NEUROPSYCHOLOGICAL SEQUELAE OF TRANSIENT ISCHAEMIC ATTACKS

BY

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Summary

The present study aimed at investigating the neuropsychological sequelae of transient ischaemic attacks. Transient ischaemic attacks are defined as those neurological disorders in which there is complete resolution of neurological symptoms within twenty-four hours. Transient ischaemic attacks may or may not reveal evidence of brain infarcts on imaging studies. In the present study, the neuropsychological sequelae of transient ischaemic attacks in the carotid circulation were investigated since, within the perspective of cognitive neuropsychology, it was assumed that localized changes in cognitive functions could be demonstrated. Since several psychological, medical and neurological factors are known to influence scores on neuropsychological tests, regression analyses were performed to determine which factors contributed significantly to the variance of scores on neuropsychological tests in the transient ischaemic attack and control groups. Two transient ischaemic attack groups, each comprising forty left and forty right hemisphere involvement patients, were then compared with each other and with a control group of forty general medical patients. Stenosis of the carotid artery formed a significant predictor of test scores in the combined transient ischaemic attack group. When the groups were analyzed independently, in the left transient ischaemic attack group stenosis predicted performance on the same tests reaching significance for the combined group, and for the Wisconsin Card Sorting Test (Perseverative Score). In the right transient ischaemic attack group, stenosis significantly predicted performance on Digits Forward, Backward and Total, the PASAT (2.4 seconds) and Trails B. On the other hand, education formed a significant predictor of performance on Digits Forward, Digits Backward and Digits Total and the PASAT (all levels) in the control group. Multivariate comparisons revealed that the left and right transient ischaemic attack groups performed worse than the controls on tests of attention, concentration and conceptual flexibility. The left transient ischaemic attack group performed worse than the right transient ischaemic attack group on all tests of attention and concentration, but there was a significantly better performance of the former group on the Rey Auditory Verbal Learning Test (Trial 1), Block Designs and Verbal Fluency. The findings on the PASAT that left transient ischaemic attack patients performed significantly worse than the right hemisphere group were considered to be relatively unreported previously in the literature on transient ischaemic attacks. The findings obtained are discussed from a neurocognitive perspective of neuropsychological functioning in transient ischaemic attacks.

Declaration

" I declare that Neuropsychological Sequelae of Transient Ischaemic Attacks is my own work and that all the sources that I have used or quoted have been indicated and acknowledged by means of complete references".

Lazarus

Theophilus Lazarus

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It is the Blood that giveth Life

(The Holy Bible:John 5:11)

CHAPTER ONE

Introduction to the Study

1.1. Introduction

Neuropsychology has traditionally been defined as the study of behaviour at various levels, relating behaviour to aspects of central nervous system functioning (Kolb and Whishaw, 1996). Behaviour does not only become altered in the presence of organic variables that alter the structure and functioning of the central nervous system, but also in the presence of psychological and social variables that are mediated through the nervous system (Luria, 1980; Lezak, 1995). Neurological diseases present one form of medical condition in which the structure of the nervous system is compromised through disease (or damage). Damage to the nervous system may occur in the form of traumatic brain injury in which the damage involves physical forces of acceleration and deceleration (Stuss, Stethem and Pelchat, 1988). It becomes apparent that apart from the physical influences, there are emotional and social issues which interplay in the behavioural changes taking place in the patient.

In systemically-related neurological diseases (for example, cerebrovascular diseases and neoplasms), no apparent physical trauma is apparent. Instead these systemically-related disorders result in a single major form of neuropathology with accompanying physical and/or psychological sequelae (Lishman, 1987). Cerebrovascular diseases encompass a wide range clinical presentations, each with varying types of neuropathological processes. Stroke represents the most extreme form of a continuum of cerebrovascular diseases in which the disorder is accompanied by defined areas of brain damage (Ernst and Stanley, 1991), visualized by a series of neuroimaging techniques. It is accepted that stroke is defined as a neurological disorder with lasting neurological impairment, accompanied by documentable areas of brain damage called infarcts. In addition to the lasting neurological impairments, there are expected neuropsychological sequelae accompanying strokes (Lezak, 1995).

Strokes are considered to have one of two underlying neuropathological conditions--haemorrhage in which the rupturing of a blood vessel is associated with other medical variables, the chief of which is hypertension. In occlusive strokes, the underlying neuropathology is narrowing of the blood vessel with total occlusion of the artery resulting in the presentation of major stroke symptoms.

It may be argued that at the opposing end of the cerebrovascular disease spectrum are the ischaemic diseases in which there are varying periods of termination of vascular supply, with resulting variations in the duration of neurological symptom presentation. Ischaemic cerebrovascular diseases are therefore essentially occlusive in nature, with the occlusion of a blood vessel resulting from the thrombus formation of an underlying atherosclerotic process or the lodging of emboli from distant, but related sources, such as the heart (Rutherford, 1995). A thrombus is a build-up of plaque in the endothelial lining of arteries. An embolus is defined as a mass of tissue (such as a thrombus) or other body that travels within the arterial systems and lodges itself within the vasculature at some point distant to its site of origin (Cohen, 1995).

The study of neuropsychological sequelae in cerebrovascular disease has been guided by the findings of neurological and neurovascular studies adopted in these clinical conditions. Two major principles of neurological investigation are influential in neuropsychological studies (Bornstein and Brown, 1991). The first relates to a major anatomical principle, with regard to the organization of the cerebral vasculature. The vasculature of the nervous system comprises two interdependent systems--the anterior internal carotid and the posterior vertebrobasilar arterial systems. Since these vascular systems perfuse different areas of the brain (although there are areas of overlap), one way to approach the study of neuropsychological sequelae in transient ischaemic attacks would therefore be to examine groups of these patients in independent analyses as suggested by Taghavy and Hamer (1995). It has therefore been suggested that studying transient ischaemic attacks referable to the anterior internal carotid artery system may afford an opportunity to refine the process of identifying those functional systems that are affected by this neurological disorder, particularly in the light of the modularization theories of cognitive neuropsychology.

The second principle observation relates to the variation in the duration of neurological symptoms which has prompted the development of classification systems aimed at the diagnosis, investigation of neuropathological processes and treatment of these disorders (Norris, Bornstein and Chambers, 1991). Transient ischaemic attacks are described as cerebrovascular diseases in which the duration of neurological symptoms do not exceed twenty-four hours, and there is complete recovery of neurological functioning. In such disorders, there may or may not be evidence of infarcts on computerized tomography imaging (Norris and Zhu, 1992). The continued use of a classification system of cerebrovascular diseases based on the temporal nature of the presenting symptoms suggests that the duration of symptoms may form a critical variable in identifying the type of cerebrovascular disease, predicting its course, planning the neurological investigation of the disease in the context of time and economy, and in the overall management of the disease.

The process of understanding the dynamics of transient ischaemic attacks has been refined and greatly enhanced through the advancement of technology used in identifying the underlying neuropathology of this cerebrovascular disease. Advanced neuroimaging techniques (magnetic resonance imaging) have indicated that transient ischaemic attacks are often accompanied by stenosis of the internal carotid artery (and its subdivisions) with infarcts in areas perfused by those blood vessels affected in the transient ischaemic attack. The underlying neuropathological process of transient ischaemic attacks has been identified to be atherosclerosis in the majority of cases (Cohen, 1995) suggesting that resulting stenosis of the artery itself may be a factor influencing the type and presentation of neuropsychological sequelae. The identification of atherosclerosis as a significant contributor to the development of transient ischaemic attacks has prompted the development of various prophylactic methods to prevent the development of stroke. Some of these methods have been medical therapy in the form of aspirin or other types of anticoagulants (Cohen, 1995)). Clinical trials have reported that the clinical efficacy of aspirin therapy is of the order of 80% (SALT Collaborative Group, 1991) thus making a significant contribution to the management of transient ischaemic attacks.

Neuropsychological studies of transient ischaemic attacks have traditionally posed the question of whether there are lasting sequelae in transient ischaemic attacks, despite the complete resolution of neurological symptoms. This question has been empirically investigated in two major research strategies based on the type of intervention strategy adopted by medical professionals treating this category of patient. In one methodological design whereby studies have not employed surgical intervention, the guiding principle of the investigations has been that transient ischaemic attack patients suffer lasting neuropsychological sequelae beyond the period of neurological resolution. The number of reported studies employing this strategy appears to have steadily reduced as indicated by a the review of recent literature based on Medline (1997 July) and Psychlit (1997) searches. One major reason that may contribute to this finding is that vascular intervention in the form of carotid endarterectomy or artery bypass surgery has been given additional impetus with the demonstration of their clinical efficacy (Moore, 1995) and is routinely undertaken in patients meeting certain criteria. However, research suggests that in view of the several complicating variables that influence the decision of whether to undertake surgery or not, this route to prophylactic care in transient ischaemic attacks is not always routine (Cohen, 1995).

Apart from psychological variables, intraoperative factors related to the surgery have been identified in vascular studies on this patient group. Intraoperative ischaemia (Ahn and Concepcion, 1995) for example, has been identified as a major surgical variable influencing neurological outcome and this factor has not been considered with regard to its potential influence on post-endarterectomy neuropsychological test scores. The identification of intraoperative ischaemia has led some researchers to call for the inclusion of methods monitoring intraoperative ischaemia as an important variable, and various forms of guidelines for such monitoring have been proposed (Ahn and Concepcion, 1995).

The finding of continued transient ischaemic attacks (and possibly strokes) even after surgical intervention procedures like endarterectomy has been another reported concern among certain authorities (Chervu, 1995). In what appears to be support for restraint in practicing exclusively vascular-based intervention in transient ischaemic attacks, some authorities have called for the reinstatement of medical-based therapy, aimed also at reducing or eliminating risk factors (Cohen, 1995). This form of prophylactic therapy, which is largely aspirin-based therapy, (according to Cohen, 1995) suggests that there may be benefits equal to that of carotid endarterectomy in transient ischaemic patients.

Within this context of the diagnostic and management issues related to transient ischaemic attacks, several neuropsychological studies have reported neuropsychological sequelae in patients with transient ischaemic attacks within the carotid circulation. Neuropsychological studies themselves have been guided by the development of neuropsychological theories and associated psychometric instruments. In 1982, Dull, Brown, Adams, Shatz, Diaz and Ausman reported that in their sample of transient ischaemic attack, reversible ischaemic neurological deficit and stroke patients, Average Impairment Ratings based on the Halstead-Reitan Neuropsychological Battery were directly related to the duration of associated neurological symptoms associated with the longest ischaemic attack. The duration of ischaemia was assumed to be related to the underlying neuropathological process and the presentation of symptoms and therefore forms an important variable in neuropsychological research.

In further investigations of transient ischaemic attacks, other medical risk factors were found to influence the probability of developing transient ischaemic attacks. Soelberg-Serensen, Marquardsen, Pedersen and Heltberg (1989) reported that among females, hypertension and age had a differential effect in determining the risk for transient ischaemic attacks. The authors indicated that younger females with hypertension or diabetes, in comparison to males, had a lower probability of developing transient ischaemic attacks. Soelberg-Serensen et al. (1989) suggested that the role of medical risk variables, particularly hypertension and diabetes, in neuropsychological test performances deserved attention, particularly in the context of transient ischaemic attacks.

Other studies have suggested that laterality effects on neuropsychological test performances in transient ischaemic attacks may be demonstrated in studies of patients who had undergone endarterectomy for lateralized stenosis to carotid arteries. Greiffenstein, Brinkman, Jacobs and Braun

(1988) found that right transient ischaemic attack patients undergoing carotid endarterectomy showed significant post-operative gains on Performance IQ scores as well as on a speed/concentration composite score. The authors interpreted these findings to suggest that neuropsychological functions may be strongly lateralized emphasizing that studies need to identify left and right transient ischaemic attack patients with a view to documenting the relative changes in neuropsychological functions.

In further investigations of transient ischaemic attacks, some studies have tended to employ serial neuropsychological test performances in patients undergoing carotid endarterectomy as a measure of outcome after surgery. In one such study, Casey, Ferguson, Kimura and Hachinski (1989) reported that the post-endarterectomy neuropsychological test scores of transient ischaemic attack patients were similar to a control group tested at equivalent intervals, and thus raised the issue of practice effects as an important factor influencing neuropsychological test scores.

In more recent studies, Taghavy and Hamer (1995) have tended to question the rationale underpinning the study of left and right hemisphere groups independently since atherosclerosis, the aetiological disease process of the majority of transient ischaemic attacks (Cohen, 1995), is presumed to be a generalized disease affecting the generalized vasculature. Instead, Taghavy and Hamer (1995) have argued for the more refined study of the domains of neuropsychological functioning in relation to electrophysiological measures of neuronal function in patients with asymptomatic internal carotid artery stenosis. Their findings suggested that symptomatic (transient ischaemic attacks) and asymptomatic (carotid stenosis without clinical symptoms) patients did not differ on those dimensions of behaviours measured on block arrangement, delayed recall of verbal stimuli, recognition memory and naming objects. Implicit in their report is that stenosis of the carotid arteries may result in changes in defined domains of neuropsychological function, even in the absence of neurological symptoms (that is, transient ischaemic attacks).

Taghavy and Hamer (1995) suggested therefore that more sensitive measures of brain functions be adopted to identify neurophysiological markers of neuropsychological dysfunction. Based on the electrophysiological findings of P300 latency and N250 amplitude values, the authors reported that the transient ischaemic attack patients as well as the asymptomatic patients with carotid artery stenosis demonstrated significantly abnormal values when compared to controls with no evidence of vascular disease. They also reported that these significantly prolonged P300 latency values and reduced N250 amplitudes were recorded in the hemispheres contralateral to the symptomatic hemispheres, supporting the view that atherosclerosis is not a localizable disease process. Alternatively, the findings of Taghavy and Hamer (1995) may reflect the participation of circumscribed brain areas in the execution of certain tasks. Thus, it appears that while atherosclerosis is a generalized disorder, there may be some vasculature areas that have a predilection for the atherosclerotic disease process, resulting in early neuropsychological sequelae consistent with the localization of function.

The current literature on transient ischaemic attacks therefore suggests that a variety of variables (medical, neurological and psychological) may influence the neuropsychological test scores of patients. The identification of these variables as exerting independent influences on test scores indicate that it is largely undeterminable from the studies reviewed what are the relative contributions of these variables to neuropsychological test scores. While the literature has suggested that carotid endarterectomy is of noted benefit in reducing strokes, the efficacy of this surgical procedure for neuropsychological outcome requires further clarification.

Studies should therefore aim to investigate the relative contributions of these variables to neuropsychological test scores. In particular, degree of carotid stenosis appears to have undergone more refined classification (Norris et al. 1991), providing an opportunity to relate this variable to neuropsychological test performance. Studies identifying the relative roles of neurovascular factors (such as stenosis) and those variables related to the psychometric properties of neuropsychological tests may in fact contribute to the decisions regarding the overall management of transient ischaemic attacks.

The present study was designed to advance current information regarding what factors contribute to the neuropsychological findings in transient ischaemic attack patients. The investigation was conducted on a sample of patients with transient ischaemic attacks who had not undergone surgery. The non-surgical patient group was selected for several reasons--accessibility to patients in the city of Durban, South Africa, where the study was conducted, the difficulty in obtaining measurement values of critical variables related to the surgical procedure (for example, risk for intraoperative ischaemia), as well the difficulty in obtaining a adequate sample size to meet rigorous statistical standards.

1.2 Aims of the study.

Using a sample of transient ischaemic attack patients and a control group, the study had the following aims:

1. to investigate whether there were significant differences in age, education and SES as indexed by per capita income between the left and right transient ischaemic attack and control groups.

2. to determine which variable (s) formed significant predictors of neuropsychological test scores in the combined transient ischaemic attack group.

3. to determine which variable (s) formed significant predictors of neuropsychological test scores in the left and right transient ischaemic attack groups, respectively.

4. to investigate whether age, education and per capita income formed significant predictors of neuropsychological test scores in a control group of medical patients.

5. to investigate if there were significant differences in neuropsychological test scores between the left and right transient ischaemic attack groups.

6. to investigate if there were significant differences in neuropsychological test scores between the left transient ischaemic attack and control groups.

7. to investigate if there were significant differences in neuropsychological test scores between the right transient ischaemic attack and control groups.

1.3 Hypotheses.

In accordance with the stated aims, the following hypotheses were advanced:

1. There were no significant differences in age, education and SES (as indexed by per capita income) between the left and right transient ischaemic attack and control groups.

2. Stenosis did not form a significant predictor of neuropsychological test scores in the combined transient ischaemic attack group.

3. Stenosis did not form a significant predictor of neuropsychological test scores in the left and right transient ischaemic attack groups.

4. Age, education and per capita income did not form significant predictors of neuropsychological test scores in a control group of medical patients.

5. There were no significant differences in neuropsychological test scores between the left and right transient ischaemic attack groups.

6. There were no significant differences in neuropsychological test scores between the left transient ischaemic attack and control groups.

7. There were no significant differences in neuropsychological test scores between the right transient ischaemic attack and control groups.

The present study was conducted on a group of eighty carotid transient ischaemic attack patients (forty left and forty right carotid transient ischaemic attack patients) and forty control, general medical patients. Several regression analyses and multivariate tests of group comparison with appropriate post-hoc tests were performed to investigate the hypotheses stated above.

In Chapter 2, issues relating to neuroanatomy, as well as the classification, diagnosis and the neuropathology of cerebrovascular diseases are discussed.

CHAPTER TWO

Issues in Anatomy, Classification, Diagnosis and Pathology of Cerebrovascular Diseases

2.1 Introduction

According to Walsh (1987), cerebrovascular disorders may be considered as those that arise as a result of some pathology in the vasculature of the central nervous system. The vascular pathology may take varied forms, e.g., there may be alterations in the structural features of the walls of the blood vessels, rupturing of the blood vessel itself, narrowing (stenosis) or total occlusion of the lumen of the vessels, or changes in the characteristics of the blood itself. Consequently, it is now accepted that cerebrovascular diseases do not constitute a homogeneous disorder, but rather consist of divergent subtypes, all having in common resulting damage to the brain. Apart from the clinical examination, several diagnostic methods are employed routinely in an effort to elucidate the underlying pathological mechanism of a cerebrovascular disease. This chapter thus has a fourfold purpose. First, an outline of the vascular supply of the brain will be given. Second, the classification criteria for the various cerebrovascular diseases will be elucidated, emphasizing the features of a transient ischaemic attack.

Third, an overview of the diagnostic methods that are used, with greater emphasis on those employed for the diagnosis of transient ischaemic attacks, will be given. Fourth, the pathogenesis of transient ischaemic attacks will be elaborated.

2.2 The Vascular System of the Human Brain

The human brain is supplied with blood by two major systems, i.e., the internal carotid and the vertebrobasilar systems (Walsh 1987; Niedermeyer and da Silva, 1987). Transient ischaemic attacks may involve either or both of these arterial systems, producing differing clinical signs and symptoms. Each of these systems will be described individually since they serve different areas of the cerebral structures. However, in keeping with the major aims of this study, the anatomical distribution of the anterior internal carotid artery system will form the major focus of discussion.

2.2.1 Internal Carotid Artery System

Brown, Baird and Shatz (1986) and Caplan and Stein (1986) reported that a pair of common carotid arteries (left and right) arise from the aortic arch, and initiate the carotid systems. Other authors, for example, Osborn and Tong (1996) report that the right common carotid is really a branch of the first offshoot of the aorta, the innominate artery. On the other hand, in approximately 75 per cent of all cases, the left common carotid artery arises slightly to the left of the innominate artery. The implications of this lateral differentiation for both circulation and neurological function are not clear. Despite these variations in the description of the origins of the internal carotid artery system, the intimate relationship between the heart and the cerebral vasculature becomes obvious (see Figure 1).

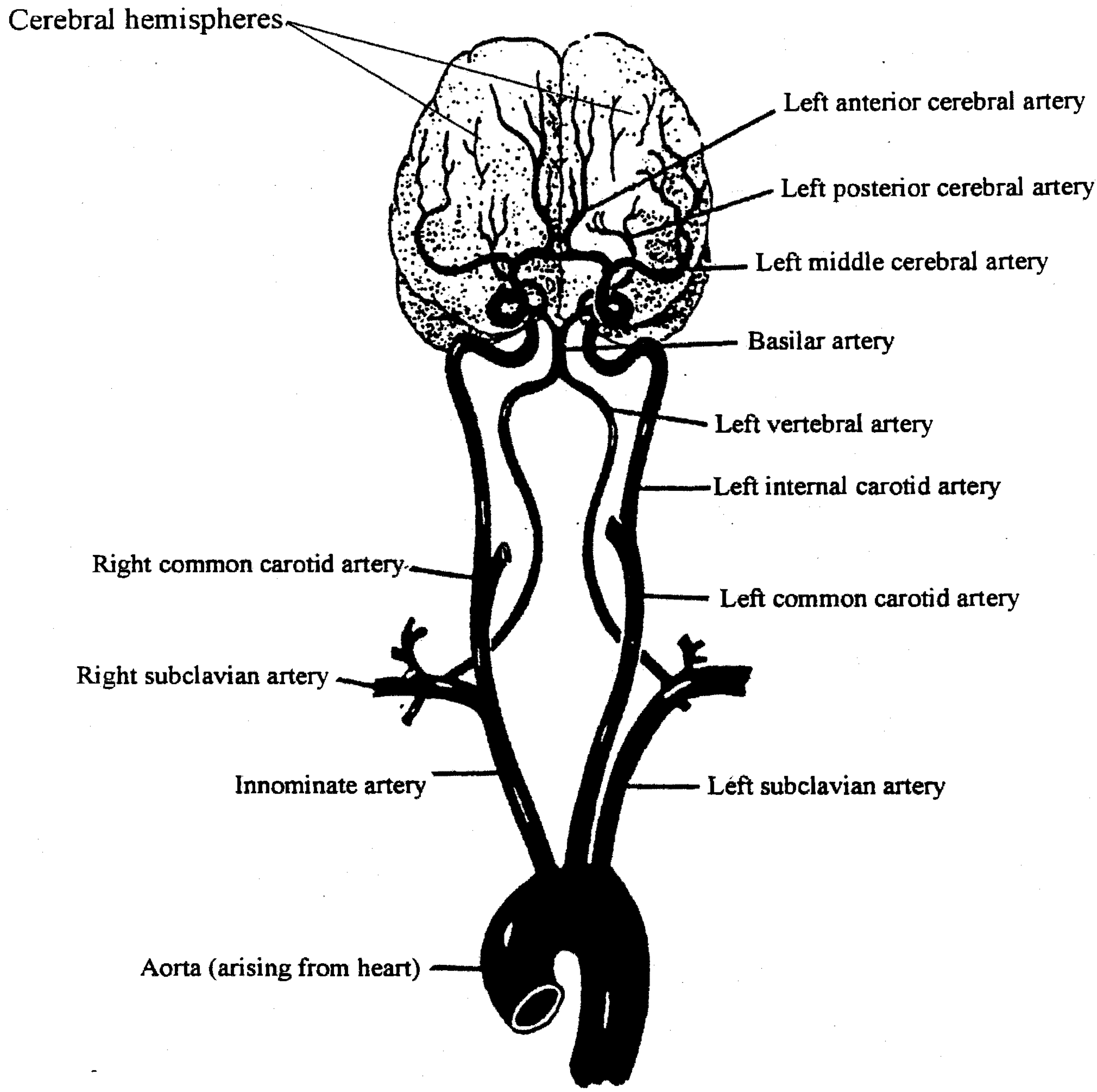


Figure 1. Illustration of the relationship between the heart and the brain vasulature (Adapted from DeGroot and Chusid, 1988)

Each common carotid artery bifurcates into the internal and external carotid arteries at the mid-cervical level (about C3 or C4). However, Osborn and Tong (1996) note that the common carotid bifurcation may be as high as the first cervical vertebra or as low as the second thoracic vertebra. In addition, Gibbs, Wise, Leenders and Jones (1984) report that the left common carotid bifurcation is higher than the right in 50 per cent, and the right bifurcation higher in 22 per cent of all cases. The significance of this finding with respect to neurological functioning has not been elaborated. Osborn and Tong (1996) and Niedermeyer and da Silva (1987) state that the cervical internal carotid artery (which is that part of this vessel that traverses the neck region) is relatively constant in diameter throughout its course, but may normally have a slight bulbous dilatation called the carotid sinus at its origin. The major branches of each internal carotid system are the anterior choroidal artery, and the anterior and middle cerebral arteries. The former artery will not be described any further since the areas of supply of this vessel are largely subcortical and include the visual system, optic systems (part of the lateral geniculate tract), internal capsule, basal ganglia, the diencephalon and the midbrain. The internal carotid artery terminates below the anterior perforated substance by bifurcating into the smaller anterior and the larger middle cerebral arteries. In addition, a discussion of the circle of Willis as the major source of collateral supply in the cerebral vascular system will be pursued.

