Preparation of Data Submitted: Data should follow the MIAME checklist (for more information see http://www.mged.org/Workgroups/MIAME/miame_checklist.html).

- Accessibility of Data: Authors of papers that include genomic, proteomic, or other high-throughput data are required to make their data easily accessible for the reviewers and the editors during the review process.

□ You may submit your data to the NCBI gene expression and hybridization array data repository (GEO, http://www.ncbi.nlm.nih.gov/geo/) and provide the GEO accession number; or,

□ You may provide a link to a secure or publicly accessible Web site which hosts the data. Prior to publication, the data must be submitted and an accession number obtained. Access to the information in the database must be available at the time of publication. GEO has a Web-based submission route, suitable for a small number of samples, or a batch submission tool (called SOFT). GEO is accessible from http://www.ncbi.nlm.nih.gov/geo/ The submission FAQ is available at (http://www.ncbi.nlm.nih.gov/projects/geo/info/faq.html).

• Guidelines for Proteins and Nucleic Acid Sequences:

- Newly reported nucleotide or protein sequences must be deposited in GenBank or EMBL databases, and an accession number must be obtained. Access to the information in the database must be available at the time of publication. Authors
are responsible for arranging release of data at the time of publication. The authors must also provide a statement in the manuscript that this sequence has been scanned against the database and all sequences with significant relatedness to the new sequence identified (and their accession numbers included in the text of the manuscript).

- GenBank
  GenBank Submissions
  National Center for Biotechnology Information
  8600 Rockville Pike, Building 38A
  Room 8N-805
  Bethesda, MD 20894
  Tel: (301) 496-2475

- EMBL Nucleotide Sequence Submissions
  European Bioinformatics Institute
  Hinxton Hall
  Hinxton, Cambridge CB10 1SD, UK
  Tel.: 44-1223-494401; Fax: 44-1223-494472
  e-mail: support@ebi.ac.uk
  On the web at: http://www.ebi.ac.uk

- DNA Data Bank of Japan
  Center for Information Biology
  National Institute of Genetics
  Mishima, Shizuoka, 411, Japan
  Tel.: 81-559-81-6853; Fax: 81-559-81-6849
  On the web at: http://www.ddbj.nig.ac.jp

- Submission to any data bank is sufficient to ensure entry in all.

- **Discussion**: This section should not reiterate the results but put the results in appropriate context regarding relevant literature and the importance of new observations contained in the manuscript.

- **Summary/Conclusions**: A brief paragraph summarizing the results and their importance may be included but is not required.

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**References**

- Accuracy of reference data is the author's responsibility. Verify all entries against original sources, especially journal titles, inclusive page numbers, publication dates, accents, diacritical marks, and spelling in languages other than English.

- Do not list the month/issue/day (the number in parentheses) in the reference.

- **NEW:** References with more than 6 authors should list the first 6 authors followed by et al.

- Cite references in numerical order according to first mention in text.

- Personal communications, unpublished observations, and submitted manuscripts must be cited in the text, not in the references, as "([name(s)], unpublished data, 20XX)."

- References must be from a full-length publication in a peer-reviewed journal.

- Abstracts may be cited only if they are the sole source and must be identified in the references as "Abstract."

- “In-press” citations must have been accepted for publication and the name of the journal or book publisher included.

- Example of a journal reference:
• Example of a book chapter reference:

• Example of a publish-ahead-of-print reference:

• Example of a website reference:
  CDC Chronic Disease Indicators: Indicator Definition. Hospitalization for cerebrovascular accident or stroke. National Center for Chronic Disease Prevention and Health Promotion web site.

• Web sites generally follow this format: Author names (if any). Title of information or page. Name of website. URL. Publication date (if any). Access date.

**Figure Legends**

Provide figure legends on a separate page of the manuscript.

**Tables**

• Each table must be typed on a separate sheet and double-spaced, if possible. The table number should be Arabic, followed by a period and a brief informative title.

• Use the same size type as in text.

• Tables should be cell-based (i.e., constructed using Microsoft Word tables or Excel). Do not use tabs or hard returns. Do not supply tables as graphics.

• Tables should be used to present comparisons of large amounts of data at a glance. Tables with only 1 or 2 rows of data should be incorporated into the text.

• Tables should be as compact as possible. Avoid unnecessary rows and columns.