2.2.1.1 The Anterior Cerebral Artery.

Once derived, the anterior cerebral artery courses medially and anteriorly, traversing over the optic nerve and chiasm to reach the interhemispheric fissure. According to Niedermeyer and da Silva (1987) as well as Osborn and Tong (1996), the proximal or horizontal portion of the anterior cerebral artery (A1 segment) extends from the origin of the anterior cerebral artery to its union with the contralateral anterior cerebral artery via the anterior communicating artery. Osborn and Tong (1996) contends that the A1 segment tends to course somewhat more inferiorly with increasing age.

Powers, Tempel and Grubb (1989) note that patients with anomalies of the A1 segment also have a slightly higher incidence of anterior communicating artery aneurysms. Before joining via this vessel, the anterior arteries give off deep penetrating arteries which supply anterior diencephalic nuclei, the subfrontal area, the anterior commissure and the genu of the corpus callosum. A long branch, known as the medial striate artery or recurrent artery of Heubner, described by Patten (1996) as inconstant in both its terminations and structure, supplies the anterior part of the internal capsule and part of the putamen, pallidum and caudate nucleus (Walsh 1987; Niedermeyer and da Silva, 1987), and may reach parts of the Sylvian fissure (Osborn and Tong, 1996).

Patten (1996) notes that the anterior communicating artery completes the anterior part of the circle of Willis (described later in this section) and allows collateral flow to the contralateral hemisphere if the carotid artery is ligated on either side. According to Osborn and Tong (1996), the branching of the anterior cerebral artery is quite variable. The first cortical anterior cerebral artery branch usually seen is the orbitofrontal artery which supplies the gyrus rectus and inferomedial surface of the frontal lobe. The frontopolar artery, which occurs in approximately one-third of all cases, originates from the anterior cerebral artery near the genu of the corpus callosum. This vessel is claimed to supply the ventromedial surface of the frontal lobe. Osborn and Tong (1996) as well as Patten (1996) further caution that both these vessels may also, instead, arise from a common trunk of the anterior cerebral artery. Furthermore, at a variable point near the genu of the corpus callosum, the anterior cerebral artery divides into its two terminal branches.

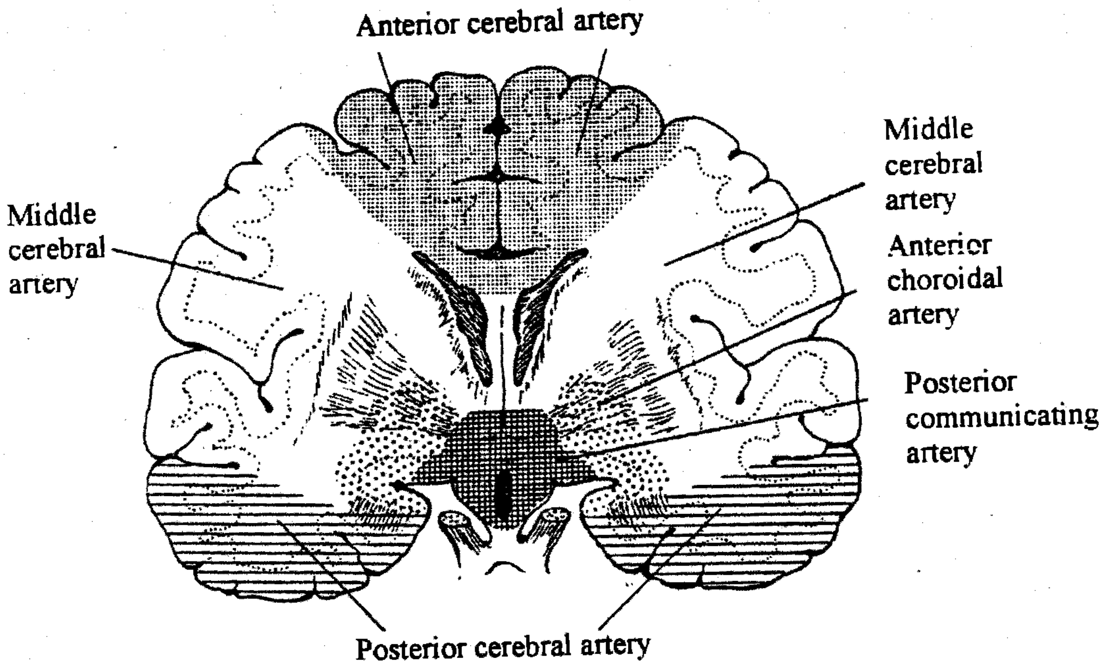


Figure 2. Coronal section through cerebrum at level of anterior commissure to show major arterial supply.
(Adapted from DeGroot and Chusid, 1988)

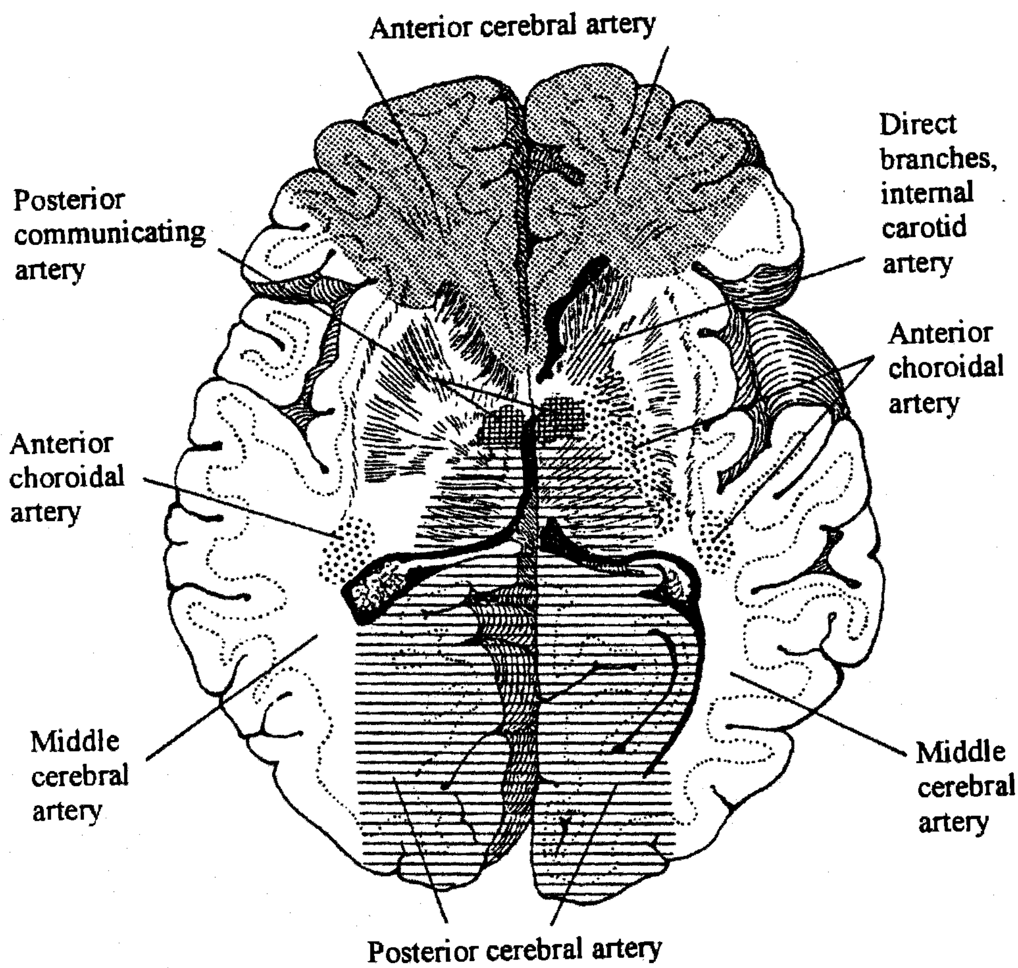


Figure 3. Horizontal section through cerebrum showing arterial supply
(Adapted from DeGroot and Chusid, 1988)

The usually smaller callosomarginal artery, which is present in approximately one-half of all persons (Robertson, Welch, Tilley and Ewing, 1988), passes over the cingulate gyrus to run within the cingulate sulcus. The larger pericallosal artery is considered a continuation of the anterior cerebral artery, running posteriorly at a variable distance above the corpus callosum. Its major branch, the superior internal parietal or precuneal artery courses upward to supply the precuneus and superior parietal lobule, with smaller branches supplying the paracentral lobule and the inferior aspect of the precuneus.

Osborn and Tong (1996) assert that branches of the pericallosal artery also supply the pial plexus which covers the corpus callosum. Patten (1996) note that when the callosomarginal is absent or small, then multiple branches arise from the pericallosal artery to supply the usual distribution of the callosomarginal artery. They note further that anterior, middle and posterior internal frontal arteries arise either from the callosomarginal or pericallosal trunk to supply the medial surface of the hemispheres as far posteriorly as the precentral gyrus. Cortical branches of the anterior cerebral arteries extend over the apex of the brain to supply a small strip of cortex along the anterior two-thirds of the superolateral surfaces of both hemispheres where they anastomose with small branches of the middle and posterior cerebral arteries. This so-called watershed area is considered a common site for cerebral infarction.

2.2.1.2 The Middle Cerebral Artery.

The middle cerebral artery, which arises at the bifurcation of the internal carotid artery above the cavernous sinus, is the larger of the two terminal branches of the internal carotid artery. Its proximal segment extends laterally and horizontally in the lateral fissure beneath the anterior perforated substance to reach the Sylvian fissure. According to Osborn and Tong (1996) and Niedermeyer and da Silva (1987), this portion of the middle cerebral artery is also termed the M1 segment (analogous to the initial or A1 segment of the anterior cerebral artery). The vessel then provides a series of six to twelve (Patten, 1996), or six to 20 (Osborn and Tong, 1996) thin, deep penetrating branches, known as the lateral lenticulo-striate arteries, which supply parts of the globus pallidus, internal capsule and caudate nucleus (Patten, 1996). The course of the proximal middle cerebral artery appears to vary with age. In children below the age of five or six years, Osborn and Tong (1996) note that the horizontal middle cerebral artery frequently courses superiorly, while with increasing age it usually becomes horizontal or often convex inferiorly. According to Patten (1996), the origin and course of the cortical middle cerebral artery branches are so variable that the only truly constant anatomic finding is in their terminal distribution. Hence, this discussion is based on the more common patterns of distal branching as described by Osborn and Tong (1996) and Caplan and Stein (1986).

Lateral surface

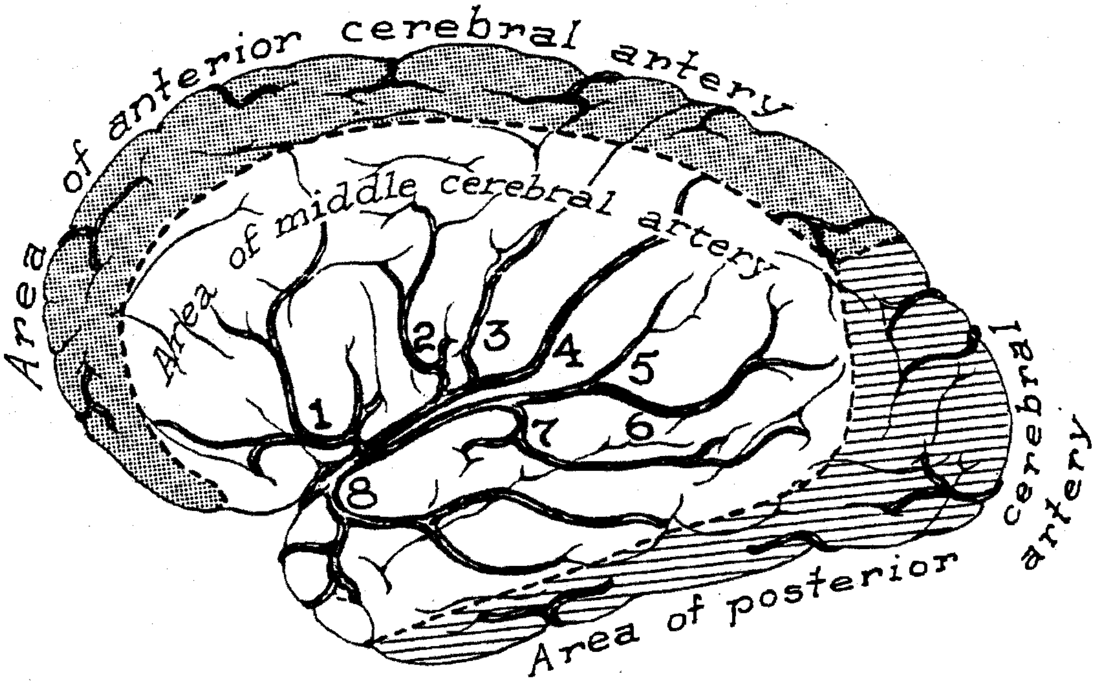
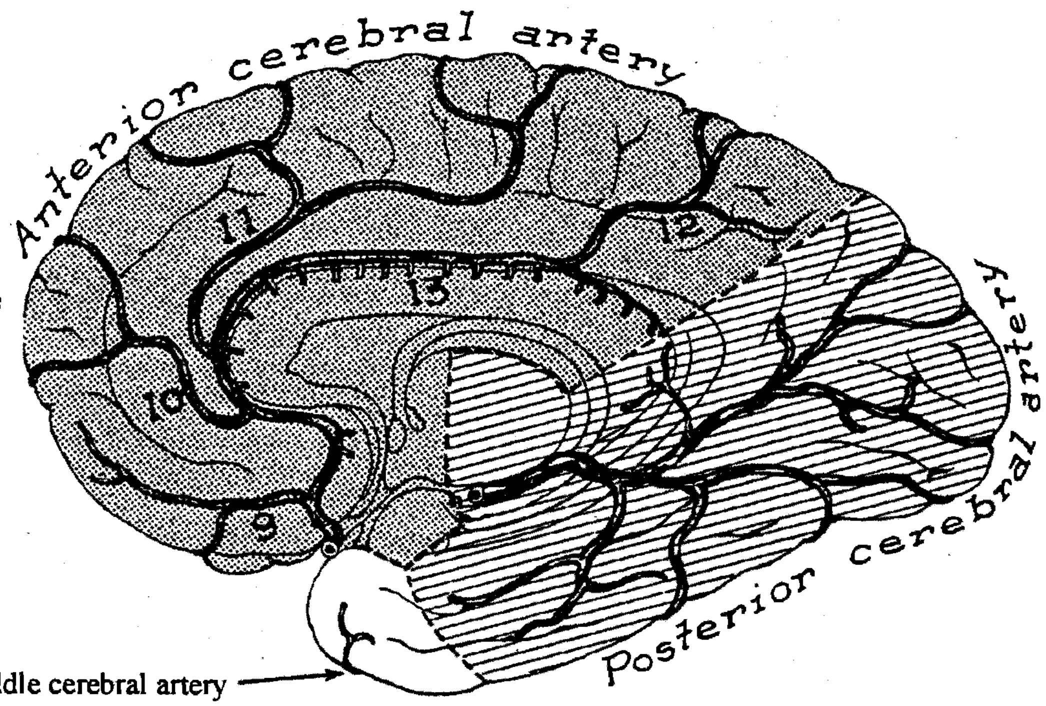


Figure 4. Scheme of the arterial supply of the cerebral cortex: Lateral surface
(Adapted from DeGroot and Chusid, 1988)

Median surface



Middle cerebral artery

1. Orbitofrontal artery.
2. Prerolandic artery.
3. Rolandic artery.
4. Anterior parietal artery.
5. Posterior parietal artery.
6. Angular artery.
7. Posterior temporal artery.
8. Anterior temporal artery.
9. Orbital artery
10. Frontopolar artery.
11. Callosomarginal artery.
12. Posterior internal frontal artery.
13. Pericallosal artery.

Figure 5. Scheme of the arterial supply of the cerebral cortex: Median surface
(Adapted from DeGroot and Chusid, 1988)

The small anterior temporal artery frequently arises before the main middle cerebral artery bifurcation, passing anteriorly and inferiorly over the temporal lip. The main middle cerebral artery trunk usually bifurcates into anterior and posterior groups. The anterior or ascending frontal artery includes both the operculofrontal and central sulcus arteries. The ascending frontal complex occasionally arises as a single trunk but more often originates as two or three separate vessels. The first branch of the complex is usually the orbitofrontal artery which occasionally arises from the horizontal middle cerebral artery. This artery courses anteriorly and slightly superiorly to supply the inferolateral portions of the frontal lobe. The next branches of the ascending frontal complex, the operculofrontal arteries, include all the branches anterior to the central sulcus arteries. The operculofrontal arteries supply most of the middle and inferior frontal gyri, including Broca's and the premotor areas. The posterior division of the middle cerebral artery usually has three branches which arise within the depths of the Sylvian fissure, loop upward over the insula and then turn posterolaterally to exit from the Sylvian fissure and ramify over the cerebral hemisphere. The major posterior branch of the middle cerebral artery is the posterior parietal artery. This vessel exits from the Sylvian fissure and courses posterior-superiorly to supply the parietal lobe immediately behind the sensory strip.

The angular artery is the terminal continuation and usually the largest cortical branch of the middle cerebral artery. The proximal portion of the angular artery initially lies within and runs parallel to the axis of the Sylvian fissure. Emerging from the apex of the Sylvian fissure, the angular artery courses posteriorly and superiorly to supply a variable area that includes the posterolateral parietal and lateral occipital lobes, and the superior temporal gyri.

The third major posterior branch of the middle cerebral artery is the posterior temporal artery which descends over the lateral aspect of the temporal lobe. Its size and area of distribution vary widely, often including virtually the entire temporal lobe except for its anterior portion.

While the preceding description attempts to provide an average view of the middle cerebral artery, Osborn and Tong (1996) Patten (1996) point out that the branching patterns are highly variable. According to their surveys, the middle cerebral artery bifurcation was found in 50 per cent of cases, and trifurcation in 25 per cent of cases, both types occurring near the insula. It has been suggested that such diversities may have implications for neurological functioning, particularly in the context of changes imposed on the dynamics of cerebral circulation.

2.2.2 The Vertebrobasilar System

The main aim of this study is to investigate the neuropsychological sequelae of transient ischaemic attacks involving the anterior internal carotid circulation. However, in order to gain a more complete impression of the dynamic organization of the cerebral vascular system, a brief discussion of the vertebrobasilar system is presented. This presentation is therefore primarily to inform on the posterior circulation of the brain and its involvement in the circle of Willis system.

Two vertebral arteries arise from the left and right subclavian arteries, respectively. These vessels proceed on either side of the vertebral column, and on entering the foramen magnum fuse to form the basilar artery at the anterior aspect of the upper medulla. The basilar artery bifurcates in the inter-peduncular space to give rise to several branches, namely, the pontine arteries, internal auditory arteries, the anterior inferior cerebellar arteries, the superior cerebellar arteries and the posterior cerebral arteries (Osborn and Tong, 1995).

Only the posterior cerebral artery will be described in any great detail since this vessel also supplies the major part of the posterior cortex.

According to some authorities (Walsh, 1987; Osborn and Tong, 1996), each posterior artery passes around the cerebral peduncles which lie between the medial surface of the temporal lobe and the upper brain stem. Along its length, each gives off vessels supplying the inferior medial surface and the hippocampal area of the temporal lobe (Patten, 1987; Niedermeyer and da Silva, 1987; Grant and Adams, 1986).

A series of penetrating vessels supplies the dorsolateral brain stem, the thalamus, posterior internal capsule and sublenticular and retrolenticular visual radiations. Patten (1996) asserts that the posterior cerebral artery terminates as the calcarine artery, supplying the visual cortex with the exception of the macular cortex at the tip of the occipital pole. This artery therefore subserves the function of vision including ocular reflexes, eye movements, the transmission and integration of visual information and memory, and perception (Osborn and Tong, 1996).

The macular cortex is supplied by the middle cerebral artery, which probably accounts for the phenomenon of "macular sparing" in the event of posterior artery occlusive disease (Patten, 1996).

2.2.3 The Circle of Willis

The circle of Willis is a vascular ring at the base of the brain that connects the two internal carotid systems with each other and with the vertebrobasilar circulation. The anastomoses thus provided by this vascular ring are of great significance when one of the major arteries supplying the brain becomes occluded. The neurological as well as the neuropsychological deficits suffered, including the ability of the patient to withstand occlusion of one or more of these vessels, depends on the presence of collateral circulation to the affected area.

The circle of Willis is considered the most important potential source of this collateral circulation. Hence, thorough knowledge of the normal anatomy of this vascular structure is essential for understanding the sequelae suffered in cerebrovascular disease. According to Osborn and Tong (1996) and Caplan and Stein (1986), the anterior portion of the classical circle of Willis consists of the two internal carotid arteries, the horizontal segments of both anterior cerebral arteries, and the anterior communicating artery. The posterior part of the circle consists of the proximal segments of both posterior cerebral arteries, and the two posterior communicating arteries themselves. The posterior communicating arteries are said to arise from the posteromedial surface of the internal carotid artery and course backward to join the posterior cerebral arteries above the third cranial nerve. Thus, they connect the anterior (carotid) circulation with the posterior (vertebrobasilar) system. In addition, numerous small branches, which are often too small to be seen in routine angiographic studies, arise from the circle of Willis to supply important structures at the base of the brain such as the optic nerves, chiasm, optic tracts, infundibulum, internal capsule, and portions of the basal ganglia and thalamus.

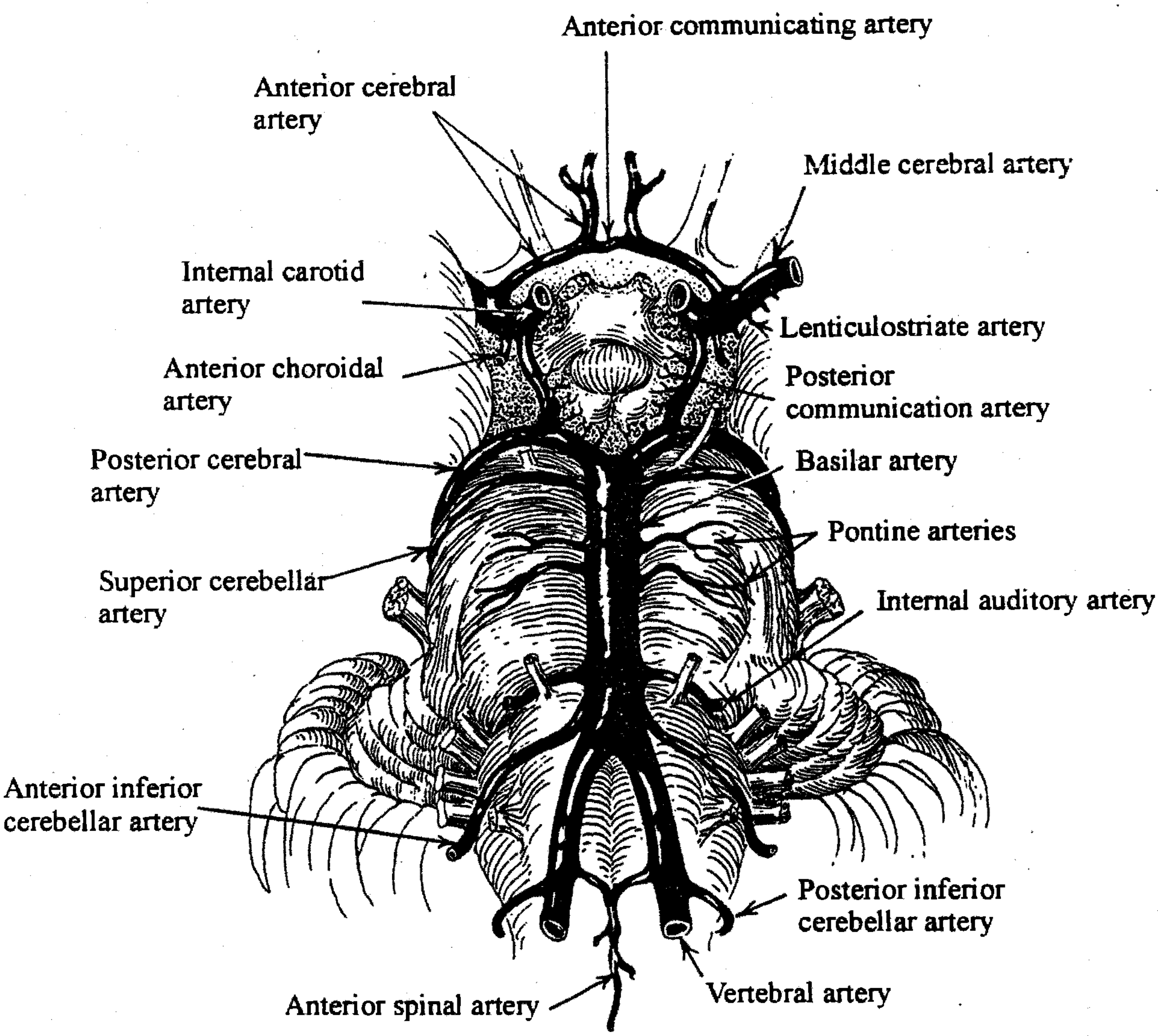


Figure 6. Circle of Willis and principal arteries of the brain: Ventral view
(Adapted from DeGroot and Chusid, 1988)

Osborn and Tong (1996) note that the components of the circle of Willis are notoriously subject to frequent variations, resulting often in a failure of adequate collateral flow in stressful conditions. Walsh (1987) states that the effectiveness of alternative supply routes will depend in large part on the rate of occlusion. A slowly occluding vessel will allow time for adequate anastomotic channels to open up so that complete occlusion of a vessel as major as the internal carotid artery may occur without observable clinical evidence. On the other hand, the sudden occlusion of a smaller vessel may bring serious lasting neurological deficit. To such structural factors may be added dynamic factors such as pressure changes and blood viscosity. From the foregoing discussion, it seems clear that while there are several anatomical landmarks which are consistent, there appear to be a surprisingly high number of idiosyncrasies which may also influence the outcome of cerebrovascular diseases.

Next, the several issues influencing the classification of cerebrovascular diseases will be discussed.

2.3 Issues of Classification in Cerebrovascular Diseases

Moore (1993) defines stroke as the acute (or, less often, subacute) onset of neurological deficit referable to disturbed brain circulation. While the authors maintain that the term stroke is preferred, Orsini, Van Gorp and Boone (1988) have noted that the terms cerebrovascular disease, stroke and apoplexy have been used interchangeably to refer to disorders of the central nervous system resulting from pathology involving the blood vessels. A survey of the literature seems to suggest that all of these terms may be employed, but once selected, a term must be used consistently throughout. For the purposes of this thesis, cerebrovascular diseases (CVD) will be employed. Virtually all enduring effects of vascular disease on the brain can be reduced to two essential pathological processes--infarction and haemorrhage (Besson, Robert, Hommel and Perret, 1995).

2.3.1 Infarction

According to Okazaki (1983), a cerebral infarct is the result of temporary or permanent occlusion of a feeding artery, extracranially or intracranially and results from the process of necrosis, which refers to the process of dying tissue. Necrosis results from a failure in the delivery of well-oxygenated blood to the particular cerebral area served by the vessel. According to Okazaki and Scheithauer (1988), the most important vascular lesions are atherosclerotic narrowing of the arterial lumen with or without its occlusion. The occlusion is caused either by superimposed thrombotic material which is a cumulative process, or by thrombotic tissue from other sites, known as emboli. The consequence of the occlusion is the reduction of oxygen (ischaemia) to the brain. When cerebral ischaemia is sufficiently severe, all local elements including neurons, glia and blood vessels will die--a process called infarction. Okazaki and Scheithauer (1988) propose that if ischaemia is less severe, only more vulnerable neurons will die resulting in selective neuronal damage. Very mild reduction, sufficient to cause only functional and reversible damage to neurons, is thought to underlie transient cerebral ischaemic attacks. It is noteworthy that the terms severe and mild ischaemia are used arbitrarily and are related to the temporal nature and reversibility of neurological symptoms. This is elaborated later in this chapter.

2.3.2 Haemorrhage

Okazaki and Scheithauer (1988) report that infarction is commoner than haemorrhage in a ratio of 3:1. A haemorrhage is due to a rupture of an abnormal artery or arteriole allowing blood to flow directly into the brain parenchyma or the subarachnoid space (Osborn and Tong, 1996). Intracranial haemorrhage, representing some 25 per cent of all cerebrovascular diseases, may therefore be divided into primary intracerebral and subarachnoid haemorrhage. The former is intimately associated with hypertension as the main aetiological factor, and the latter with the rupture of an aneurysm or angioma. Lishman (1987) maintains that the differentiation is not always absolute, since bleeding may occur into brain tissue in the vicinity of a ruptured aneurysm or angioma. Similarly, blood may gain access to the ventricular system and subarachnoid space after primary intracerebral haemorrhage. The most common site of haemorrhage is in the putamen and internal capsule, resulting from the rupture of the lenticulostriate artery. It is often found that a secondary consequence of this haemorrhage is the formation of a blood clot or intracerebral haematoma, which may lead to secondary effects because of the resulting tentorial herniation and brain stem compression.

The differentiation of cerebrovascular diseases due to infarction or haemorrhage has important implications for neuropsychological assessment. It becomes clear that infarctions result in brain damage to relatively specific areas when compared to haemorrhages which causes more diffuse damage. Thus, notwithstanding the role of other factors, the prediction of sequelae regionally in the case of infarcted cerebrovascular diseases is less difficult as opposed to such predictions for haemorrhages. Grouping patients with both types of cerebrovascular diseases into one group for the analysis of behavioural sequelae is therefore a serious methodological error.

Caplan and Stein (1986) note that there is now consensus that cerebrovascular diseases embrace a multitude of subtype disorders, characterized chiefly by the symptom presentation as well as features of the underlying pathogenesis. Thus, the diagnosis of <u>reversible ischaemic neurological deficits</u> refers to the condition of partial neurological deficits which last more than 24 hours, but resolve with time. The resolution period in these cases has been specified by some authors, for example, Levy and Werdelin (1988) to be within four weeks of onset of symptoms. Others (Wilson, Veith, Hobson and Williams, 1987) differentiate between <u>partial nonprogressing stroke (PNS)</u> and <u>completed stroke</u>, the former being an incomplete permanent ischaemic neurological deficit that does not advance to a greater deficit. The latter type is a focal neurological deficit that occurs abruptly and stabilizes.

<u>Transient ischaemic attacks</u> in the brain have been consistently defined as transient, focal cerebral dysfunction of ischaemic origin, which disappears within 24 hours (Werdelin and Juhler, 1988; Levy and Werdelin, 1988). Dennis, Bamford, Sandercock and Warlow

(1989), in their study, defined transient ischaemic attacks as an acute loss of focal cerebral or ocular function with symptoms lasting less than 24 hours and which, after adequate investigation, were presumed to be due to embolic or thrombotic disease. There appear to be three clinical criteria necessary for the diagnosis of transient ischaemic attacks--complete resolution of all symptoms, a resolution period of 24 hours or less and an ischaemic process underlying the disease. Waxman and Toole (1984) have argued that it is necessary to reserve the term transient ischaemic attacks for episodes of focal deficit in which no evidence of the ischaemic event is found on computed tomography.

Gewertz and McCaffrey (1991) add to these observations by noting that it is necessary to define transient ischaemic attacks as corresponding to a brief period of cerebral ischaemia without cerebral infarction, or to a small brain infarction with rapid and complete clinical recovery. They state further that a computed tomogram may be positive for an infarct in up to ten per cent of transient ischaemic attack cases. Gewertz and McCaffrey (1991) report that it is possible that the transient ischaemic attack may be due to an old, silent infarct, and therefore the documentation of these CT findings will add to the diagnosis and treatment of such patients. Despite the strong argument for computed tomography in transient ischaemic attacks, Towne, Weiss and Hobson (1990) note that diagnosis is based entirely on clinical criteria, and that laboratory studies are aimed at excluding causes of nonvascular origin, and at discovering potential aetiologic factors in those patients who have true transient ischaemic attacks. Waxman and Toole (1984) and Toole (1991) argue that while the clinical examination is aimed at an objective assessment of the patient's symptoms, the process has a component of subjectivity which is dependent on the clinical experience of the neurologist, and report that they have encountered several patients who by their own account were completely without sequelae, but whose close associates describe them as having altered judgment or a personality change. These authors quote the findings of the Italian Multicentre Study on Reversible Cerebral Ischaemia which reported that in the diagnosis of transient ischaemic attacks, agreement between examiners varied from 2 per cent to 76 per cent for history, and between 21 per cent and 92 per cent for neurologic signs.

Three major observations emerge from the preceding discussion. First, the diagnosis of a transient ischaemic attack is based initially on the findings of a clinical examination and the resolution time of neurological symptoms, an temporally-based arbitrary definition. There appears to be an artificial continuum separating transient ischaemic attacks from reversible ischaemic neurological deficits. It appears that absolute dependence is placed on the adequacy of the neurological examination as a sensitive measure of brain function and, as suggested by the findings Italian Multicentre Study, neurological findings may be subject to variation in terms of diagnostic outcome.

Second, a proper diagnosis should include computed tomography which may confirm the development of an infarct, exclude nonvascular events, and uncover possible aetiologic factors in transient ischaemic attacks. Thus, the above discussion urges researchers to distinguish between infarcted and non-infarcted cases when investigating the sequelae of such episodes.

Third, the distinction between the subtypes of cerebrovascular diseases that are ischaemic in nature is based on arbitrary temporal phenomena. It appears possible that a condition diagnosed at one time as a transient ischaemic attack could, at a later time be a reversible ischaemic neurologic disorder, or still later, a completed stroke. It is perhaps for this reason that Hachinski and Norris (1985) suggested that presumed transient ischaemic attack is a preferable designation in most cases. However, Dennis, Bamford, Sandercock and

Warlow (1989) also strongly argue that the maintenance of a distinction between transient ischaemic attacks and minor strokes is important since they have different implications for these respective patients.

This section emphasizes the importance of performing computed tomography on transient ischaemic attack patients to determine the presence of infarcts. In addition, the detection of infarcts, even among those patients falling within the temporal definition of transient ischaemic attacks, need to investigated with respect to their influence on neuropsychological test performance.

2.4 Investigative Techniques in Cerebrovascular Diseases

As indicated in the foregoing section, two main investigative techniques are employed in the diagnosis of transient ischaemic attacks. These are the detailed clinical examination and laboratory investigations, respectively.

2.4.1 The Clinical Examination

Cerebrovascular diseases are initially diagnosed on the basis of clinical presentation (Caplan and Stein, 1986). Deveshwar, Welch, Ramadan and Levine (1991) state that patients who have apparently suffered a transient ischaemic attack present a special diagnostic challenge since there are often no objective signs on examination. Thus, diagnosis is based almost entirely on a retrospective evaluation of the patient's symptoms. It is perhaps for this purpose that these authors, together with others (Werdelin and Juhler, 1988; Patten, 1996) note that the clinical examination should have two distinct phases--history taking and a neurological examination.

2.4.1.1 History taking.

This aspect of the clinical examination is generally aimed at establishing the mechanism of the cerebrovascular disease, or in this case, the transient ischaemic attack. Therefore, several steps fundamental to this diagnostic process have been proposed by Patten (1996).

(a) Establishing the ecology of the disease.

The ecology of the disease refers to the physiological context in which cerebrovascular disease is identified. The context may therefore refer to the historical context of the disease as well as the presence of possible aetiological factors at the time of disease identification. This step of history taking involves the documentation of prior medical diseases and demographic data that might predispose the patient to one or more of the stroke mechanisms. For example, Caplan and Stein (1986) note that on discovering that a patient has had two prior heart attacks, diabetes and hypertension, the physician will be led to favour a mechanism of atherosclerosis of the extracranial cervical arteries, associated with a thrombotic mechanism of the transient ischaemic attack. On the other hand, the presence of prior heart disease raises the possibility of arrhythmia, mural thrombosis, ventricular aneurysm, and valvular heart disease--all potential sources of cerebral embolism. Hypertension raises the possibility of intracerebral haemorrhage. Other details are then brought to diagnostic focus. For example, epidemiological data suggest that 60 per cent of all cerebrovascular diseases are thrombotic, 20 per cent embolic, 12 per cent due to intracerebral haemorrhage, and 8 per cent to subarachnoid haemorrhage. Age and sex are important data, and if in this case the victim is a woman in her twenties, then thrombosis is unlikely and a haemorrhagic mechanism is strongly favoured. The above examples suggest that the skill of the clinician in detailing the ecology of the cerebrovascular diseases is a necessary feature of this process.

(b) Determination of previous Cerebrovascular Symptoms.

Caplan and Stein (1986) and Patten (1996) note that establishing whether neurological symptoms had previously occurred is an essential feature of history taking. They suggest that transient ischaemic attacks in the same vascular territory are frequent precursors of thrombotic cerebrovascular diseases.

An important aspect of this aspect of history taking is the strong reliance on the memory of the patient. Moreover, the almost complete dependence on the patient to supply such critical and sophisticated medical information is frowned upon by several authors (Dennis et al., 1989; Caplan and Stein, 1986). Another criticism of this aspect is that it may well be that some patients cannot provide information about a transient ischaemic attack, for example, because of aphasia, altered level of consciousness (Levy and Werdelin, 1988), or amnesia.

(c) Recording the Activity of the Patient at onset of symptoms.

Garcia, Lassen, Weiller, Sperling and Nakagawara (1996) and Caplan (1987) note that traditional teaching states that most thrombotic cerebrovascular diseases occur when the circulation is least active and most sluggish, possibly in the non-rapid eye movement stage of sleep. Embolism and haemorrhage would be more likely to occur when the circulation is more active or when blood pressure rises. Thus, it may add to diagnostic efficiency to document the physical activity of the patient at, or immediately preceding, the onset of symptoms.

(d) Establishing the Temporal Course of the Deficit.

This aspect of the examination is vital to decide, in terms of classification criteria, the type of neurovascular episode suffered by the patient. As indicated in the previous sections, if symptoms and signs disappear completely within 24 hours, the episode is termed a transient ischaemic attack. Okazaki (1983) and Werdelin and Juhler (1988) suggest that determining whether the progression of deficits could be described as maximal at onset, fluctuating or progressive, yields valuable data that may be deployed in the diagnostic process. For example, an improvement shortly after onset of the deficit argues strongly against an intracerebral haemorrhage. A deficit maximal at onset and unassociated with headache, is most compatible with an embolic mechanism. On the other hand, the gradual development of a progressive focal deficit associated with gradually developing symptoms of increased intracranial pressure suggest intracerebral haemorrhage.

(e) Documentation of Accompanying Symptoms.

It is often found that together with the primary symptoms of neurological dysfunction are other associated symptoms which may guide diagnosis. For example, Caplan and Stein (1986) note that headache is an invariable symptom of subarachnoid haemorrhage. The authors contend that the sudden release of blood into the subarachnoid space increases intracranial pressure and usually leads to severe headache, vomiting and a decrease in the level of consciousness. In intracerebral haemorrhage, the focal deficit usually develops progressively, and only later, when there has been an enlargement of the haematoma, do headache, vomiting and decreased concentration develop. Loss of consciousness is common in subarachnoid haemorrhage and rare in ischaemic cerebrovascular diseases, unless there is bilateral involvement of the brainstem.

(f) Concluding Comments on History Taking.

An analysis of the history taking process reveals two common and consistent features. Firstly, the clinical investigator should be keenly aware of the variables influencing the clinical presentation of cerebrovascular diseases. Second, the dependence of the clinician on the patient (or close associates) for the documentation of vital information is striking. It is perhaps for this reason that several authorities (Werdelin and Juhler, 1988; Levy and Werdelin, 1988) strongly suggest the importance of other assessment techniques (for example, computerized tomography) to confirm clinical impressions.

2.3.1.2 The Neurological Examination.

The neurological examination that follows the clinical interview is guided by the latter. According to Caplan and Stein (1986), neurological findings do not impact heavily on the diagnosis of stroke mechanism--the findings do help, though, with the anatomical location of the lesion. With respect to a transient ischaemic attack, the authors stress that the most frequently missed signs of dysfunction involve abnormalities of higher cortical function, level of alertness, the visual and oculomotor systems, and gait. For example, in cerebral lesions, higher sensory functions such as position sense, object recognition, and extinction are more affected than elementary pin or touch perception.

Welch and Levine (1991) have proposed classical types of focal cerebral infarction which present clinical symptoms associated with different vascular involvement, a broad dichotomy being the carotid and vertebrobasilar vascular beds, respectively. The various clinical neurological syndromes related to the carotid system may be described as follows.

1. Superficial middle cerebral artery syndrome. This syndrome is said to involve any one or a combination of several signs, for example, face-arm sensory-motor weakness or hemiparesis. In this clinical presentation, the lower limb may be involved, but less so than the face and arm, and the intensity of the paresis varies from very mild to complete paralysis. Aphasia, when the dominant hemisphere is involved, can occur without hemiparesis. Visual impairment may be present in the form of a loss of vision in one half of the visual field on the side of the hemiparesis. Visual neglect of the left side of the body, may be observed in some cases of right-sided cerebral involvement.

2. Deep middle cerebral artery syndrome. This syndrome consists of a pure motor hemiparesis or hemiplegia (without sensory or visual impairment) involving the entire side of the body, i.e., face, arm and leg.

3. Complete middle cerebral artery syndrome. This syndrome combines the hemiparesis or hemiplegia of the deep middle cerebral artery syndrome with the sensory, visual and language dysfunctions of the superficial middle cerebral artery syndrome.

4. Anterior cerebral artery syndrome. This syndrome typically features a sensory-motor monoparesis of a lower limb or a more widespread hemiparesis that predominates clearly at the lower limb and at the proximal end of the upper limb. Often found is urinary incontinence, as well as an involuntary grasping reaction of the affected hand (grasping reflex).

The neurological examination may thus be guided by a systematized syndrome analysis (as that suggested above) in order to make decisions regarding arterial location of the lesion. From the preceding discussion, it would appears clear that the different syndromes, together with their constituent symptoms, may also be influenced by the arterial tree involved, as well as the location of the thrombus or embolus.

The next part of the investigative process is the use of laboratory techniques.

2.4.2 Laboratory Investigations.

These analyses are planned in order to test, confirm, and elaborate upon hypotheses regarding the mechanism, and subsequently on the type of cerebrovascular disease implicated. Several diagnostic techniques may be employed largely to determine two basic phenomena--the existence of a vascular lesion, thereby excluding other aetiologic agents in the cerebrovascular disease such as neoplasms, as well as the development of a lesion in the cerebral parenchyma, that is, an infarct. It is within this context that the various techniques will be discussed.

2.4.2.1 Brain Imaging Tests.

The advent of brain imaging techniques has largely revolutionized the diagnostic process, particularly with respect to cerebrovascular diseases. However, the exorbitant cost of some of these tests preclude their routine employment in several countries. On the other hand, others have been discarded because of their dubious predictive validity. Thus, this discussion is based on those brain imaging techniques that are more routinely used, that is, cranial computed tomography (CT) and magnetic resonance imaging (MRI), according to Patten (1996) and Caplan and Stein (1986).