• Use indenting within the stub column to indicate subgroups. Do not use bold, shading, rules, etc.

• Tables should not contain vertically merged cells; horizontally merged cells are permitted when necessary in the heading row.

• Internal headings are not permitted outside of the stub column. If internal headings are required, the table should be split into 2 tables.

• No internal shading is permitted.

• Units of measure should be in the heading row or stub column rather than the body of the table whenever possible.

• Indicate footnotes in the table in this order: *, †, ‡, §, | |, #, * *. Follow AMA 9th edition for footnote styles.

• Tables should be concise.
Figures

- Authors should be pleased with the figure submission quality before submission. We recommend that you print the figure at its final publication size to check the quality.

- Figures should be submitted as high-resolution TIFF or EPS files. PowerPoint files can be accepted but is a less preferred file format, as elements within the figure (such as axis labels) may shift location or drop out during conversion. JPEG, Word, and Excel files should not be used. See Artwork and Table Guidelines (PDF) for instructions for creating high-quality digital art in various software applications.

- Color figures should be in RGB (red/green/blue) mode. If a figure is supplied in CMYK (cyan/magenta/yellow/black) mode, there may be a shift in the appearance of colors, especially fluorescents. Figures that will appear in black and white should be submitted in black and white.

- Figures should be supplied at the highest resolution possible for optimal clarity. Color figures should be at least 300 dpi; halftones, 600 dpi; and line art, 1200 dpi.

- Figures should be submitted at the final publication size. Please note that most figures will be sized at 1 column wide. Dimensions for figures are:
  - 1 column: 3.25 inches wide
  - 2 columns: 6.80 inches wide

- For line and bar graphs and pie charts, ensure that the colors/lines/symbols used for the different sets of data are easily distinguishable.

- Graphs and charts should have a white background. Do not use dark PowerPoint backgrounds.

- Labels for panels should be uppercase letters (A, B, C, etc) in boldface Arial or Helvetica.

- Multipart figures may have no more than 4 panels.

- Multipart figures may be set at 2 columns across the page and should be laid out horizontally if appropriate.

- Use the same font (typeface) throughout the figure. Sans serif fonts, such as Arial and Helvetica, work best.

- Use the largest font size possible without distorting the figures. Text should be no smaller than 6 points.

- Whenever possible, all text within a figure should be the same size. If this is not possible, the font size should vary by no more than 2 points.

- Label units of measure consistently with the text and legend. Follow the AMA for unit abbreviations.

- Incorporate figure keys into the legend rather than including them as part of the figure whenever possible. Titles should be included in the figure legends.

- Any abbreviations or symbols used in the figures must be defined in the figure or figure legend.
Follow AMA 9th edition for footnote style in legends.

If the figure is reprinted/adapted from another source, please provide a permission letter and include the source in the legend. If no language is provided in the permission letter, use the following sample:
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Supply a scale bar with photomicrographs.

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See AMA, 10th edition, Section 4.2 for more information on figures.
Appendix B

Additional Risk factor data

<table>
<thead>
<tr>
<th>Participant (with risk factor cholesterol identified) N=4</th>
<th>Other risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Hypertension, pre-existing heart condition</td>
</tr>
<tr>
<td>E</td>
<td>Diabetes, pre-existing heart condition, hypertension</td>
</tr>
<tr>
<td>H</td>
<td>Nil reported</td>
</tr>
<tr>
<td>J</td>
<td>Hypertension, pre-existing heart condition, alcohol use</td>
</tr>
</tbody>
</table>

Table 1: Participants with risk factors additional to cholesterol.

<table>
<thead>
<tr>
<th>Lesion Location</th>
<th>Number of participants with PCOM variation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterolateral</td>
<td>1</td>
</tr>
<tr>
<td>Dorsal</td>
<td>2</td>
</tr>
<tr>
<td>Anterolateral</td>
<td>2</td>
</tr>
<tr>
<td>Medial</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 2: Participants with PCOM variation by lesion location

<table>
<thead>
<tr>
<th>Gender</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>4</td>
<td>75.00</td>
<td>7.071</td>
<td>3.536</td>
</tr>
<tr>
<td>Male</td>
<td>6</td>
<td>77.17</td>
<td>5.193</td>
<td>2.120</td>
</tr>
</tbody>
</table>