1. Cranial Computed Tomography (CT) Scan. Since the internationally acceptable term is computed tomogram, this term will be adopted for the remaining discussion. The basic principle of CT scans is the attenuation of x-rays as they pass through the body (Deveshwar et al., 1991). The authors note that with CT the calibrated x-ray beam is passed through the patient, and the degree of the attenuation varies with regard to the type of tissue. X-rays emerging from the patient are recorded by detectors and several x-ray beams are passed in various directions through the subject yielding attenuation data for a three-dimensional slice of the region being studied. Computer algorithms are used to resolve attenuation data from the slice of tissue under investigation into volume elements that are then mapped onto a matrix of square picture elements (pixels) which thus constitute the CT image. The degree of shading of each pixel's gray level represents the average linear attenuation coefficient of a small volume of the object under investigation. Each coefficient is expressed as attenuation relative to water in Hounsfield units (HU). The value of a Hounsfield unit is given by the formula

$$HU = \frac{(\text{tissue}) - (\text{water}) \times 1000}{\text{water}}$$

where u represents the linear attenuation coefficient, and 1000 the scaling factor. The Hounsfield units represent the basic data acquired from CT imaging.

The analogue image generated is based on the assignment of gray levels to a range of Hounsfield units. Dense structures that markedly attenuate x-rays fall at the bright end of the scale (showing a white), while those with lowest attenuation fall toward the dark end. The actual level of gray level scale is constrained to relatively few steps but may be manipulated within the range of acquired data. If the range of HU values were wide relative to the number of steps in the gray level scale, each tone in gray scale would represent a broad range of HU values, and diminished contrast discrimination would result. In addition to altering the range of numerical values to sampled, CT data acquisition can also vary the thickness of the slice of the reconstructed image. Slice thickness depends on the collimation of the x-ray beam and can vary from 1.5 to 10.0 millimetre in most contemporary machines (Ernst and Stanley, 1991)

Images may be acquired as overlapping or contiguous sections. Computer technology permits a variety of enhanced or refined CT images. High resolution scans obtain data over a narrower field, which results in improved spatial resolution but also increases noise in the image. The data in the CT are typically obtained and displayed in the axial (horizontal) plane (Naeser, Hayward, Laughlin, and Zatz, 1981).

- A frequent augmentation to the CT procedure involves the use of intravenous contrast materials. Contrast media contain iodine, which can enhance some bright features of a CT image. With the injection of contrast medium in the blood, normal brain does not enhance because the contrast agent does not cross the blood-brain barrier, whereas pathological tissue containing compromised blood-brain barrier does enhance (Stevens, Valentine and Kendall, 1988). Stevens et al. (1988) further note that enhancement occurs in two stages although the second, slower phase appears to be best for differentiating between normal and pathological brain tissue. Enhancement may thus persist for many hours or maybe days and appears to be unrelated to lesion vascularity. Contrast enhancement is often needed when lesions are suspected in regions where CT artifacts are likely (e.g., posterior fossa and pituitary region) or when the lesion is isodense compared with surrounding brain tissue. Contrast-enhanced CT improves sensitivity in approximately 10% of arteriovenous malformations and in some cerebral infarctions between one and three weeks, post-infarct (Stevens et al., 1988).

Several findings with respect to the CT scan in ischaemic cerebrovascular disease have been reported. According to Wall, Brant-Zawadzki, Jeffrey and Barnes (1981), approximately 80% of strokes are detectable by CT within 24 hours after infarction. Other researchers (Kohlmeyer and Grazer, 1978) reported that CT scans may be normal in as many as 25% of cases with well documented infarction and this situation is thought to be related to averaging of low and high density components of the lesion, resulting in an isodense appearance of the lesion. Ischaemic infarctions typically result in dark areas of low attenuation as opposed to haemorrhage infarctions which produce bright areas of high attenuation. The low density areas associated with acute infarction correlate with increased water content. Early water changes are caused by cytotoxic oedema, a form of intracellular oedema caused by alterations in cell membrane permeability (Wall et al. 1981).

According to Russell (1984), the typical CT appearance of stroke changes as the lesion evolves. With acute infarctions (the first five days), low-density lesions corresponding to oedema are the most frequent findings. During the subacute period, the CT scan often reveals a lesion of lower density, with less mass effect than during the acute stage. In the chronic stage, the infarct appears as a well defined area of decreased attenuation with density similar to that of cerebrospinal fluid. Russell (1984) emphasize that in the later stages, there may be atrophy of cerebral gyri with resultant enlargement of subarachnoid spaces, which in turn may appear as a prominence of the sulci or fissures and there may be associated dilatation of the adjacent ventricular system.

Thus Caplan and Stein (1986) and Okazaki and Scheithauer (1988) have proposed that computed tomography has definite advantages as well as disadvantages in cerebrovascular diseases. They list the following major strengths of this technique to be in:

(a) Confirming or excluding intracerebral haemorrhage in a patient with recent-onset symptoms.

(b) Defining the location, size and mass effect of intracerebral haemorrhage, and helping to establish whether blood has drained into the ventricles and subarachnoid space.

(c) Confirming the presence of a subarachnoid haemorrhage.

(d) Describing the site of the aneurysm and the probability of development of vasospasm by an analysis of the location and extent of bleeding.

(e) Sometimes directly imaging an aneurysm, arteriovenous malformation or an elongated fusiform dilatation of a vessel.

(f) Identifying the vascular territory and size of infarcts, especially those that are within the cerebral hemispheres.

(g) Occasionally providing a direct image of the thrombotic process by demonstrating a fresh occlusion of a cerebral vessel due to recent embolization.

(h) Uncovering an unsuspected nonvascular lesion, such as a meningioma, glioma or subdural haematoma.

(i) Providing useful prognostic data. A normal computerized tomogram in a patient with prominent neurological abnormalities is more likely to indicate the possibility of reversible damage. On the other hand, a large hypodense lesion, or area revealing decreased attenuation suggesting infarction, is unlikely to be reversible.

(j) Differentiating between haemorrhagic and ischaemic cerebrovascular diseases, as suggested by Okazaki and Scheithauer (1988).

A commonly cited limitation of computed tomography is that the result may be normal in a patient with recent infarction. In addition, infarcts less than one centimetre in diameter may not be consistently imaged by computed tomography (Okazaki and Scheithauer, 1988). Although Werdelin and Juhler (1988) suggest that the interpretation of findings of computed tomography is evolving, certain landmarks are used routinely. The presence of mature infarcts indicates previous major ischaemic episodes, and atrophy may be present. An area of low density (hypodense, or decreased attenuation) may be interpreted as an infarct. An isodense area is interpreted by most as reflective of an ischaemic event (Okazaki and Scheithauer, 1988; Patten, 1996).

The use of computed tomography in transient ischaemic attacks has been strongly advocated despite the varying figures of positive outcomes quoted in the literature. For example, Deveshwar et al. (1991) and Patten (1996) assert that computed tomography findings may be positive for an infarct in up to 10% of transient ischaemic attack cases. Werdelin and Juhler (1988) report that positive computed tomography findings suggestive of infarction were found in 30 per cent of their transient ischaemic attack sample, yet their cases revealed a transient ischaemic attack rate of 4.2 per patient over a 72 hour period.

Calandre, Gomara, Bermejo, Millan and Del Pozo (1984) found that in their transient ischaemic attack study, 75 per cent of cases showed normal computed tomogram findings, with 25 per cent revealing infarcts. However, the authors noted that the size of the low-density lesions was not significantly different from those found among the reversible ischaemic neurologic deficit and ischaemic stroke with minimum residuum groups.

Thus, while computed tomography helps to clarify the abnormal brain pathologic anatomy, it is less useful in eliciting the stroke mechanism and the precise location and severity of the occlusive lesion within the vessel. Furthermore, the usefulness of computed tomography in the individual patient depends on two factors, viz., the adequacy and completeness of the available clinical data, and the experience and neurological sophistication of the physician caring for the patient.

2. Magnetic Resonance Imaging (MRI). The underlying principles of MRI involves establishing a baseline condition in a system, activating the system, and obtaining measurements as the system returns to normal. The advantage of magnetic resonance imaging over computed tomography is that the former has higher resolution capabilities, thereby generating cerebral matter sections which permits superior visualization. Like computed tomography, magnetic resonance imaging provides little information about the mechanism of the transient ischaemic attack, in particular, the intravascular process. Both CT and magnetic resonance imaging are costly diagnostic procedures and therefore do not readily allow their deployment in many diagnostic settings, particularly in developing countries Within the context of prohibitive cost and accessibility, documentation of the role of MRI ischaemic cerebrovascular diseases has been consistent.

Experimental and human studies agree that ischaemic changes can be detected by MRI within the first few hours following the ictus (Unger, Gado, Fulling and Littlefield, 1987). The authors note that the increased contrast of MRI allows for the identification of smaller regions of infarction, including lacunar infarcts, than CT scans. Additionally, MRI is reported to be sensitive to stroke in the intermediate stages when oedema dissipates and before frank cavitation appears, a period when CT images of stroke often appear isodense with surrounding tissue (Deveshwar et al., 1991). At this intermediate stage of the ischaemic event, MRI is reported to detect a rim of hyperintense signal on the image surrounding the darker zone, representing the core of the infarct (Awad, Johnson, Spetzler, & Hodak, 1986).

Thus, MRI improves the clinician's ability to determine the stage of a patient's infarction and elucidates the anatomy of smaller lesions. Salgado, Weinstein, Furlan, Modic, Beck, Estes, Awad and Little (1986) report that MRI is particularly useful in studying patients with transient ischaemic attacks. They report that abnormalities of CT are typically observed in TIAs less than 29% of the time, whereas with MRI abnormalities have been observed in up to 80% of such patients. Other authors, for example, Awad, Spetzler, Hodak, Awad, and Carey (1986) have emphasized the role of age in interpreting MRI in cerebrovascular diseases.

3. Cerebral Angiography.

According to O'Hara (1991) and Moneta, Saxon, Taylor and Porter (1995), cerebral angiography by arterial catheterization remains the standard and tested manner of defining the nature of vascular lesions in the extracranial and intracranial vessels. The preferred method uses the Seldinger technique which selectively catheterizes and opacifies individual arterial circulations. According to several authorities (Osborn and Tong, 1996; Bigler, Yeo and Turkheimer, 1988), angiography should be tailored to the clinical question and therapeutic alternatives. For example, in a transient ischaemic attack with symptoms of transient aphasia and right hemiparesis, the lesion is most likely within the left internal carotid artery territory. In that circumstance, the first procedure should be to selectively catheterize the left common carotid artery and gain fluoroscopic information about the carotid bifurcation before proceeding further.

Some researchers, for example, Norris and Zhu (1992) reported that they found essentially normal angiograms in transient ischaemic patients. These authors suggest that such cases should be differentiated from those with a positive angiogram, and should rather be included in a subcategory for which the source of the embolic aetiology cannot be defined using existing diagnostic techniques. Others propose that the quality of the angiogram is important as conditions such as mild to moderate atheroma may easily be missed.

The role of angiograms has been initially noted in the identification of narrowing of blood vessels, known as stenosis. The degree of stenosis has been a motivating factor in the use of carotid endarterectomy, a surgical process in which atherosclerotic plaques are removed from carotid arteries. Stenosis can either be neurologically symptomatic or asymptomatic. The definition of asymptomatic but clinically significant carotid stenosis is usually related to the magnitude of stenosis present at the carotid bifurcation and proximal internal carotid artery (Ernst and Stanley, 1991). According to Hobson (1991), by convention, this generally has been defined as a 50% per cent reduction in luminal diameter of the artery as seen on arteriography. The percentage of stenosis, when present, is determined by comparing the least transverse diameter at the stenosis with the diameter of the distal uninvolved internal carotid artery. The percentage is then expressed as the function of the diameter and of the cross-sectional area. Hobson (1991) further notes that the 50 per cent stenosis becomes the threshold lesion for considering surgical intervention.

Hobson (1991) and Towne, Weiss and Hobson (1990) report that is now customary to identify those patients with less than 50 per cent stenosis as not significant for surgical intervention, referred to as mild stenosis. Patients evidencing 50 to 75 per cent stenosis are classified as having moderate stenosis with possible recommendation for surgery. Those patients with degrees of stenosis between 75 and 99 per cent are classified as high grade or severe stenosis and surgical intervention is mandatory or highly recommended. This classification system of degree of stenosis provides an opportunity to study what the neuropsychological implications are in the presence of varying degrees of carotid stenosis, in a systematized and empirical manner using regression and correlation statistics.

The discussion in this section suggests that although magnetic resonance imaging is the favoured investiagtive tool in transient ischaemic attacks, computed tomography and angiography may also form useful diagnostic techniques supplementing the clinical examination in the diagnosis of transient ischaemic attacks. The use of computed tomography is also shown to be important in differentiating those cases with cerebral infarcts from those without this evidence. The documentation of this evidence, within the limitations imposed by the resolution power of computed tomography, may assist in excluding patients with other forms of neurological diseases from the study sample.

2.5 Pathogenesis of Transient Ischaemic Attacks

Ernst and Stanley (1991) note that there are two basic types of pathophysiological mechanisms in cerebrovascular diseases--ischaemic and haemorrhagic. The process underlying transient ischaemic attacks is essentially ischaemic in nature (Levy, 1988; Okazaki and Scheithauer, 1988; Dennis et al., 1989) which invokes a series of neurovascular processes.

The ischaemic process may be caused by a variety of pathological phenomena, both of vascular or non-vascular origin. Of the vascular types, atherosclerosis and embolism constitute the major forms.

2.5.1 Cerebral Atherosclerosis

Atherosclerosis is a degenerative vessel-wall disease that causes progressive narrowing of arteries. In the cerebral circulation, atherosclerotic plaques develop at the major arterial bifurcations (for example, the bifurcation of the internal carotid artery), branch points, and the cardiac vasculature from which the anterior cerebral vessels originate (for example, the aortic arch). Common sites of predilection include the internal carotid artery origin, the junction of the basilar and vertebral arteries, the initial segment of the middle cerebral artery (M1) and the proximal posterior cerebral artery (Zarins, 1991). Cohen (1995) notes that as cerebral atherosclerosis progresses, signs of cerebral ischaemia may arise as a thrombosis or critical narrowing of the arterial lumen reduces blood flow to distal vascular channels or as embolic debris from the atherothrombotic site dislodges and travels within the vessel. Neurological deficits may be minimized if adequate collateral blood flow channels form to nourish the ischaemic brain tissue.

Clinically, internal carotid artery occlusion may be heralded by transient ischaemic attacks with reports of monocular visual loss. Since no collateral flow occurs between the origin of the internal carotid artery and the ophthalmic artery, thrombosis anywhere between these points should result in a similar infarction in a given case. The literature indicates that there is a relative lack of consistency of this symptom in the diagnostic criteria adopted by various researchers. For example, Spencer, Thomas, Nicholls and Sauvage (1990) found that 14 of their transient ischaemic attack subjects reported monocular visual loss, whereas this figure was reported in 17% of the transient ischaemic attack sample of Dennis et al. (1989). On the other hand, Werdelin and Juhler (1988) note that none of their transient ischaemic patients reported this symptom. The significance of reporting this symptom therefore appears unclear, although Mansour, Mattos, Faught, Hodgson, Barkmeier, Ramsey and Sumner (1995) proposed from their study that patients with monocular visual loss may have a lower risk of subsequent strokes than those with transient cerebral ischaemic attacks. Their conclusions are based on their findings that patients with monocular visual loss are more likely to seek medical attention than those with transient ischaemic attacks without this accompanying symptom.

Okazaki and Scheithauer (1988) reported that in the presence of unimpaired cardiac function, severe atherosclerotic stenosis can be tolerated if collateral circulation is sufficient. The authors contend that the ischaemic lesions that develop secondary to significant stenosis and thrombosis of the internal carotid artery vary considerably in size (determined largely by the arterial tree involved), as well as in type. Once again, the efficacy of the collateral circulation is the most critical factor determining these parameters.

2.5.2 Cerebral Embolism

As early as 1959, Fisher suggested that embolism might account for the transient focal attacks often described by patients with carotid occlusion. Rutherford (1995) asserted that there are two main sources of cerebral emboli--the heart and the cerebral vessels themselves (artery-to-artery embolism).

2.5.2.1. Cardiac Sources of Emboli.

Dennis et al. (1989) and Caplan and Stein (1986) reported that there are several types of cardiac emboli that may induce cerebral ischaemia. Some of the types proposed are those from myocardial infarction, cardiac rhythm disturbances, valvular disease, cardiac tumours and cardiomyopathies. Each of these offer differing risk levels for cerebral embolization. For example, cardiac tumours, myocardial infarction and cardiomyopathies offer reportedly lower risk for cerebral infarction. Rhythm and valvular diseases are common cardiac disorders that may be associated with transient ischaemic attacks (Lees and Hertzer, 1981) .

The importance of documenting the cardiogenic emboli is important in view of the available evidence implicating the role of certain personality factors associated with coronary heart disease. Thus, to further the understanding of the way transient ischaemic attacks influence neuropsychological test performance, patients who have such cardiac-related aetiologic evidence need to be studied independently from those with other probable causes.

2.5.2.2 Artery-to-artery embolism.

The idea of intra-arterial emboli was reported as far back as the early 1900s by Chiara. Caplan and Stein (1986) note that after large vessel occlusion, emboli arise from atherosclerotic plaques. Despite their sources, emboli are treated indiscriminately by the vessels in which they are eventually lodged. Moneta et al. (1995) note that on reaching the bifurcations or narrowing of cerebral vessels, the embolus migrates more distally, fragments, or lyses. It is supposed that the duration of symptom presentation corresponds with the time for which the embolus remains lodged. Because of the process involved, symptoms that are due to emboli have a sudden appearance, and are maximal at onset.

2.6 Overall Comment

Several issues have become clear in the preceding discussion which may serve to inform future research on transient ischaemic attacks. One major issue is that the resolution period of neurological symptoms appears to be an important variable that needs documentation. This may be difficult since symptom clearing is often complete at medical examination and the patient often arrives at a hospital or surgery long after the symptoms have resolved (Toole, 1991). Thus, the nature and duration of symptoms are based on the careful documentation of the history of the symptoms elicited from the patient or family and/or friends.

The author goes on to report that more than fifty per cent of TIAs resolve within thirty minutes, while a slightly lower proportion have a resolution time of one hour. Only a few subjects appear to have a symptom resolution time of between one and twenty-four hours. This categorical information of less than thirty minutes, between thirty and sixty minutes and greater than sixty minutes may provide a useful classification system to analyze performance on neuropsychological tests. Even such arbitrary categories may lend insight into the various neuropsychological functions, their organization and the recovery patterns in ischaemic cerebrovascular disease. It should be noted that Toole (1991) has reported that even in history taking there is variation in the degree of consistency among clinical examiners. However, estimating interrater reliability coefficients (where possible) and reporting correlation or regression analyses relating symptom clearing periods to neuropsychological test performances may be helpful in examining this issue. Such analyses may offer new insights on the recovery of function in transient ischaemic attacks.

Furthermore, the duration of clinical symptomatology and its relationship to computerized tomography findings deserves investigation. The literature surveyed (Levy and Werdelin, 1988; Waxman and Toole, 1983; Werdelin and Juhler, 1988) treat transient ischaemic attacks resolving within 24 hours homogeneously, although it is reported that most transient ischaemic attack episodes last for fifteen minutes (Toole, 1991). The homogeneous treatment of transient ischaemic attack episodes with such varying resolution times may be more usefully recategorised by short and long duration, which in turn may be used in studies correlating this variable with neuropathology.

Particularly within single case studies, it may also be worthwhile to attempt some documentation of collateral or anastomotic activity, if possible, from angiographic studies. The literature persistently relates to these phenomena as possible mechanisms for either recovery of function (or resolution of symptoms) or, alternatively, the persisting deficits seen in some instances (Walsh, 1987; Caplan and Stein, !986).

The inclusion of monocular visual loss in studies of outcome in inconsistent. As indicated previously, there still appears to be poor consensus on whether this symptom forms part of the transient ischaemic attack. In neuropsychological studies, the presence of monocular visual loss, especially since it also presents for varying durations, may confound findings regarding performances on neuropsychological tests. Studies may therefore benefit from a systematic documentation of the prevalence of monocular blindness, and its relationship to symptom resolution period and neuropsychological test performance among transient ischaemic attack patients. Alternatively, studies of patients who have not presented with this clinical symptom during the transient ischaemic attack, may be beneficial.

A final issue that deserves reporting is the pathogenesis of the transient ischaemic attack. Some studies (Levy and Werdelin, 1988) seem to deal with transient ischaemic attacks homogeneously, even in the presence of differing pathogenic factors (Deveshwar et al., 1991). There appears to be strong evidence that cardiac patients, for example, those who have suffered episodes of myocardial infarction, may be influenced by independent psychological dynamics. Despite its controversial status, a widely-quoted phenomenon related to myocardial infarction, is Type A Behaviour patterns (Friedman, 1990). Therefore, there seems to be some indication for an analysis of the personality characteristics as an intervening variable in transient ischaemic attack patients, particularly among those with cardioembolic involvement.

What becomes apparent is that transient ischaemic attacks occur within the context of a multitude of interacting medical variables, reflecting the systemic nature of the disorder. Each of these variables (e.g., hypertension) may independently or, in an interactive manner, influence performance on neuropsychological tests. Also, given the wide variability in the aetiological significance and pathology of transient ischaemic attacks, together with the idiosyncratic nature of the cerebral vasculature and the variability in diagnostic techniques used, it appears that studies conceptualized within the framework of multivariate statistical analyses will offer a useful way of investigating the neuropsychological sequelae of transient ischaemic attacks.

Next, a conceptual view with converging ideas from neuroanatomy and cognitive neuropsychology is proposed for the study of transient ischaemic attacks.

CHAPTER THREE

A Neuroanatomical-Cognitive Theory of Neuropsychological Functions in Carotid Transient Ischaemic Attacks (TIAs)

3.1 Introduction

The history of the role of cerebrovascular diseases in the study of brain function predates even the seminal reports of Broca (1861) (Burrows, 1848; Bechmann, 1858, cited in Bornstein and Brown, 1991, p. 14). In modern times, Geschwind (1970) has argued strongly for the systematic study of cerebrovascular diseases in the investigation of neuropsychological functions, in particular aphasia, noting that "thrombotic cerebrovascular disease is by far the most important cause of aphasia in adults" (p.70). Benton (1991) has extended this principle to the study of other cognitive abilities. As becomes apparent from the discussion in Chapter 2, the internal carotid arterial system has a distribution area that may be defined in terms of its various arterial branches. With technically advanced brain imaging techniques, it appears that the branches and distribution of the anterior and middle cerebral arteries (the major branches of the internal carotid artery system) may be defined more clearly thereby offering some elucidation of those brain areas that are affected by occlusion to specific regions of the vascular system of brain (Bornstein and Brown, 1991).

Therefore a review of the major anatomical and psychological systems underlying neuropsychological functioning appears appropriate. This review is appropriately based on the structural features of the human brain and the neuropsychological functions of areas perfused and presumably compromised by occlusion of the internal carotid system. First, a proposal for the anatomical organization of the human brain pertinent for studying the neuropsychological sequelae of transient ischaemic attacks in the carotid circulation is presented. Second, a cognitive approach to the study of neuropsychological functioning in carotid transient ischaemic attacks will be presented.

3.2 Anatomical Organization of the Human Brain

The neurons that make up the human brain display regional variations in architecture, connectivity and transmitter neurochemistry (Kolb and Whishaw, 1996). These variations formed the basis of contemporary theories and studies in neuropsychology (Walsh, 1987). In keeping with the goals and objectives of this study, the functional significance of those areas perfused by the carotid arterial system will be discussed.

3.2.1 Principles of Gross Neuroanatomical Organisation

Many frameworks have been proposed for subdividing the cortical surface of the human brain on the basis of regional variations in the architectonic arrangement of neurons and myelin (Mesulam, 1985; Kolb and Whishaw, 1996). These schemes may be classified into two major groups--those that focus on the unique properties of individual regions and those that focus on patterns formed by regions sharing common characteristics. The latter school of thought dominates this discussion since it appears to be consistent with findings from neuropsychological research (Posner, 1986).

Mesulam (1985) proposes that in adopting the anatomically-based regional approach, the entire cortical mantle can be subdivided into only five subtypes which display a gradual increase in structural complexity and differentiation. This structural typology has major implications, and offers an anatomical framework, for the understanding of the distributions of neural connectivity and the neuropsychological consequences of cerebrovascular disorders.

To demonstrate the hierarchical arrangement of this structural typology, Mesulam (1985) has presented the following model, reflected in Figure 7.

EXTRAPERSONAL SPACE

primary sensory and motor
areas

IDIOTYPIC CORTEX

modality-specific (unimodal)
association areas

**HOMOTYPICAL
ISOCORTEX**

higher-order (heteromodal)
association areas

temporal pole;caudal orbitofrontal
anterior insula;cingulate;parahippocampal

PARALIMBIC AREAS

septum;substantia innominata;
amygdala;piriform cortex;hippocampus

**LIMBIC AREAS
(CORTICOID + ALLOCORTEX)**

HYPOTHALAMUS

INTERNAL MILIEU

Figure 7. Cortical zones of the human brain

(Modified from Mesulam, 1985)

On reviewing this model of the organization of the brain, some important implications for the distribution of neuropsychological function may be derived. Firstly, the limbic structures comprising the corticoid and allocortical areas have the closest association with the hypothalamus. The hypothalamus represents the head ganglion of the internal milieu and is a major generator of drives and instincts that promote the survival of the self (Kolb and Whishaw, 1996). Areas in the limbic zone of the cortex assume an important role in the regulation of four types of behaviours--memory and learning, the modulation of drive, the affective colouring of experience and the higher control of hormonal balance and autonomic tone.

The most highly specialized primary sensory and motor areas lie at the other pole in the model. These areas of the cortex are most closely associated with extrapersonal space, i.e., sensory input from the environment has its first cortical relay in the primary sensory areas while the motor cortex coordinates actions that lead to the manipulation of the extrapersonal world. Adjacent to the primary sensory and motor areas lies the unimodal association cortex which provides the neuronal machinery for the subsequent processing of sensory input (Mesulam, 1985).

The two remaining zones of heteromodal and paralimbic formations provide neural bridges that mediate between the needs of the internal milieu and the realities of the extrapersonal world. According to Mesulam (1985), these zones provide two major types of neural transformation--the further associative elaboration of sensory processing and the integration of this information with drive, affect and other aspects of mental content.

The model presented in Figure 7 also provides an anatomical basis for the patterns of cortico-cortical interconnections that are found in the human cortex (Kolb and Whishaw, 1996). Components of each zone have vertical connections with components of other zones and also form horizontal connections with each other. With reference to the connectivity between the hypothalamus and the cortex, Mesulam, Mufson, Wainer and Levey (1983) reported that the most profuse interconnectivity of this nature is with the limbic structures. This pattern of interconnection suggests that the hypothalamic influence on the cortex is likely to be felt most intensely within the limbic zone.

At the cortical connectivity level, the paralimbic areas have vertical connections with the paralimbic and heteromodal areas (Kolb and Whishaw, 1996). With respect to the heteromodal areas, Mesulam (1985) reports that there are extensive connections with components of the paralimbic zone, on the one hand, and with those of the unimodal zone, on the other. These connections appear to provide a substrate for the interactions between motivational factors and extensively pre-processed sensory information.

Many cortical areas also have horizontal cortical connections with other components of the same zone. These are reported to be extremely well developed within the limbic, paralimbic, and heteromodal zones (Mesulam, 1985; Kolb and Whishaw, 1996). For example, these authors note that of all the cortical neurons that directly projected to a subsector of prefrontal heteromodal cortex, 26 per cent were located within unimodal regions, 13 per cent within paralimbic areas, and 61 per cent in heteromodal areas. Furthermore, within the paralimbic zone, the insula and the cingulate cortex have interconnections with virtually every one of the other paralimbic regions of the brain. However, Mesulam (1985) and Kolb and Whishaw (1996) emphasize that while the unimodal regions may receive extensive input from other association areas in the same modality, there is essentially no interconnectivity among areas belonging to different modalities. These patterns of interconnections suggest that within the limbic, paralimbic and heteromodal zones there is emphasis on channel width, whereas the emphasis is on "modality restriction" within the unimodal and primary zones (Mesulam, 1985, p. 143).

The principles of neural arrangement that have been outlined have a strong bearing on the patterns of behavioural deficits that emerge in the psychological profiles of individuals who have disruptions to these pathways. In particular, cerebrovascular disorders of the occlusion type tend to result in highly localized or discrete neural disruptions. Such neural disruptions are likely to result in the impairment of behaviour in specific psychological domains.

The next section will focus on the distribution of the zones presented in the model in Figure 7. Two major issues, which are interlinked, will be used as a guide to the ensuing discussion. In the first instance, in keeping with the major aims and objectives of this thesis, emphasis will be placed on those areas of the brain that are perfused by the carotid arterial system. Secondly, in keeping with the psychological nature of this study, the role of heteromodal cortex will be expanded upon.

3.2.1.1 Primary Areas (The Idiotypic Zone).

The discussion in chapter two suggests that the only destination of the carotid system in the idiotypic zone is the region around the Fissure of Rolando, comprising the primary motor and primary somatosensory areas. This vascular supply takes place through the anterior cerebral artery division of the internal carotid artery in each hemisphere (Walsh, 1987). Thus, the discussion in this subsection will focus on these areas.

In terms of the earlier discussions on the functional role of the idiotypic zone (Mesulam, 1985), the primary somatosensory area is the major recipient of projections from the ventroposterior thalamic nucleus, which in turn, is the thalamic relay of the ascending somatosensory pathways. The contralateral half of the body surface is somatotopically mapped onto the primary somatosensory area in each hemisphere. The mouth and face areas are represented most ventrally and the hand, arm, trunk, and thigh more dorsally, while the foot and leg more medially. Most parts of the somatosensory area have callosal connections with homologous parts in the opposite hemisphere, with the exception of the hand and foot representations (Mesulam, 1985). In accordance with the structural composition of this area, it has been well established that damage to this region is associated with a selective impairment of cortical sensations such as two-point discrimination, touch localization, position sense and stereognosis (Lezak, 1983; Walsh, 1987).

While the primary motor cortex which is located in the precentral gyrus contains a body representation closely paralleling that of the somatosensory area, there are essential differences between these two areas. According to Luria (1980), these differences are related to the cortical organization of the entire frontal lobe which plays a major role in the performance of coordinated and goal-directed acts by the organism in relation to the external world in response to perceived groups of stimuli. These important structural differences relate to the presence of giant Betz cells and to the large contingent of pyramidal tracts which convey impulses of voluntary movement to the motor centres of the skeletal muscles situated in the brain stem and spinal cord. These features are in contrast to the elements of cortical organization adapted for perception of afferent impulses from the subcortex.

Luria (1980) further noted that the isolated projection points within this zone should not be considered as being static in construction, but rather dynamic in nature. He reported that electrical stimulation of the same point of the motor cortex may give rise to different effects, the nature of the effect depending on the intensity of the current being applied and on the previous state of the particular part of the cortex. Mesulam (1985) notes that while the clinical consequences of damage to the primary motor area are still poorly understood, it is widely reported that impaired fractionated distal limb movements are found in such cases. The term fractionated means that a function may be deconstructed into individual components, each recognizable and identifiable as comprising a functional system. Mesulam (1985) notes further that there may be some forms of apraxia that result from an inability to convert verbal commands into skilled movements which require fractionated control of distal limb musculature. Fractionated refers to complex isolated components of control that are required for the accomplishment of a skill or behaviour. Such apraxias are reported to arise from lesions that interrupt the multisynaptic pathways leading from language areas to the primary motor areas.

3.2.1.2. Modality-Specific (Unimodal) Association Areas.

The remaining discussion of this aspect will focus on the frontal lobe (the area of cortical tissue anterior to the Fissure of Rolando) since this region is the main supply area of the internal carotid artery. Mesulam (1985) together with Kolb and Whishaw (1996) identify the region immediately anterior to the primary motor cortex as the modality-specific association area of the motor type. Luria (1980), on the other hand, preferred to designate this region as the secondary premotor area. Both groups of authorities agree, however, that the principal function of this area is the performance and automization of more complex coordinated movements, i.e., those taking place over a period of time and requiring the joint activity of various groups of muscles. The projection provides links between the premotor cortex and the subcortical formations that constitute an important part of the extrapyramidal system of the cortex. This system, in contrast to the direct pyramidal tract, reaches the terminal motor centres of the brain and spinal cord through a series of relays in the subcortical levels of the central nervous system.

Mesulam (1985) proposes that the supplementary motor area, the posterior aspect of Brodmann's area 8 and Brodmann's area 44 (a component of Broca's region) should be included together with the secondary motor area in the category of motor association cortex. With respect to Brodmanns's area 8, this author as well as Luria (1980) agree that its function is in the realm of coordinated eye movements during the modulation of the motor aspects of exploration and scanning in the process of directed attention. In the left hemisphere, damage that includes Brodmann's area 44 is often associated with Broca's aphasia, a clinical phenomenon that has many complex linguistic features. One of the most salient manifestations of this phenomenon is an impairment in the generation of speech-related motor programmes. This is a category-specific motor impairment, since it is reported that some of these patients have no difficulty coordinating the same muscles groups in the act of singing or whistling.

With regard to the supplementary motor area, Laplane, Talairach, Meninger, Bancaud and Bouchareine (1977) reported that patients with lesions in this region of the brain present with an impairment of rapidly alternating movements. The findings of the cerebral blood flow study by Roland, Larsen, Lassen and Skinhoj (1980) suggested that the supplementary motor area may provide a covert plan for intended movements. They showed that actual finger movements yielded local blood flow increases in this part of the brain as well as in the primary motor region. However, when these investigators asked their subjects to think about performing the same movement without actually executing it, only the supplementary motor area still showed activation. This region has therefore been reported to be important for motor planning.

Other investigators (Freedman, Alexander and Naesar, 1984) on the other hand have suggested that this area modulates the initiation of motor responses and the ability to sustain motor output. For example, the paucity of speech output in transcortical motor aphasia may result from a disconnection between the supplemenatry motor area and Broca's area.

From the previous discussion, it appears that the unifying feature of the components of the motor association area is that they modulate the sensory guidance, as well as the initiation, inhibition, planning and learning of complex movements.

3.2.1.3. Higher-Order (Heteromodal) Prefrontal Association Areas.

The discussion in this section will be guided by two interrelated principles. The first relates to the anatomical organization of the prefrontal cortex and the second refers to the domains of behaviour associated with demarcated areas.

On the basis of extensive neuroanatomical evidence (Mesulam, 1985; Luria, 1980), two major divisions of the prefrontal cortex have been identified--the dorsolateral and orbitomedial zones. The dorsolateral system is extensively connected with secondary sensory association areas in parietal, occipital, and temporal lobes--a reciprocal relationship that corresponds with the presumed role of dorsolateral frontal zones in integrating sensory information from multiple modalities. The orbitomedial zone is connected with limbic structures in the cingulate and anterior temporal lobes, and hence is well situated to integrate motivational and emotional processes.

Thus, Mesulam's (1985) designation of the dorsolateral zone as heteromodal cortex and the orbitomedial zone as paralimbic cortex aptly captures the functional differences of these two regions (see Figure 7).

Research aimed at elucidating the functional significance of the prefrontal cortex is therefore aimed at identifying the clinical syndromes associated with these zones. There are consistent reports (Luria, 1980; Walsh, 1987; Malloy, Bihrie, Duffy and Cimino, 1993) that two associated groups of neuropsychological syndromes are associated with dysfunction or damage to these respective zones. Dorsolateral lesions seem to cause deficits in temporal and sensory integration, planning, maintenance of goal-directedness, and behavioural flexibility. These syndromes are characterized by various froms of deautomatization of motor, speech, and intellectual acts while states of consciousness remain relatively intact (Luria, 1980).

Lesions of the orbitomedial division, on the other hand, result in the disruption of inhibitory and emotional mechanisms, with impulsive and socially inappropriate behaviour resulting. Thus, it becomes apparent that the orbitomedial zones are predominantly concerned with the regulation of nonspecific activation processes (Luria, 1980).

What seems apparent from the above discussion is that several anatomical areas of the brain involving varying levels of neuropsychological functional significance may be comprised in carotid transient ischaemic attacks. One contemporary method of investigating these neuropsychological changes is to employ the cognitive approach (Anderson, 1994; Mapou and Spector, 1995), which is presented next.

3.3 Cognitive Approaches to Neuropsychological Functioning

One of the initial assumptions underlying this approach is that cognitive systems are organized in a modular way (Caramazza, 1984). According to this principle of modularity, mental abilities are made up of separate cognitive subsystems or modules. A logical justification for the assumption that cognitive systems are organized in a modular way is to be found in the vision research work of Marr (1982), who argued in computer terms that complex systems are easier to debug (to correct and correct system errors) and to upgrade (to add to, or to improve) if they are organized in a modular way. If they are not, argued Marr (1982), then small changes to improve one part have to be accompanied by many simultaneous compensatory changes elsewhere. Empirical evidence from neuropsychological studies, showing a wide array of different selective impairments observed in neurological cases, appears strongly to support the notion of modularity (Mapou and Spector, 1995). Thus the operation of spoken word retrieval may be made up of one set of modules, written word recognition another, and visual recognition yet another.

Fodor (1983) listed what he thought to be the properties of cognitive modules. Important among these was the property of informational encapsulation, meaning that a module must carry out its own form of processing in complete ignorance of, and isolation from, the processes going on elsewhere in the total cognitive system. If, for example, there is a module or set of modules which process the emotional expression on a face, and a separate module or set of modules which recognize that face and determine who the person is, then informational encapsulation demands that the modules processing the emotion on the face must operate independently of any activity within those modules processing the identity of the face.

Fodor (1983) also proposed that modules must be domain-specific, that is, each module can only accept one particular sort of input. For example, the module processing the emotional expression of faces would not also be able to process the emotional tone of voices--such processing would require a separate domain-specific module. Shallice (1984) noted that if the assumptions of informational encapsulation and domain specificity were combined with the assumption of neurological specificity, whereby modules are distinctly represented within the brain itself, there is the possibility that brain lesions will selectively impair certain modules while leaving others intact and operating at normal, pre-injury levels of efficiency.

Fodor (1983) also proposed that the operation of modules is mandatory, that is, modules are unstoppable--they are beyond voluntary control, and if the appropriate input is present a module will carry out its particular type of processing whether the person wishes it or not. Ellis and Young (1988) note that this feature is not uniform across cognitive modules and suggest, for example, that the system from which the names of people and things are retrieved appears to be mandatory, yet the retrieval of the name of a person or object seems to be more voluntary than mandatory. They argue that while we cannot stop ourselves recognizing a familiar person we see, we do seem to have some voluntary control over whether or not we activate the module from which the person's name is retrieved. It appears therefore that the property of the mandatory nature of modules refers more to input modules than to output modules.

Deriving from this view of the modular nature of cognitive skills is the second assumption which states that the individual modules can fractionate, so that acquired brain damage can selectively impair some modules while leaving others intact (Caramazza, 1984). Thus, one might expect to observe cases, for example, in which spoken retrieval is disordered, while written word recognition remains relatively preserved. One might also expect to observe instances of selective damage within sets of modules, so that for example, within the domain of spoken word retrieval, one may discover a case in which naming pictures is impaired, while reading picture names is considerably more successful (Hillis and Caramazza, 1992).

Underpinning careful cognitively-based neuropsychological studies that aim to reveal precise patterns of impairment (and abilities that remain relatively intact) is the third assumption of subtractivity, the view that the performance of an individual patient reveals the usual cognitive apparatus employed in a particular task, minus those systems that have been damaged (Caramazza, 1984). The final assumption of subtractivity holds that the nature and function of a particular cognitive component will be reflected in an undistorted way in the patterns of acquired disorder that are observed to occur. As Caramazza (1984) has cogently noted, performance on a task after brain damage reflects a variety of factors, including disruption to processing systems other that the component one has targeted, and including strategic and compensatory mechanisms that do not normally come into play. Mapou and Spector (1995) have argued that in order to confirm these models, confirmatory data from experimental studies (converging operations) as well as the search for reliability and validity through replication of results must be sought.

The discussion of those neuropsychological functions influenced by transient ischaemic attacks of the carotid circulation is guided by two important principles. Firstly, there are clearly identifiable brain areas of distribution associated with the carotid arterial system. As indicated in chapter two, these cortical areas are the frontal lobes and the anterior temporal lobes. Secondly, there are strong findings of the major neurocognitive functions mediated by the frontal and anterior temporal lobe regions. Since the type of neuropsychological pattern of function and dysfunction will be guided by the neuroanatomical areas affected in transient ischaemic attacks, the role of the frontal lobe in the cognitive functions under investigation will be discussed. Using these principles in tandem with the proposals for the cognitive functions subserved by these neuroanatomical regions, the following functions are discussed.

3.3.1 Attention and Concentration

All too often attention is conceptualized and consequently treated as a unitary entity. This follows the implicit assumption that attention is a basic cognitive skill underlying and supporting the higher cognitive functions. Attention however consists of a number of basic capacities and thus models of attention have typically involved elucidating a system for attention (Mirsky, Fantie and Tatman, 1995). Several authorities (Anderson, 1994; Mirsky et al, 1995; Lezak, 1995) propose approaches with converging features that attempt to conceptualize attention and concentration. These authors generally argue that the ability to detect the nature and contents of the environment through sensory receptors, is not sufficient for survival in a complex habitat. When necessary, one must be able to select the appropriate stimulus on which to act from all the information that bombards the sensorium. Having selected, one must then be able to maintain fixation on the target, thereby resisting the tendency to be attracted by competing, but irrelevant or redundant, stimuli (Mirsky et al., 1995). When required, one must be able to terminate one's fixation and switch one's focus to another target. Sometimes one must carry out two functions simultaneously, splitting one's attention between a main target while monitoring what is happening on the periphery. The specific dysfunction will determine the nature of the behavioural deficit.

The prefrontal cortex is among the many structures involved in attention (Lezak, 1995). Significant frontal activation is said to occur during selective attention activities among patients considered to be neurologically intact (Naatenen, 1988). The role of the prefrontal cortex in attention has been described in various ways. These range from the capacity to make and control shifts in attention (Mirsky, 1989) to Luria's (1973) suggestion that the prefrontal lobes are involved in modulating the level of vigilance. Thus, attentional functions are frequently impaired with patients with frontal lobe involvement. Symptoms have been described as sluggish in reacting to stimuli or being unable to maintain an attentional focus (Stuss, 1993).

Cognitive psychologists are reported to have been quite fruitful in their exploration and discovery of a number of the more finely grained aspects of attention. These include arousal, effort and intensity (e.g., Cohen, 1993); focussed and divided attention (e.g., McDowd and Craik, 1988); search and detection, automatization, consistency and complex attentional processing (Schneider, Dumas and Shiffrin, 1984). Within the context of specifying the character of attention defect, studies of several populations of patients (Mirsky, 1989; Jones, Duncan, Brouwers; Mirsky, 1991) have yielded a model of attention proposed by Mirsky et al. (1995) comprising four factors--perceptual-motor speed, flexibility, vigilance and numerical-mnemonic processing. Elements of attention that respectively correspond to these factors are purported to be focus-execute, shift, sustain and encode. Other researchers (Lezak, 1995) appear to support this model in part.

According to Mirsky (1989) and Posner, Inhoff, Friedrich and Cohen (1987), evidence from neuroanatomical, clinical, and neuropsychological studies suggest that an attention "system" can be described within the brain. According to Cohen (1993) although attention, concentration and tracking can be theoretically differentiated, in practice they are difficult to separate. Purely attentional defects appear as distractibility or impaired ability for focussed behaviour. Several authors (Cohen, 1993; Mirsky et al., 1995) argue that intact attention is a necessary precondition of both concentration and mental tracking activities. Mirsky et al. (1995) notes that concentration problems may be due to a simple attentional disturbance, or to inability to maintain a purposeful attentional focus.

3.3.1.1 Vigilance. Vigilance is described as the ability to sustain and focus attention in itself (Mirsky et al., 1995). Cohen (1994) has defined vigilance as a state of readiness to respond despite long intervals of empty waiting. According to Lezak (1995) psychological tests assessing this aspect of attention typically involve the sequential presentation of strings of stimuli (numbers or words) over a period of time with instructions for the patient to indicate when a given number or letter (the target item) is perceived. One such test described by Lezak (1995) is the Cancellation Task which reportedly measures many functions including motor responses and visual scanning. In a variation of this test, Ruff, Evans and Light (1986) presented the Two and Seven Test which required the skills of identifying target items in the presence of distractors. Ruff, Niemann, Allen, Farrow and Wylie (1992) reported that left anterior lesion patients generally performed better than right anterior lesion patients on this task. Anterior lesion patients performed better than posterior lesion patients. This finding suggest the frontal lobes are involved in the vigilance function of attention.

3.3.1.2 Short-Term Storage. Research on memory has provided considerable evidence for a verbal memory system that is involved in tasks in which subjects must retain small amounts of information over brief delays (Waters, Caplan and Hildebrandt, 1991). Waters et al. (1991) also note that research into the structure of short-term memory system has shown that speech-based or phonological information plays an important role in its functioning . Shallice (1988) noted that the short-term memory system is also involved in language comprehension. He argued that the phonological store mechanism (for verbal material) plays a role in the comprehension of auditorily presented sentences.

According to Mirsky et al. (1995), the attentional system operates on both speed and quantity of processing. This author suggests that the functions of speed and quantity may be considered to have both an independent as well as an inter-dependent relationship with each other. Shum, McFarland and Bain (1990) note that these two dimensions therefore need to be assessed independently. The most common way of assessing the function of quantity (or short-term storage) is by employing the Digit Span test as reflected in the Wechsler Scales of Intelligence. The test consists of a Forward string recall and a Backward recall, the scores on each combined to constitute a Total Digit Span score. While Total Digit Span score is used routinely as a measure of short-term attention, cognitive psychologists (e.g., Storandt, Botwinick and Danziger, 1986) have emphasized that the processes involved in Digits Forwards and Digits Backwards are quite different. Storandt et al. (1986) proposed that Digits Forwards may involve rote learning while Digits Backwards involves both rote learning and mental manipulation which requires some function of mental control. The neuroanatomical substrates subserving these functions have not yet been elucidated.