Table 3: Mean Age of males and females
### Independent Samples Test

<table>
<thead>
<tr>
<th></th>
<th>Levene's Test for Equality of Variances</th>
<th>t-test for Equality of Means</th>
<th>95% Confidence Interval of the Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F</td>
<td>Sig.</td>
<td>t</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Equal variances assumed</td>
<td>0.270</td>
<td>0.617</td>
<td>-0.563</td>
</tr>
<tr>
<td>Equal variances not assumed</td>
<td></td>
<td></td>
<td>-0.526</td>
</tr>
</tbody>
</table>

Table 4: Statistical significance of difference in mean age between males and females
## Appendix C

### Additional Outcome Data

<table>
<thead>
<tr>
<th>Lesion Location (number of participants)</th>
<th>Reported outcome (number of participants reporting)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterolateral (1)</td>
<td>Memory (1), use of hands (1)</td>
</tr>
<tr>
<td>Medial (4)</td>
<td>Memory (3), tired/energy (1), unable to write (1), coordination (2), balance (1), grip/drops things (1)</td>
</tr>
<tr>
<td>Dorsal (3)</td>
<td>Balance (1), memory (3), anxiety (1), mobility/walking (2), mood (1), concentration (1), tired/energy (1)</td>
</tr>
<tr>
<td>Anterolateral (2)</td>
<td>Energy (1), memory (1), balance (1), reduced movement in legs/mobility (1), dribbling (1)</td>
</tr>
</tbody>
</table>

**Table 5: Reported outcomes for different lesion locations**

<table>
<thead>
<tr>
<th>Correlations</th>
<th>Location of thalamic lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory</td>
<td>Pearson Correlation -0.086</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed) 0.825</td>
</tr>
<tr>
<td></td>
<td>N 9</td>
</tr>
<tr>
<td>Fluency</td>
<td>Pearson Correlation 0.142</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed) 0.715</td>
</tr>
<tr>
<td></td>
<td>N 9</td>
</tr>
<tr>
<td>Visuospatial</td>
<td>Pearson Correlation 0.045</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed) 0.907</td>
</tr>
<tr>
<td></td>
<td>N 9</td>
</tr>
<tr>
<td>Language</td>
<td>Pearson Correlation 0.616</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed) 0.077</td>
</tr>
<tr>
<td></td>
<td>N 9</td>
</tr>
<tr>
<td>Attention</td>
<td>Pearson Correlation 0.053</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed) 0.892</td>
</tr>
<tr>
<td></td>
<td>N 9</td>
</tr>
<tr>
<td>SOW</td>
<td>Pearson Correlation -0.324</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed) 0.394</td>
</tr>
<tr>
<td></td>
<td>N 9</td>
</tr>
<tr>
<td>ARCS</td>
<td>Pearson Correlation 0.402</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed) 0.283</td>
</tr>
<tr>
<td></td>
<td>N 9</td>
</tr>
</tbody>
</table>

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

**Table 6: ARCS scores correlated with location of lesion**
Appendix D

Evidence of Journal Submission

>>> <stroke@strokeahajournal.org> 11/02/12 10:39 AM >>>
MS ID#: STROKE/2012/681106
MS TITLE: Thalamic stroke: pre-cursors and outcomes for 10 patients.

Dear Mick Hunter,

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Your Manuscript Number is: STROKE/2012/681106. Please take note of this number for future reference.

To follow the progress of your paper under review please go to:
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Thank you for your submission.
Yours sincerely,

Editorial Office
Stroke
Appendix E

Demographic Questionnaire

Demographic and behavioural data interview sheet (Version 2)

Participant number:____________

Date:________________________

PARTICIPANT QUESTIONS:

Date of birth:

Gender:

Date of stroke:

Is English your first language?

Do you have any illnesses/injuries apart from your stroke?

Have you ever been diagnosed with a mental illness?

Have you ever sustained a head or brain injury apart from your stroke?

Premorbid functioning:

Work, community activities, hobbies prior to stroke
Post stroke functioning:

Observed behavioural, physical and cognitive changes since stroke

PARTNER/CARER QUESTIONS:

Premorbid functioning:

Work, community activities, hobbies prior to stroke

Post stroke functioning:

Observed behavioural, physical and cognitive changes since stroke