3.3.1.3 <u>Mental Tracking.</u> According to Lezak (1995), the ability to hold information long enough to perform an operation on them and then proceed to new information, constitutes this function. The simplest test of mental tracking is reportedly Digit Span Backward, which reportedly tests how many bits of information a person can attend to at once and repeat in reverse order (Cohen, 1993; Anderson, 1994). Tests of mental tracking involve some perceptual tracking or more complex mental operations as well, and many of them involve some form of scanning. In addition to Digit Span Backwards, Paced Auditory Serial Addition Test (PASAT) has been reported to be a sensitive indicator of the mental tracking. The cognitive operations required to perform this function are several-fold. Most obvious is that successful performance is dependent on education since operations are based successful mastering of the operations of addition (Delaney, Prevey, Cramer and Mattson, 1988). The role of the frontal lobe in this skill has not been reported in the literature. The most effective deployment of the test reported in the literature has been with postconcussion patients who reportedly are assessed for recovery of function, more importantly speed of processing (Roman, Edwall, Buchanan and Patton, 1991).

The cognitive function of memory, which is closely related to attention and concentration, will be discussed next.

3.3.2 Memory

Memory may be defined as the capacity to register, retain, and retrieve information (Ellis and Young, 1988). According to Squires (1987) there are three distinct but related, psychologically and biologically validated forms of memory: sensory memory, short-term memory, and long-term memory. Sensory memory (also called registration by Lezak, 1995) holds sensory information for a second or two (Neisser, 1967). It is neither strictly a memory function nor a perceptual function but rather a selecting process by which perceptions enter the memory systems (Nauta, 1966). The information decays continuously, and new inputs erase residual traces of previous inputs. The first traces of the stimulus may be experienced as a fleeting visual image (iconic memory, lasting up to 200 milliseconds) or auditory replay (echoic memory, lasting up to 2000 milliseconds indicating early stage processing in terms of sensory modality (Neisser, 1967).

Short-term memory is a limited-capacity store that retains information for a minute or two depending on rehearsal and may itself be comprised of three stages (Squires, 1987). Immediate memory temporarily holds information that has been retained from the registration process. While theoretically distinguishable from attention in the models of most authors, Squires (1987) reports that immediate memory represents neuronal activation in which the relevant perceptual components have been integrated. Although immediate memory is thus usually conceptually distinct process, Baddeley (1992) shows how this system itself may operate as a set of subsystems controlled by a limited capacity executive system which he collectively called working memory. He postulates two working memory subsystems--one for processing language (the phonological loop) and one for visuospatial data (the visuospatial sketch pad). In the model used to explain the processing of verbal material, working memory consists of a limited-capacity supervisory controlling system, the central executive, and a slave system, the articulatory loop. In the slave system, there is an articulatory control process and a phonological store that is specialized for processing verbal material.

Baddeley (1992) identifies rehearsal as a second stage of short-term memory describing this stage as any repetitive mental process that serves to lengthen the duration of the memory trace. He argues that since rehearsal maintains the memory trace for hours, there is an increased likelihood that a given bit of information will be permanently stored, although this is not ensured at this stage.

As early as 1975, Barondes proposed a third kind of short-term memory that lasts for an hour to about a day. This author suggested that short-term memory may last longer than a reverberating circuit (rehearsal) could be maintained by even the most conscientious rehearsal efforts, but is not yet fixed as learned material in long-term memory storage. Cohen (1993) reports that despite the clinical interest in this form of short-term memory, there is a relative lack of empirical data on this phenomenon particularly with its incorporation into existing models of short-term memory.

Long-term memory is a lasting memory process and refers to the person's ability to store information (Anderson, 1994). According to Cohen (1993), the process of storing information as long-term memory is known as consolidation and this process is reported to occur quickly or continue for considerable lengths of time without requiring active involvement. Squires (1987) reports that learning, i.e., the acquisition of new information, implies consolidation--that is, what is learned is consolidated. Squires (1986) further defines consolidation as a hypothesized process of organization within "representations of stored information, which continues as long as information is being forgotten" (p. 241). Learning often refers more specifically to effortful or attentive activity on the part of the learner. While most of the learning in long-term storage appears to be organized on the basis of meaning (Broadbent, 1970), Baddeley (1978) argues that rote repetition and association built on superficial, relatively meaningless stimulus characteristics can also lead to learning.

Impairment in learning and memory are among the most common symptoms and neuropsychological deficits in neurological patients Learning and memory can be impaired in the context of relatively preserved intellectual functions in cases of amnesias (Kapur, 1988). In addition to accurate diagnostic assessment, there has been an increasing emphasis on accurate and relevant measurement of memory.

Memory disorders have a long history of being associated with prefrontal lesions. For example, Stuss and Benson (1986) described a "forgetting to remember" in which an intended act or memory is forgotten. Lezak (1995) however notes that these patients typically do not have a disorder of the memory system but they rather seem not to use context to facilitate recall, a finding reported in the study of Moscovitch and Umlita (1991). These patients are reported not to order or organize what they learn although with appropriate cueing adequate recall can be demonstrated (Jetter, Poser, Freeman and Markowitsch, 1986). These phenomena of frontal amnesia demonstrate how inertia and executive disorders in particular can interfere with cognitive processes (Walsh, 1987).

Within populations of cerebrovascular patients, Stuss and Benson (1986) report that the most common source of reports of memory impairment in cerebrovascular disease concerns the rupture and surgical correction of anterior communicating artery aneurysms. Neurosurgeons have long been aware of impaired function as a common and serious residual of this disorder. It had been interpreted that frontal lobe damage underlies the memory loss, suggesting that the medial, posterior orbital frontal area be included among neuroanatomical loci of memory function.

In an effort to study learning and memory empirically, several psychometric instruments have been devised (Lezak, 1995). The use of words, more popularly in word lists, has been deployed in many settings. The use of word lists has been based on the observation that the number of words normal subjects recall immediately remains relatively stable through the early and middle adult years (Talland, 1965; Miller, 1973). Word learning lists have reportedly been useful in delineating memory system deficits in a variety of disorders. Head trauma patients tend to have somewhat lower recall for each measure but demonstrate a learning curve with little gain appearing on delayed recall but a near normal performance on the recognition trial (Peck and Mitchell, 1990). In the case of a specific word list, Rey Auditory Verbal Learning Test, frontal lobe patients perform consistently less well than control subjects on recall trials. However, on a recognition format, their performance reaches a normal learning curve (Janowsky, Shimumura and Squires, 1989). These findings suggest a significant retrieval problem among frontal lobe patients. Similar problems with the retrieval process among frontal lobe patients have been documented in the literature.

Luria (1973) noted that the accumulated evidence implies that lesions of the frontal lobe do not cause a primary disturbance of memory, but they do interfere with mnestic activity. He further exemplified that while frontal lobe damage leaves the operative function of memory intact, the ability to create stable motives of recall and maintain the active effort required for voluntary recall is impaired. In other words, the frontal lobes are involved in the process of organizing methods of memorization and retrieval and in comparing the results with the original intention. Luria's (1973) studies of learning and memory were based on the presentation of long lists of words (spoken or written) to frontal lobe patients. He reports that those items that make a direct impression and require little effort to memorize are best remembered. The total number of items remembered does not significantly increase with repetitions of the list as it does in normal subjects, and different words may be recalled on subsequent trials. It is suggested (Stuss and Benson, 1986) that the passive imprinting of material is intact but that a deficit exists in the control of retrieval. Furthermore, Luria (!973) and Stuss and Benson (1986) report that if given one series of words to remember, followed by a second series to remember with a subsequent request to remember the first list, frontal lobe patients perform less well than normal subjects. The findings in the studies cited above suggest strongly that the frontal lobes are involved in the processes of learning and memory. Any form of change in the status of the frontal lobe may therefore result in changes in this psychological function. However, since the process of learning is reflected in recall and retrieval of information, systematic studies of learning and memory in different patient groups are likely to further elucidate these processes.

Next, the role of the frontal lobe in executive functioning, specifically the capacity for cognitive flexibility and the capacity to shift set, is presented.

3.3.3 Executive Functioning

There are several categories of behaviour that may be identified as comprising executive beviours (Stuss and Benson, 1986; Anderson, 1994; Lezak, 1995). The principles of carotid circulation (Chapter 2) as well as the literature review of neuropsychological sequelae in transient ischaemic attacks in this vascular bed (see Chapter 5) suggest certain categories of psychological functions that may be of importance in the present investigation. These findings provide the guidelines for the discussion the functions comprising executive function.

3.3.3.1 Flexibility and the Capacity to Shift Set. According to Luria (1973) and Pribram (1987), the prefrontal lobes have been interpreted as serving an executive function, a diverse set of interrelated but theoretically independent functions (Anderson, 1994). The ability to regulate one's own behaviour is considered part of the executive functions of the frontal lobe (Lezak, 1995; Stuss and Benson, 1986) and has long been established as a function of the prefrontal cortex (Luria, 1973). Defects in the control, regulation and integration of cognitive activities tend to predominate in patients with dorsolateral lesions (Lezak, 1995; Walsh, 1987). As indicated by Mesulam (1985), the the designation of the dorsolateral zone as heteromodal cortex suggests that the dorsolateral cortex is involved in supramodal sensory regulation, together with the maintenance of goal-directedness and facilitating behavioural flexibility. Difficulties in making mental shifts have typically been referred to as perseveration or rigidity (Walsh, 1987). Goldberg and Tucker (1979) and Walsh (1987) both argue that while perseveration may be found in lesions of lobes other than the frontal, this behavioural deficit appears only in conjunction with the patient's specific deficits. In frontal lobe patients on the other hand, perseveration tends to be supramodal, i.e.. occurs in a variety of situations and a variety of tasks (Lezak, 1995).

The Stroop Colour-Word Test (Golden, 1978) has also been established as a measure of the ability to shift perceptual set to conform to changing demands (Lezak, 1995). Golden (1978) operationalizes this skill as an ability to suppress an automatic word-reading response in favour of a colour-naming response. Trenerry, Crosson, DeBoe, and Leber (1989) reported that patients with left hemisphere cerebrovascular diseases performed at the lowest level of brain-damaged patients suggesting the sensitivity of this test to left hemisphere lesions. In another study, only patients with left frontal lobe lesions, or those with bilateral lesions displayed slowed performance on the Stroop Interference trials most prominently (Holst and Vilkki, 1988).

Despite the established sensitivity of the Stroop Colour Word Test Interference trial to the suppression of automatic responses, some authorirites provide alternate interpretations to lower perfromances on this aspect of the test. Zajano and Gorman (1986) reported failure on this test to be due to impairment in selective attention. Lezak (1995) maintains that although the capacity for fluently adaptive behaviour is certainly involved in this task, it is as a measure of concentration effectiveness that this technique appears to make its greates contribution.

Some attempts have been made to develop an equivalent non-verbal cognitive productive task as represented in the Ruff Figural Fluency Test which requires the subject to draw series of different designs (Ruff, Light and Evans, 1987). According to Anderson (1994), no localization studies have been reported for this test making interpretation difficult. Also, the author indicates that there is a serious lack of adequate validity and reliability data on this test.

Another aspect of the flexibility and capacity to shift function is the ability to sorting stimuli. Lezak (1995) describes sorting tests as the most common form of abstraction and concept formation. The capacity for abstract thinking, in turn, has been commonly reported to be impaired in frontal lobe patients (Goldstein, 1948; Stuss and Benson, 1986; Walsh, 1987;). Several tests have been developed in an attempt to assess these sorting behaviours in patients and normal subjects. Most sorting tests assess the ability to shift concepts as well as the ability to use them According to Lezak (1995) and Stuss and Benson (1986), the Wisconsin Card Sorting Test (WCST) remains a widely used measure of abstract thinking and shift of set. The studies of Milner (1963) are probably those that firmly established the WCST as a measure of frontal dysfunction. Support for these findings have been provided by the studies of Drewe (1974) who reported the frontal lobe patients obtained fewer categories on this test.

Studies have reported inconsistent findings with respect to lateralization in the performance on the WCST. Taylor (1979) found that perseverative errors more often associated with left-sided dorsolateral lesions than those with right-sided lesions. Robinson, Heaton, Lehman and Stilson (1980) reported that in contrast, right frontal patients produce more perseverative errors than left frontal lesion patients. Lezak (1995) has pointed out that the question of whether these differences arise from difference in the nature of the lesions or other patient variables need exploration. She suggests that these discrepancy in the findings may relate to the type of lesion patients included in the study samples. For example, Taylor's (1979) subjects all reportedly had surgical excision of frontal tissue while the Robinson et al. (1980) study included subjects with diffuse head injury.

The role of the frontal lobe in the executive function of sorting and shifting set has been controversial in the light of other research findings. Anderson, Damasio, Jones and Tranel (1991) found that reviewing the performances of frontal and nonfrontal patients on the WCST offers no privileged WCST competency in differentiating anterior from posterior lesions. Mountain and Snow (1993) in their review of the WCST data suggest that while caution must be exercised against identifying lesion sites with this test, the test itself is a strong assessment instrument of the functions of sorting and set shift behaviour.

3.3.4 Concluding Comments

While it is widely acknowledged that the frontal lobes are involved in a wide range of cognitive behaviours (Lezak, 1995; Kolb and Whishaw, 1991; Luria, 1973), it is beyond the scope of this chapter to review all of these functions for the present study. Three categories of behaviour have been targeted for review based on their commonality in findings among cerebrovascular studies (Bornstein and Brown, 1991). In proposing a model for the organization of cogntive abilities, Mapou and Spector (1995) indicate that cognitive skills may be conceptualized as comprising a hierarchy. In this hierarchy, the cognitive domains of attention and concentration and learning and memory may be considered to be representative of the level foundation and integrated skills in the structure of cognitive abilities (Mapou and Spector, 1995), which represents a base level for cognitive functioning. On the other hand, Mapou and Spector (1995) also suggest that sorting and set shift skills may also be representative of a cognitive ability at the foundation skill level, while Luria (1980) conceptualized attention and concentration as more fundamental than sorting and set shift skills.

The present study is aimed at investigating the neuropsychological sequelae in transient ischaemic attacks of the carotid circulation. The theoretical framework presented in this chapter, which is based on the cognitive structure of abilities of relevance in this neurological condition, forms the framework for the ensuing investigation. The theoretical framework also draws to some extent on neuroanatomical organization, but to an even greater degree on the findings of neuropsychological investigations using psychometric tests. The present study is itself an empirical study of the neuropsychological sequelae in transient ischemic attacks investigating, by definition, the psychological consequences in the presence of such cerebrovascular diseases. Thus, psychometric issues relating to neuropsychological assessment are discussed next in Chapter 4.

CHAPTER FOUR

Issues in Neuropsychological Assessment

4.1 Introduction

The science of the measurement of human behaviour in its broadest sense, and of behaviour in the presence of neurological dysfunction,. is underpinned by several theoretical issues. These issues relate primarily to the scientific principles underlying the measurement process in psychology, generally called psychometric theory and practice, and to the factors influencing the score values elicited in the various measurement processes. Thus, in order to elucidate these two broad issues, the purpose of this chapter is twofold. First, the psychometric principles of psychological assessment and its application to neuropsychological assessment will be outlined. Second, the influence of the demographic variables of age, education and SES on neuropsychological test performance, pertinent to the present study, will be reviewed.

4.2 Psychometric Issues in Neuropsychological Assessment

As implied in the name, clinical neuropsychology draws from more than just one discipline. From examining the name, there is the simplified view of the different disciplines of neurology and psychology from which clinical neuropsychology draws. The assessment methods involve everything from behavioural observation to timed pencil-and-paper tests and responses to computerized tests (Anderson, 1994).

Several theories have been influential in the process of psychological testing. With respect to the primary issues of psychometric theory, classical test theory has been reported to be the primary influence on conceptions of validity and reliability. Since it was proposed by Spearman (1904), the classical test theory (also known as true-score model) has undergone both change and expansion.

According to this model, an observed score is conceived as consisting of two components--a true score and an error component.

In symbols:

$$X = T + E$$

where X is the fallible, observed score; T is the true score; and E is random error. Conceptually, the true score can be thought of as the score that would be obtained under ideal or perfect conditions of measurement. Since such conditions never exist, the observed score always contains a certain amount of error (Pedhazur and Schmelkin, 1991). Although (4.1) is theoretically meaningful, classical test theory assumes that the traits measured are constant and that measurement errors are random. Accordingly, if a person were to be measured many times, assuming that he or she remains unchanged, a series of equations such as (4.1) would be obtained, each consisting of the same true score (because it is assumed to be constant) but differing observed scores because of variations in errors.

Franzen (1989) reports that progress in the science of psychological measurement has meant that psychometric theory is no longer associated just with classical test theory. He reports that there have been developments in measurement to include different forms of scaling, nonparametric as well as parametric statistics, and different theoretical conceptions of the process of measurement.

Michel (1986) discussed three different theories of measurement with reference to acceptable statistics: representational theory, operational theory and classical theory (different from classical test theory). Very briefly, representational theory can be described as the use of numbers to represent the empirical relations between the objects of measurement. The psychometric tradition is often seen to be embedded in representational theory (Franzen, 1989).

The process of measurement results in numbers that reflect or represent a level of skill (or some other construct) that can be related to a level of some other skill when both skills are measured on the same scale. Or, alternately, the first number can be correlated with a number reflective of some other property, such as cognitive flexibility (Lezak, 1995). In the strictest sense, representational theory applies only to single scores (Franzen, 1989).

Operational theory views measurement as an operation that produces numbers. The measurement and production of numbers involved in summing qualitative signs are associated with operational theory. The operation of challenging the subject to perform certain behaviours and then summing the successes results in a number that does not necessarily reflect a skill, but that can be analyzed by statistical manipulations.

Classical theory views measurement as the assessment of quantity. Here, numbers are not necessarily assigned; instead, numerical relations are discovered (Franzen, 1989). When a battery is interpreted on the basis of profiles, the applicable body of thought is classical theory.

The present study is based on the administration of psychometric tests that yield scores that purportedly reflect the skill measured by that test. Various theories underpinning the measurement of psychological traits have been formulated. These theories also have implications for demonstration of test validity and the estimation of test reliability. Thus, the concepts of validity and reliability become important issues in neuropsychological assessment and these will be discussed next.

4.2.1 Validity

Validity is the most important consideration in test development and use. This concept refers to the degree to which both theory and empirical evidence support inferences and actions based on test scores (Lezak, 1995; Anderson, 1991; Sbordone, 1996). In an empirical sense, validity may be defined as a statistical relationship between the results of a particular procedure and a characteristic of interest, that is, between a contrived procedure and other independently observed events (Anastasi, 1982: Nunnally, 1978). These relations may be defined in terms of the content of the test, in terms of related criteria, and in terms of underlying constructs. All of these can be quantified in terms of contextual variables and subject variables. Validation thus appears to be the process of developing a sound scientific argument that supports proposed interpretations and actions based on test scores that are validated, not the test itself. Thus, a demanding feature of this assumption is that each intended use of the test must be validated (Sbordone, 1996).

4.2.1.1 Content Validity

Content validity is defined as the degree to which a test adequately samples behaviour from the domain of interest (Nunnally, 1978). Test content refers to the themes, wording, and format of the items, tasks, or questions on a test, as well as the procedures regarding administration and scoring. Therefore evidence based on test content involves logical and empirical analyses of the relevance and representativeness of the test content to the defined domain including the conditions of testing and scoring.

In neuropsychological assessment, if a test is intended to be sensitive to the global aspects of memory dysfunction, there need to be sufficiently representative tasks that access the construct defining global memory processes as understood by the test developer. Thus the process of content validation begins when the initial test items or procedures are selected during the design of an instrument. According to Hopkins and Antes (1978), most arguments used to support content validation are theoretical and logical. Moreover, content validation may be most easily evaluated or demonstrated when the procedure is an operationalization of a well-defined theory or a component of a theory.

Items for a test are usually derived by a variety of methods ranging from examples of behaviour that are directly stated in the theoretical model (e.g., the expectation of increased skin conductance as anxiety increases) to the selection of items by expert judges. In neuropsychological procedures, the sensory modality (visual, auditory, or tactile) through which a stimulus is presented and the likely internal processes used to achieve a solution (rote or reasoned) are all as important to content validity as to construct validity (Nunnally, 1978) . This author argues that the pertinent issue is likely to be generalizability of the information derived from an item and, consequently, the likely generalizability of the test as a whole. In dealing with content validity, there is the ever-present prospect of a tradeoff between lack of specificity or insufficient sampling of the domain and tedious redundancy that does not usefully articulate the characteristic of interest. Therefore when tests are shown to have limited content validity, the issue raised is insufficient generalizability to the domain of interest.

The causes of limited content validity are usually incomplete understanding of the underlying theory, lack of a guiding theory, or a tendency to assume greater generalized interpretations of item performance at the time of construction. Therefore one's intent may be to design a widely applicable neuropsychological screening test, but the items may all require that the subject copy simple geometric designs. There is a large subset of brain-impaired subjects (e.g., subjects with specific impairments in language skills) for whom performance on such a test will not be diagnostically useful.

Face validity is often erroneously employed synonymously with content validity. However, Anderson (1991) reports that face validity is a category of content validity and refers primarily to the perceptions of the examinee, the test compiler as well as that of the test user. The subject forms some conclusions about what the test is measuring on the basis of the content or language of the test procedures. In more ambiguous test situations (for example, personality assessment), the examinee's assumptions about the nature of test is relatively disparate from the examiner's intent. Face validity thus becomes an important concern in that the perceptions of the examinee affect his or her performance on the test--the results may be confounded in comparison to the intended measurement purpose of the test user. Franzen (1989) argues that an examinee is more likely to participate in an assessment that uses procedures that appear to provide information that will answer his or her concerns or provide feedback regarding his or her anticipations regarding personal health status.

From the discussion above, it can be seen that content validity plays a large role in the assessment process. Nunnally (1978) suggested a few ways in which content validity can be evaluated. For example, if a scale is thought to measure a single construct, the items can reasonably be expected to demonstrate a fair amount of internal consistency, a relation that can be tested empirically. For those constructs thought to be affected by experience, content validity can be evaluated by demonstrating improved performance following a training procedure. Content validity can also be evaluated by comparing performance on the test in question with performance on other tests thought to tap the same or similar constructs. Anastasi (1982) suggested a qualitative method of checking content validity by having subjects think out loud during the testing process. Despite inherent limitations for deployment in brain-impaired populations particularly those comprising language-impaired patients, this method may nonetheless be useful in determining content validity (Pedhazur and Schmelkin, 1991).

Another method used to assess content validity is error analysis. When persons of similar brain dysfunction fail an item, a review of their error patterns for signs of consistency may suggest how the brain dysfunctions translates into behaviour (Kaplan, Fein, Morris and Delis, 1991). An example of this is the analysis of errors on the Block Design subtest of the WAIS-R. The authors proposed, for example, that breaking the external configuration of the target design while retaining its detail in a poorly configurated fashion may be related to right cerebral dysfunction.

A concluding comment about content validity is that demonstrating this feature of a test is limited by the extent to which extraneous factors affect test performance. The relative contributions of motivation, academic experience, prior intellectual status, sex and psychological status must be understood before an accurate assessment of content relevance and generalizability can be conducted. Differences in timing procedures, administration instructions, or scoring procedures may cause relations with external criteria to vary considerably.

4.2.1.2 Criterion Validity

Anastasi (1982) described criterion-validating procedures as those that demonstrate a test's effectiveness in a given context. Thus criterion validity is commonly expressed as a correlation between a test score and some external variable which may be another test that is assumed to demonstrate the characteristic of interest. It is typical to speak of concurrent validity as allied behaviour (observations recorded on an equivalent instrument) measured at the same time. Predictive validity is usually the term of use, as performance on the test being evaluated is used to temporally predict the criterion, whether it is a diagnostic group membership or behavioural change. The statistical expression of validity is called the validity coefficient, which is discussed next.

4.2.1.3 Validity Coefficient

A validity coefficient is often computed as an index of the correlation between the score achieved on a particular test and some criterion variable. For example, one may correlate the relation between a score on the Wisconsin Card Sorting Test and a dummy-coded variable indicating diagnostic group (that is, 1 - normal, 0 - brain-impaired). Dummy coding consists of 1's and 0's, with 1 signifying membership in a category under consideration and 0 signifying no membership in that category. This coding scheme is also referred to as binary coding, or indicator variables (Pedhazur et al., 1991).

In this case, a significant positive correlation value derived to reflect the relationship between group and error scores on Wisconsin Card Sorting Test would indicate that a high error score on this test was associated with a subject's membership in the brain-impaired diagnostic group. Assignment to the diagnostic group would have to made on the basis of external, independent criteria, such as neurological evaluation, the results of neuroradiological evaluation, or previous history (Reitan and Wolfson, 1985). The validity coefficient that is derived can be negatively affected by the degree of homogeneity of the sample. This can occur both numerically and conceptually. Numerically, the magnitude of the correlation coefficient decreases as the overall sample becomes more similar in test scores because of the restriction of range. Conceptually, a high validity coefficient may be associated with one particular type of brain impairment, but not with others. This finding is becoming more obvious in cognitively-based neuropsychological studies in memory disorders (Butters, Delis and Lucas, 1995). Validity coefficients can also be affected by gender, level of education, age, socio-economic status and other pertinent variables.

The relation between a validity coefficient and decision theory is important in deciding the significance of the validity coefficient. Decision theory, as applied to tests, is reported to be a mathematical operationalization of the decision-making process. Early models of the theory were based on the net improvement in accuracy over the base rate (the natural frequency of occurrence of a given phenomenon) that one would gain at various levels of validity.

An elaborate alternative to computing a validity coefficient is a research design sometimes referred to as the method of contrasted groups (Anastasi, 1982). The researcher evaluates the results of testing two groups that are assumed to be different on the criterion that is of interest. To elaborate on this issue, persons with no known brain impairment and persons with known brain impairment are both given the Luria-Nebraska Neuropsychological Battery. The scores are then compared by some statistical technique. A traditional method of comparing test performance has been to test for significance of the difference between mean scores for the two groups. Unfortunately, the two groups may contain members whose scores lie in the region of overlapping distributions of the two groups. An alternate and preferred method begins with a use of the statistical technique known as discriminant function analysis. The results of such an analysis produce a linear composite that may be used to demonstrate maximal separation between the two diagnostic groups. The weightings derived from this analysis may then be used to assign the subjects statistically to predicted groups. Predicted group membership is then compared with actual group membership and an accuracy rate, or "hit rate", is then computed. The latter part of this analysis is referred to as classification analysis.

Two important issues need to be kept in mind when these statistical procedures are employed. First, discriminant function analysis identifies those variables that significantly contribute to the function that statistically separates the groups of interest. Classification analysis applies an equation based on those significant variables in order to predict group membership. Optimally, applying the equation to the group on which it was derived should result in a relatively high hit rate. Second, demonstrating a significant hit rate in such a derivation sample is only the first step in determining predictive validity. It is not until the derived equation can significantly predict group membership in a second, or cross-validation sample that predictive validity can be said to have been demonstrated for that set of test procedures (Anastasi, 1982; Franzen, 1989).

While the design described above is considered to be sophisticated in demonstrating validity (Greiffenstein, Baker & Gola, 1994), there are still many sources of contamination (Oakes, 1990). One of the major sources of contamination is sample representativeness. If the procedure being evaluated is intended to have broad applications rather than demonstrate the presence of a particular type of brain impairment, and if the effects of ancillary subject characteristics are to be ruled out, both the diagnostic subgroup of brain impairment and the subgroup characteristic of "normality" ought to be as heterogeneous as possible. To the extent that they are not heterogeneous, the generalizablity of the validating investigation needs to be clearly defined. Additionally, the usual subject matching procedures in the contrasting-groups methodology ought to be observed just as they would be in any clinical research.

Some authors have suggested that the hit rate itself may be contaminated. For example, Willis (1984) demonstrated that the meaning of a given rate of accuracy may be inflated if one does not take into account the prior probabilities of group membership (base rate). Thus, when one is comparing two diagnostic groups, 50% accuracy is not the correct point for chance assignment if prior membership is 70% and 30% for the two groups.

4.2.1.4 Concurrent Validity

Concurrent validity is considered to be a little more complex than is a similar analysis of generated neuropsychological measures. Although neuropsychological tests may be related to other tests that purport to measure similar brain functions, concurrent neurophysiological measures (i.e., a CT or MRI) can also provide a major source of validation. The cost of such validational exercise may be prohibitive even if it is rewarding. Several issues therefore need to be considered when such demonstrations are reviewed. First, what is demonstrated by these methods? Although the CT scan may be accurate in detecting acute subdural haemorrhage, or a MRI an area of infarct of adequate dimension, the CT scan is significantly less accurate in detecting subtle residual subcortical or cortical changes, and the MRI equally inadequate to identify lesions less than half a millimetre in diameter, that may leave an individual profoundly perseverative or memory-impaired (Osborn and Tong, 1996). Thus the individual may look impaired on the neuropsychological test but not on the CT or MRI scan. Thus if one wants to demonstrate the general utility of the neuropsychological measure, a series of behavioural measures may be a more accurate set of criteria.

Second, what is the population to which the measures will be applied? Although severely impaired individuals may be more likely to present classically demonstrable physiological findings, unless such individuals are the intended population, such criterion-validational exercises are likely to be inappropriate because of their limited generalizability. In those cases, it may be necessary to use other forms of criteria (Nunnally, 1978).

Third, how will the test instrument be used in clinical settings? Physiological criteria may be useful for instruments that will be used primarily for diagnostic or localisationist purposes. On the other hand, behavioural measures may be more appropriate instruments that are intended to provide information for intervention programmes or to document the course of recovery (Lezak, 1995).

The foregoing discussion emphasizes that greater numbers of criteria and greater degrees of heterogeneity in the sample used in the validation of an instrument will enhance the clarity with which the utility of a test can be defined. Thus, it appears that in validating an instrument it is important to remember that the identification of the populations, the context, and the questions for which a particular instrument a inappropriate is just as important as the identification of the populations, the context, and the questions for which an instrument is appropriate.

4.2.1.5 Construct Validity

Cronbach and Meehl (1955), who introduced construct validity conceptually, defined this term as that aspect of the validation process that attempts to demonstrate the dimensions or traits that the test was designed to measure. It is now widely recognized that construct validation is an ongoing process and in addition to the demonstration of content and criterion validity, construct validity is developed from exploratory and confirmatory hypothesis-testing of the procedure of interest. The goal of construct validation is to build a nomothetic net or inferential definition of the characteristics that a test seek to measure. In many ways, the process of construct validation returns the investigators to the beginning of the design of the instrument because the relation between the test and its underlying theory is constantly at issue. Thus, no test instrument or procedure should be assumed to be completely finished at the time of introduction. Instead, as the investigation of a technique refines our understanding of that instrument, and knowledge in the area of brain-behaviour relationships grows, the technique itself, if viable, should evolve.

Several common ways to investigate the construct validity of a test exist. The most basic research method is theory testing. By using a theory or a set of alternative theories of brain-behaviour relationships, it is possible to test hypotheses regarding test performance following definable brain injuries. In this way it is expected that the items of a test that tap those functions attributed to the damaged area will show the most frequent failures, and the those items tapping functions not usually attributed to the damaged area will be relatively error-free. At a simpler level, the scores on such a test should vary with the degree of brain compromise or cognitive inefficiency. Therefore, psychiatrically impaired persons, especially those with major psychiatric disorders, might also be expected to show varying degrees of impaired performance on the test (Franzen, 1989; Anderson, 1994; Lezak, 1995).

Serial testing during the recovery stages from brain damage can also provide a useful test of construct validity. For example, oedema is known to cause general widespread impairment (due to diffuse pressure effects) during the first few weeks after brain injury and thus more impaired test performance is expected in the early course of recovery. Improvement in test performances is expected following reduction in oedema following anticipated recovery time lines. In a similar manner, as compensatory skills are taught in rehabilitation programmes or as the individual learns to compensate for the deficits with feedback from the environment, significant changes in some functional areas are seen. In terms of the proposals of Finger and Stein (1982), it is expected that the most severely and directly damaged functions would show deficits more impervious to recovery. An alternate approach to construct validation tends to focus on predictions regarding performance on other tests that are postulated to measure the same traits as the original test or other tests that measure the same underlying traits. With this method it is expected that a measure of a certain cognitive skill would show moderate correlations with measures of general intelligence, little or no relation to a measure of trait anxiety, and a strong correlation with a test purported to measure the same cognitive skill.

Campbell and Fiske (1959) operationalized this design into a model that evaluates a measurement technique in terms of discriminant and convergent validity. The authors propose that discriminant validity is defined by relations with tests assumed to unrelated to the test of interest. Divergent coefficients are expected to be nonsignificant or very low (Nunnally, 1978). Convergent validity, on the other hand, is demonstrated by positive significant correlations with tests assumed to measure the same or similar construct (Campbell and Fiske, 1959). Furthermore, high correlations are expected between two procedures that use the same methodology instead of different methodologies (for example, behavioural observations versus self-report). This method of analysis is usually identified as the multitrait-multimethod matrix (Nunnally, 1978).

In the latter type of analysis, the postulated dimension is measured by a variety of procedures, including the test under consideration, using both the same and different methodologies. At the same time, those methodologies are used to measure a different trait. In this way, traits are crossed with the methods. The intercorrelations among the measures constitute the multitrait-multimethod matrix. The results thought to support the instrument under evaluation include a pattern of positive correlations with other tests measuring the same trait and low to zero correlations with instruments measuring unrelated traits. Several criticisms have been levelled at the multitrait-multimethod designs.

Jackson (1969) argued that the Campbell and Fiske (1959) approach compares individual correlations without examining the overall structure of the relations. This appears to be an important point since the pattern of correlations may be affected by the way in which variance is distributed in measuring the traits under consideration. Jackson (1969) proposed factor analysis of the monomethod matrix as an alternative to obviate these problems. During such an analysis, the correlation matrix is first orthogonalized and submitted to a principal-components analysis, followed by a varimax rotation. The number of factors is set to equal the number of postulated underlying traits. Although Jackson's (1969) suggestions offer some advantages, they may be of limited use in cases in which relations exist among the traits under consideration, as is the case in the neuropsychological assessment of many interrelated cognitive skills. Secondly, when the monomethod matrix is used, the influence of different measurement methods may not be examined. Cole, Hoard and Maxwell (1981) investigated the result of using a mono-operationalization of constructs and reported that the overall effect is to spuriously deflate validity coefficients. Therefore, the two methods of Campbell and Fiske (1959) and Jackson (1969) may be regarded as complementary in nature and thus both need to be applied in any rigorous attempt at construct validation.

Cole (1987) also criticized the multitrait-multimethod matrix in general and suggested an alternative. Some of Cole's (1987) criticisms appear to parallel those made by Jackson (1969). For example, Cole (1987) noted that there are no specific guidelines for the evaluation of the size of the resulting zero-order correlation coefficients. Moreover, the collection of multiple measures of multiple constructs is an endeavour that is extremely expensive and often unattainable in clinical settings so that it is rarely performed. Cole (1987) also noted that the multitrait-multimethod matrix is sensitive to the presence of correlated errors. The errors may be correlated because of a similarity in the time of day at which certain aspects of the assessment are conducted or because of certain criteria of the instruments being administered by the same person.

Thus, Cole (1987) proposed the use of confirmatory factor analysis to analyze the data and investigate discriminant and convergent validity. Confirmatory factor analysis allows for a statistical test of the hypothesis, unlike examination of the multitrait-multimethod matrix, which allows for only a description of the relations among variables. Confirmatory factor analysis can also test for the presence of correlated errors and can control for their effects. Thus the use of confirmatory factor analysis allows the clinical researcher to analyze less costly data sets by allowing the use of monotrait-monomethod data sets (for the evaluation of factorial validity), monotrait-multimethod data sets (for the evaluation of convergent validity), and multitrait-monomethod data sets (for the evaluation of discriminant validity), as well as the analysis of multitrait-multimethod data sets (for the evaluation of both divergent and convergent validity).

The limitations of confirmatory factor analysis are related to its requirements. Firstly, a very large data set is necessary for confirmatory factor analysis. In addition, complete data sets are required for each subject since confirmatory factor analysis does not usually handle missing data. Second, the data set must be multivariate normal, that is, the data sets must have normal distribution patterns (Delis, Cullum, Butters and Cairns, 1988). Failure to meet this requirement will affect the results of the test of significance considerably. Third, the covariance matrix must contain multiple measures of each construct.

Another requirement of confirmatory factor analysis can be seen as a benefit--that is, the factor structure must be specified before analysis and therefore, the researcher must more fully consider the implications of the chosen data analysis before analyzing the data. Exploratory factor analysis provides a way to examine construct validity. The investigator starts from the theory underlying the test or from an alternative theory thought to explain test performance. This type of factoring can be seen to be a rudimentary version of confirmatory factor analysis, as opposed to exploratory factor analysis, which makes relatively few assumptions regarding the underlying structure of a set of data. An example of this method is found in the validation work of the Luria-Nebraska Neuropsychological Battery (LNNB). For this analysis, predictions were made from Luria's (!980) theory regarding the likely number of dimensions that would underlie a given LNNB subscale. These predictions were based on operational definitions of conceptually similar tasks that represented a given component function. Oblique rotations were initially selected because factors were assumed to be interrelated. In many cases, the assumptions forming the theory were confirmed (Golden, Hammeke, Purisch, Berg, Moses, Newlin, Wilkening and Puente, 1982).

Exploratory factor analysis may be used to develop support for conclusions regarding the construct validity of a test. A test composed of a variety of subscales may be reduced to factorially simple dimensions. Once the factors have been identified, a linear-weighted composite (a factor score) may be used to determine the relative contribution of a given factor to the specified test performance. The factorial validity coefficient of a test may then be computed by correlating test scores with a factor score (Anastasi, 1982). For example, if a motor speed factor were identified, the relative contribution of motor speed to test performance could be computed.

Marker variables can also be used in factor-analytic studies of construct validation. A marker variable is usually a descriptive rather than a conceptual measure. Its meaning is relatively better understood than that of the test procedure being evaluated. Age, education, gender and IQ are common marker variables. However, the scores generated by accepted neuropsychological measures may also be included as marker variables. Thus, when reviewing the results of such a factoring procedure, the researcher looks for factors on which the marker variables are significantly loaded (Franzen, 1989). Consideration for the meaning of the marker variables contributes to the understanding of the construct meaning of the tests of interest that also loaded on that factor.

Serial factor analyses with the same sample or across independent samples demonstrate the stability of a test's underlying dimensions across time or across samples. Although temporally stable results may be less desirable for those measures thought to be sensitive to the current neuropsychological status of the individual, the latter method (that of using an independent sample) is highly desirable for those techniques that are not intended to be impairment-specific.

A final method that may used in construct validation is that of examining the homogeneity of a scale (item analysis). On scales that are assumed to measure a general underlying dimension, especially scales that use a sum across items to derive a score, the correlation of individual item scores with the total scale score may be used to identify items that are less likely to be related to the underlying trait. Items whose scores have a low correlation with total scores would be candidates for revision, a method which could improve the overall validity of the homogeneous scale. In another suggestion by Anastasi (1982), this procedure could be applied to the contrasted-groups design in order to evaluate the extent to which the trait is homogeneous across the intended subject pools. Next, the issue of ecological validity will be discussed.

4.2.1.6 Ecological Validity

Ecology, as it relates to applied neuropsychology, refers to the interrelationship between patients/clients and their environments (Acker, 1990). Sbordone (1996) expands on this definition to include the functional and predictive relationship between the patients's performance on a set of neuropsychological tests and the patient's behaviour in a variety of real-world settings. One apparent implication of this definition is that demand characteristics within these various ecological settings are idiosyncratic and fluctuate as a result of their specific nature, purpose and goals. Thus the interface between the demand characteristics within these various settings and the patient's functional cognitive strengths, goals and objectives, premorbid skills and abilities, and biological systems may either compensate for the patient's cognitive and/or behavioural impairments, or exacerbate those impairments, resulting in secondary psychological disorders. Thus, what is further apparent from this definition is that there may be a peculiar interaction of the patient and his environment resulting in a behavioural profile that is usually patient specific, consistent with the cognitively-based approach to neuropsychological assessment (Wilson, 1996). The phenomenon of ecological validity can therefore be argued to be of critical importance in the prediction and explanation of neuropsychological deficits, particularly with reference to recommendations for management or rehabilitative purposes.

Ecological validity may also form an important issue in the documentation of neuropsychological deficits and associated daily difficulties in diagnostic groups undergoing neuropsychological assessment. For example, Lezak (1995) has reported on the characterological difficulties of severe frontal lobe patients, particularly those with closed head injuries. Therefore, documenting such difficulties in specified categories of neurological patients may provide useful collateral data in support for the validity of neuropsychological deficits obtained on appropriate psychological tests.

From the foregoing discussion it can be seen that several issues may affect the meaningfulness of neuropsychological test scores obtained from a group of patients. A related psychometric issue of concern is reliability and this will be discussed next.

4.2.2 Reliability

Reliability refers to the degree of precision of measurements obtained on individuals or groups of people or other entities. An individual's score, performance or product, or behaviour almost always varies in quality from one occasion or specimen to another, even under strictly controlled conditions. The causes of this variation may or may not be related to the purposes of measurement. The subject may try harder, be more alert, have less anxiety, or enjoy better health on one occasion than another. An examinee may have knowledge, understanding or experience that is more pertinent to some questions than others in the domain represented by the test items. Some individuals may exhibit less variation than others, but no examinee is completely self-consistent. Because of this variation and for reasons related to the scoring process, an individual's obtained score or the average obtained score of a group must always be regarded as an approximation, subject to error (Nunnally, 1978; Franzen, 1989).

In classical test theory, the hypothetical average score resulting from many applications of a prescribed measurement procedure is called an individual's true score for that procedure. It is a hypothetical personal parameter, specific to the measurement procedure, and each observed score of an examinee is presumed to estimate this parameter. Under an approach to reliability estimation known as generalizability theory, a comparable concept is referred to as an examinee's universe score. Under item response theory, a closely related concept is called an examinee's ability or trait parameter, though observed scores and these parameters may not be stated in the same units. The hypothetical difference between an examinee's observed score on a particular assessment technique and his/her true or universe score for the prescribed procedure is called measurement error.

Errors of measurement are inconsistent and unpredictable. They are conceptually distinguished from consistent errors which may also affect performance on a group or individual basis. An example of consistent group error is represented by differences in the difficulty of test items which might superficially be perceived as interchangeable. When one test form, X, is known to be uniformly less difficult than another, Y, it is generally expected that an examinee will score higher on the easier form. The differences between Form X scores and Form Y scores are to some extent consistent differences among individuals that arise from the use of a mixture of forms that can be estimated by scaling or equating procedures. The consistent errors that affect some individuals are not so easily overridden as those affecting groups. For example, some examinees experience levels of test anxiety that severely lower cognitive efficiency. The presence of such a condition can sometimes be recognized in an examinee, but the examinee's performance cannot be overcome by statistical adjustment. The individual consistent error is not generally regarded as an element of unreliability. Rather, it constitutes a source of irrelevant variance and thus does not contribute to construct validity (Franzen, 1989).

4.2.2.1 Characteristics and implications of Measurement Error

In general, measurement error reduces the utility of measures. It limits the extent to which assessment results can be generalized beyond the particulars of a specific application of the measurement process. Because the errors are inconsistent and unpredictable, they cannot be removed from the observed scores.

Thus reliability estimates are attempts to measure the proportion of variance that is due to those influences that cause the measured score to deviate from its true score. According to Carmines and Zeller (1979), two different forms of error can lower the reliability of a test. Random errors are those extraneous influences that fluctuate over different occasions. An example of random error in neuropsychological assessment is the influence of the time of day. A patient who is head-injured is likely to be different in the morning than in the afternoon due the effects of fatigue (Lezak, 1995).

Nonrandom error is the result of those influences that systematically affect the observed score. Nonrandom error always raises or lowers the observed score to the same extent. For example, an individual's scores on the Wechsler Adult Intelligence Scale (WAIS-R) may be consistently lower than his or her score on the WAIS. Thus because of nonrandom error, one of these forms may be over- or under-estimating the examinee's IQ.

The concept of reliability poses special problems for neuropsychological assessment instruments. With respect to transient ischaemic attacks in particular, the underlying pathology is often considered to be a resolving lesion, since there is often resolution of the oedema that is a consequence of arterial occlusion (Moore, 1995). Therefore a transient ischaemic attack patient's score on a neuropsychological test is not expected to be stable in the few weeks following the neurological event, thus limiting the use of test scores that are not serially-based. Therefore, the index of reliability must be related to the dynamic nature of the transient ischaemic attack in order for the test to offer an element of reliability. Of course, the important consideration (and apparent contradiction) is that for reliable scores, it is not expected that score values would change in the absence of outside influences.

The information about measurement error includes the identification of the major sources of error, summary statistics bearing on the size of the errors, and the degree of generalizability across alternate forms, scorers, administrations, or other relevant dimensions (Anastasi, 1982). It also includes a description of the examinee population to whom the data apply since they may accurately reflect what is true of one population but not represent what is true of another. For example, a given coefficient derived from a nationally representative population may be significantly higher than the coefficient computed for the same test when it is used with a more homogeneous subpopulation based on one gender, one ethnic group, or one clinical condition.

4.2.2.2 Statistical Methods in Reliability

Generally speaking, reliability is measured by computing some form of a correlation coefficient (usually a Pearson product-moment correlation coefficient) and variances or standard deviations of measurement errors. Traditionally, three broad categories of coefficients have been recognized in the literature.

1) coefficients derived from the administration of parallel forms in separately timed sessions (alternate form coefficients).

2) coefficients obtained by administration of the same instrument on separate occasions (test-retest coefficients).

3) coefficients based on scores based on subsets of the test items, all data accruing from a single administration of the instrument (split-half consistency or internal consistency coefficients).

With the development of generalizability theory, the forgoing three types may now be seen as special cases of a more general classification: generalizability coefficients.

Like traditional reliability coefficients, a generalizability coefficient is defined as the ratio of true score variance to observed score variance. Unlike traditional approaches to reliability study, however, generalizability theory permits the researcher to specify and estimate the various components of true error and observed variance. Estimation is accomplished by the application of the techniques of analysis of variance. Of special interest are the separate numerical estimates of individual components of overall error variance. Such estimates permit identification of those sources that contribute the most error to the measurement process. The generalizability approach also makes possible the estimation of coefficients that apply to a wide variety of potential designs (Franzen, 1989).

Assessments derived from performances or products are especially sensitive to evaluator biases, scorer subjectivity, and intra-examinee factors that cause variation from one performance or product to another. Therefore, the methods of generalizability theory are well suited to the investigation of the reliability of the scores on such measures. Estimates of various error variances indicate the extent to which examinee scores may be generalized to a population of scores and to a domain of products or performances (Nunnally, 1978).

Generalizability coefficients and the many coefficient included under the traditional categories may appear to be interchangeable, but some may convey quite different information from others. A coefficient in any given category may encompass errors of measurement from a highly restricted perspective, a very broad perspective, or some point between these extremes. For example, a coefficient may reflect error due to scorer inconsistencies, but not reflect the variation which characterizes a succession of examinee performances or products. A coefficient may reflect only the internal consistency of items within an instrument and fail to reflect measurement error associated with day to day changes in examinee health efficiency, or motivation (Anderson, 1994).

Thus it should not be inferred that parallel forms or test-retest coefficients based on test administrations several days or weeks apart are always preferable to internal consistency coefficients. An individual's status on some attributes, such as mood or emotional state, may change significantly in a short period of time. In the assessment of such constructs, the multiple measures that give rise to reliability estimates must be obtained within the short period the attribute remains stable. Therefore the characteristics of this kind of internal consistency may be preferred.

Another consideration in the issue of measurement errors is the application of neuropsychological measures in programme effectiveness. One such application germane to the present investigation is the pre-test and post-test evaluations in endarterectomy studies of transient ischaemic attack patients. Average scores of groups, when interpreted as measures of programme effectiveness, involve error factors that are not identical to those that operate at individual level. The positive and negative measurement errors of individuals may average out almost completely in group means. However, the sampling errors associated with the random sampling of persons who are tested for purposes of programme evaluation (for example, carotid endarterectomy), remain. Thus, random variation in the mean achievement of subjects in a programme on neuropsychological tests from year to year may constitute a potent source of error on programme evaluations. Such group variation has little or no bearing on the accuracy of individual rankings within a norm group. Therefore, when an instrument is used to make group judgments, reliability data must bear directly on the interpretations specific to groups. Standard errors appropriate to individual scores are not appropriate measures of the accuracy of inferences about programmes (Anastasi, 1982; Franzen, 1989).

4.2.3 Concluding Comments on Psychometric Issues

From the previous discussion it becomes apparent that the scores on neuropsychological tests offer a primary tool for identifying empirically the behavioural consequences of neurological impairment and thus the derivation and meaning of such score values demand careful scrutiny. Kashden and Franzen (1996) have suggested that while clinical experience and judgment in neuropsychological assessment is obviously useful in such situations, they are not enough. Careful documentation of the test performances of clinical samples need to continue to advance the objective analysis of neuropsychological function. More than that, the continued documentation of subjects without significant socio-medical or psychiatric histories will serve to inform on the base rates of various neuropsychological functions and dysfunctions. Next, the influence of demographic variables on neuropsychological assessment will be discussed.

4.3 Pertinent Demographic Variables and Neuropsychological Assessment

Since the beginnings of time, the influence of certain human variables, called demographic factors, have been known to influence mental functioning. In psychological research, the most important demographic factors have been reported to be age, SES, education and gender (Lezak, 1995). In the present study, an understanding of the influences of these variables on neuropsychological test performance appears to be both appropriate and important. However, since the present study included only male subjects in the final sample (see Chapter 6), the focus of this discussion will be on age, education and SES.

One of the major problems underlying neuropsychological assessment is that psychological tests sensitive to cerebral dysfunctioning also tend to be sensitive to demographic variables (Lezak, 1995). The consistent findings of the influence of age, SES (a complex phenomenon indexed in several ways) and education have impressed the need for test norms to be stratified according to these demographic variables.

4.3.1 Age and Neuropsychological Test Performance

The effects of normal aging on neuropsychological functioning has received much attention in the past 30 years. It has been shown that different abilities change at different rates (La Rue, 1992). General assumptions have been that tasks depending on novel information processing and speed of response tend to show a marked decline with increasing age, for example, reaction time tasks and performance subtests of the Wechsler Intelligence Scales (Bleeker, Bolla-Wilson, Agnew, Meyers, 1988; La Rue, 1992). In contrast these authors note that tasks that rely more on well-established, past accumulated knowledge or language skills have been considered less influenced by age. Heaton, Grant and Matthews (1986) related this distinction to that of Horn and Cattell (1966) who distinguished between crystallized and fluid intelligence. Crystallized intelligence is knowledge and skills acquired in previous learning situations, while fluid intelligence reflects ongoing learning, conceptualizing, and problem-solving in novel situations. These constructs are useful in considering age-related declines in cognitive abilities (La Rue, 1992). Kaufman and Horn (1996) reported that as measured on the Kaufman Adolescent and Adult Intelligence Test (KAIT; Kaufman and Kaufman, 1993), fluid intelligence reaches a peak in development in young adulthood and declines thereafter, at first quite gradually but then more rapidly as age progresses into old age.

The typical way that investigators have studied the influence of age on neuropsychological test performance has been to compare performance on a measure among subjects at different ages. This cross-sectional method obviously has practical advantages, but it may also confound other variables with age. For example, the average educational level of populations in industrialized countries has been rising this century (Thompson, Heaton, Grant and Matthews, 1989). If different age groups are compared on a test performance without considering education, there is the risk of overestimating the effects of aging because the groups are likely to differ on educational background as well. Conversely, if groups are matched in terms of education, the result may be to underestimate aging effects because the older groups are likely to have been of a select sample representing the higher education levels (Benton and Sivan, 1984). Longitudinal studies, on the other hand, are very expensive and time-consuming and generally are quite rare and do not solve all the methodological problems either. Such studies are likely to underestimate age effects because of the selected attrition of less able individuals and practice effects that might obscure a decline in ability (Heaton, Grant and Matthews, 1986). A proposed solution to this difficulty has been the use of cross-sequential or age-cohort designs, which involve testing subjects in different age groups and then retesting them a few years later (Benton and Sivan, 1984).

Studies on the tests comprising the Halstead-Reitan Neuropsychological Battery (HRNB) appear to be foremost in examining age influences on neuropsychological test performance (La Rue, 1992). In a study reported by Heaton, Grant and Matthews (1991), 553 subjects ranging in age from 15 to 81 years were tested on the HRNB in three different laboratories. The participants were grouped in the age categories of 20 to 39 years, 40 to 59 years and 60 years and older. Age was found to account for 20% to 35% of variance in scores on the Category test, Tactual Performance Test and

Trail Making Test. In contrast, only one of the WAIS-R subtests, Digit Symbol, was affected to this extent by age. Further results indicated that fewer elderly subjects were classified as normal than young or middle-age adults, with this effect being more pronounced among poorly educated older individuals. Moehle and Long (1989) reported findings that tended to corroborate the results of Heaton, Grant and Matthews (1986). They reported a linear increase on the HRNB impairment index with age in a medically ill sample with an average of about 12 years of education. The mean impairment index for patients aged 65 years and older was 0.79 compared to 0.39 for 25- to 34 year-olds and 0.56 for 45- to 54 year-olds.

Memory appears to be the most-studied functional ability with respect to age, in the areas of both neuropsychology and cognitive psychology (La Rue, 1992). In fact, the Memory Assessment Scales (Williams, 1991) report the various types of memory scores, correcting for both age and education. However, in the more popularly used Wechsler Memory Scale-Revised (Lezak, 1995), the study of the effect of age on performance has indicated that not all subtests show the same amount of decline with age. For example, Albert, Heller and Milberg (1988), examining optimally healthy and well-educated subjects, found a mean Digit Span Forward score of 7.38 (SD = 0.89) for 30- to 39-year-olds compared to 7.14 (SD = 0,96) for 60- to 69-year-olds and 6.78 (SD = 0.04) for 70- to 80-year-olds.

The assessment of language functions across different age groups is based on the findings that many language functions are well preserved with advancing age (Spar and La Rue, 1990). In using the Boston Naming Test to assess this function, Kaplan, Goodglass and Weintraub (1983) reported that subjects who are 70 years or older have lower mean scores than those in younger age groups, although the magnitude of the age difference varies from study to study (La Rue, 1992). The widespread variation in the language function of naming has prompted the development of norms that are based on age decades (Spreen and Strauss, 1991). One implication of the age decade based norms is that although arbitrary, the norms may reflect cohort experiences of individuals used in the norming exercise.

Another measure of language function as well as an indicator of executive function is the verbal fluency test (or Controlled Oral Word Association Test) (Lezak, 1995). Albert et al. (1988) reported that age effects are generally small in absolute magnitude, but the downward trend is consistently observed with increasing age. When more time is given, more words are reported to be generally produced.

In terms of other specific tests, studies have shown age effects on the Trail Making Test in non-brain-damaged patients waiting for cardiac surgery (Stanton, Jenkins, Savageau, Zyzanski and Aucoin, 1984) and among healthy normals (Stuss, Stethem and Poirer, 1987). From this brief review of the influence of age on neuropsychological test performance, it becomes apparent that several neuropsychological tests show sensitivity to the effects of normal aging as well as "pathological" changes in the cerebral cortex due to abnormal aging processes. Next, the effects of educational achievement on neuropsychological test performance are reviewed.

4.3.2 Educational Achievement and Neuropsychological Test Performance

The relationship between educational achievement and neuropsychological test performance has long been in focus with the initial interest in the Wechsler Intelligence Scales. Since the Wechsler Intelligence Scales often represent the initial tests in neuropsychological assessment (Anderson, 1994), findings regarding the influence of education on test performance indicate a correlation value of 0.64 between Wechsler-Bellevue-Full Scale IQ and education. For the WAIS, Pearson correlations have been reported to be 0.66 for 25-34 year-olds and 0.72 for 45-54-year-olds (Matarazzo, 1972). For the WAIS-R, the reported correlations are 0.63 for 25-44 year-olds and 0.62 for 45-74-year-olds (Matarazzo and Herman, 1984). These high correlations on different versions of the test at different times suggest that it is a very stable finding. Education has in fact been used to determine an expected Full Scale IQ, either by itself or in combination with other demographic variables (Barona, Reynolds and Chastain, 1984; Karzmark, Heaton, Grant and Matthews, 1985).

In the study by Stanton et al. (1984) on the Trail Making Test among non-brain-damaged subjects, a strong relationship between performance on this test and education was obtained, with 50% of subjects with nine years of education or less falling in the impaired range, using the cutoff scores suggested by Russell, Neuringer and Goldstein (1970). Using the same criterion, only seven per cent of those with a college degree or more were classified as impaired.

Seidenberg, Gamache, Beck, Smith, Giordani, Berent, Sackellares and Boll (1984) used multiple regression analyses to consider the effects of various demographic variables on the neuropsychological performances of 288 subjects with seizures. The authors found that in general education was the most influential subject variable. Education was selected as the first predictor variable for 11 Halstead Reitan Neuropsychological Battery measures and was a significant predictor for two others. Moreover, education was the sole demographic variable to account for any significant portion of variance for six measures and accounted for over 12%of the variance of several measures, including the Halstead Impairment Index, Speech-Sounds Perception Test, Category Test, Trail Making Test and the Aphasia Screening Examination. The authors concluded that educational level was most evident on tests involving "linguistic and symbolic processing." (p. 661).

Heaton, Grant and Matthews (1986) investigated education effects on the WAIS-R and the Halstead-Reitan Neuropsychological Battery using a large sample of neurologically normal adults N=553). Significant correlations were found for all the WAIS-R and Halstead-Reitan Neuropsychological Battery measures, but WAIS-R scores showed a higher correlation with education than did Halstead-Reitan Battery scores. Within the Halstead-Reitan Neuropsychological Battery, education tended to correlate most highly with tests of language skills, conceptual ability, and cognitive flexibility (e.g., Trail Making Test, Category Test).

4.3.3 SES, interacting Variables, and Neuropsychological Test Performance

SES is a complex measurement variable but has long been suspected to influence scores of neuropsychological tests. In an effort to investigate the effects, experimenters have opted to measure SES in terms of associated variables--education, income and occupation. Several classification systems have been derived to measure SES based on one or a combination of these variables. However, according to Anderson (1994), little attempt has been made to relate SES per se as a variable in neuropsychological test performance. Instead, the influence of education, and to a lesser extent, occupation, on neuropsychological status, have been studied. Thus it becomes apparent SES as a variable is itself derived on the basis of other demographic factors. Therefore it is logical to assume that while the individual variables of education, income and occupation may be independently explored, more important are the interacting effects of these variables (LaBarge, Edwards and Knesevich, 1986).

Understanding the complexity of the problem of interacting demographic variables can be helpful in appreciating the limitations of studies that address only one demographic variable at a time and this may help explain contradictory results across studies. Since age appears to form the most important group variable in almost all normative studies (Anderson, 1994; Lezak, 1995), this variable will be chosen to demonstrate this principle on a commonly used verbal test, the Boston Naming Test. Normative data for the Boston Naming Test (experimental version) were first provided by Borod, Goodglass and Kaplan (1980). The authors discussed both age and education in the text of their article but did not report correlations between each variable and the Boston Naming Test scores. They provided means and standard deviations as well as cutoff scores for subjects divided into five age groups (under 40, 40-49, 50-59, 60-69, and 70 and over). They did not report mean educational levels for each age group, although they did report the number of subjects falling into each of three education ranges for each age group. The education ranges were 0-8 years, 9-12 years, and 13-16 years.

Two subsequent studies investigated performance on this version of the Boston Naming Test in normals. Nicholas, Obler, Albert and Goodglass (1985) reported means and standard deviations for subjects in four age groups (subjects in their 30s, 50s, 60s and 70s). They provided the mean educational level for each of the four age groups but did not look at the relationship between performance and education. In another study, LaBarge, Edwards and Knesvich (1986) published a study specifically looking at normal elderly subjects' performances on the Boston Naming Test. The study included subjects from age 60 to 85 and divided them into five age groups (60-64, 65-69, 70-74, 75-79, 80-85). The authors reported nonsignificant correlations between education and test performance in their sample of 58 subjects. They reported means and standard deviations for each age group although some age groups had very small subject numbers (e.g., age 60-64, n=3).

The means reported in these studies for comparable age groups and the suggested cutoffs for considering subjects "impaired" were found to be quite different. While the reasons for these findings may be quite diverse and varied, estimating the educational levels in these three studies suggests that in the Nicholas et al. (1985) study the subjects were relatively well educated and had higher scores. Thus, because education level and age are significantly related to performance on the Boston Naming Test, education differences across studies may at least partially explain the discrepant results.

In the Seidenberg et al. (1984) study using a multivariate approach, the authors selected five variables to explore their relationships to test scores: age, sex, education, SES and handedness. The authors had administered the Halstead-Reitan Neuropsychological Battery to 288 subjects, all of whom had some type of seizure disorder. They then performed stepwise regression analyses using the demographic variables as predictor variables and 18 Halstead-Reitan Neuropsychological Battery measures as criterion variables. The total variance accounted for by the demographic variables ranged from 54% for Grip Strength to less than 2% for Tactual Performance Test-Time, a Visuospatial Score, and Sensory-Perceptual errors. Five measures did not have a significant amount of variance accounted for by any of the five predictor variables. Six measures had only one subject variable that accounted for a significant amount of the variance, and in all six cases the predictor variable was education: Tactual Performance Test-Time, Tactual Performance Test-Memory, Tactual Performance Test-Location, Sensory-Perceptual errors-left hand, Speech Sounds Perception Test, and the Halstead-Reitan Impairment Index. The other seven measures were influenced by two or more variables, but no test had a significant relationship to more than three of the subject variables.

Seidenberg et al. (1984) also found only a minimal interrelationship among the predictor variables, with a significant Pearson correlation found only between educational level and SES (r = 0.40). Although the fact that the sample was comprised of seizure patients limits the generalizability of the findings, it is interesting to note that a series of regression analyses using various seizure indices as predictor variables revealed only one significant relationship among all 18 measures (Tactual Performance Test-Location--a measure of nonverbal memory). Other, potentially more serious limitations in the generalizability of the study however, include the fact that the sample was composed primarily of young adults, thereby attenuating the role of aging, and the mean WAIS Full Scale IQ of the sample was only 84. Therefore, this sample was probably not an ideal one for assessing relationships between demographic variables and neuropsychological test performance, but the methodology reflects more sophisticated thinking about how to consider the influence of demographic variables.

Abikoff, Alvir, Hong, Sukohh, Orazio, Solomon and Saravay (1987) took a similar approach, exploring age and education effects with regard to performance on the Logical Memory subtest of the Wechsler Memory scale. Age and education were both significantly related to performance, and there was a tendency for older subjects to have less education (r = -0.26). Examination of the partial correlations revealed that more of the variance in the recall was explained by education than by age. The authors used multiple regression procedures to arrive at predictor equations, which could then be used to compare obtained scores with expected scores.

A similar approach was taken by Karzmark, Heaton, Grant and Matthews (1984; 1985) in using demographic variables to predict Average Impairment Rating (a summary score for Halstead-Reitan Neuropsychological Battery variables; Russell, Neuringer and Goldstein, 1970). Five demographic variables (sex, age, race, education and occupation) were entered into a stepwise multiple regression analysis to predict Average Impairment Rating. Age and education were the most powerful predictors, accounting for 43% and 19% of the variance, respectively, but the regression formula included all five demographic variables. The formula can be used to compute an expected Average Impairment Rating, which can then be compared with the one obtained for a given individual;. Karzmark et al. (1985) also cross-validated a previously derived multiple regression formula based on demographic variables to predict WAIS Full Scale IQ that was developed by Wilson, Rosenbaum, Brown, Rourke, Whitman and Grisell (1978; cited in Seidenberg et al., 1984). The same five predictor variables were used in the formula to predict the Average Impairment Rating. In addition, Barona, Reynolds and Chastain (1984) developed a similar prediction formula based on demographic variables for the WAIS-R Full Scale IQ.

Heaton, Grant and Matthews (1986) investigated the effects of age, education and sex on the WAIS and the Halstead-Reitan Neuropsychological Battery performance, using a well-screened sample of neurologically normal adults. These authors examined the effects of the three variables individually, and also explored possible interactions between age and education. They found significant interactions on a number of measures including WAIS Comprehension, Picture Completion, Block Design, and Picture Arrangement subtests; Halstead-Reitan Impairment Index; Average Impairment Rating; Category Test; Trail Making Test-Part B; Tactual Performance Test-Memory; Tactual Performance Test-Location and Speech-Sounds Perception Test. The authors had hypothesized three possible patterns of age by education interactions: (1) Subjects at higher education levels might show less age-related decline; (2) subjects with the least education might show more age-related decline; (3) older subjects at all education levels might show a regression to the mean.

Plotting the interactions for a few of the variables yielded evidence of all three patterns, depending on which test variables and which end of the age spectrum were being reviewed. For example, of the two summary scores (Halstead-Reitan Impairment Index and Average Impairment Index), pattern (2) appeared to be occurring between the first (<40 years) and the second (40-59 years) age groups, while pattern (3) fitted the subgroup data between the second age level (40-59 years) and the third (60+ years). While not providing specific normative data, this study showed that for subjects with limited educational backgrounds, the standard cutoff scores become inadequate at a younger age than for subjects who have achieved higher educational levels.

The findings of the interactive effects of demographic variables of neuropsychological test performance have stimulated the systematic investigation of such variables in several tests. A similar study was undertaken by Vangel and Lichtenberg (1995) using the Mattis Dementia Rating Scale on cognitively intact and impaired geriatric patients. The ninety cognitively intact subjects had a mean age of 74 years (SD = 5.9) and a mean educational level of 10.5 (SD = 3.6). The 73 younger (79 years and younger) cognitively-impaired age group had a mean age of 72.3 years (SD = 4.0) and a mean educational level of 10.6 years (SD = 3.7). The 17 older (80 years and older) cognitively-impaired group had a mean age of 83.5 years (SD = 2.9) and a mean education of 10.3 years (SD = 3.1).

Pearson and point biserial correlations of demographic measures and Dementia Rating Scale Total (DRS-T) scores for the cognitively intact group were found to be significant for age ($r = -0.28$, $p < 0.01$) and education ($r = 0.24$, $p < 0.05$), such that older participants scored more poorly, and those with more reported years of education scored higher, on the DRS-T. DRS-T was not significantly correlated with race or gender. The authors also reported that both age (t (192.85) = -5.42, $p < 0.001$) and education (t (190.83 = 2.57, $p < 0.05$) were significantly different across impairment rating groups.

A stepwise regression analysis model was generated with the model accounting for 17% of the DRS-T variance (F (85,4) = 3.93, $p < 0.01$). Of the four predictors, only age had significant unique variance in the prediction of DRS-T (r = -0.27; $p < 0.05$). This finding suggests that although both age and education are correlated with DRS-T scores, the relationship of education to the DRS-T can be accounted for in terms of age. In a study on the DRS predating that of Vangel and Lichtenberg (1995), Schmidt, Freidl, Fazekas, Reinhart, Greishofer, Koch, Eber, Schumacher, Polmin and Lechner (1994) reported that performance varied with both age and education in spite of the fact that the mean education was equivalent in the samples of both studies on the DRS. Vangel and Lichtenberg (1995) argued that these disparate findings may be due to cultural differences in the quality of education, or in the opportunities available to those with lower education. These interpretations suggest the possible role of factors beyond the influence of education and may indeed point to the complex web of issues in SES.

4.4 Concluding Comments

This chapter attempts to present the major issues that are implicated in neuropsychological assessment. It becomes apparent from the foregoing discussion that the utilization of objective, actuarial-based tests are subject to several psychometric principles broadly relating to the validity and reliability of these measures. In addition to that, the interpretation of the scores in a manner that relates to the underlying construct of interest, is often subject to the interacting confounds of age, education and the complex web of SES. These issues must therefore be heeded in the interpretation of psychometric tests of neuropsychological function.

Next, a literature review of the studies investigating neuropsychological sequelae in transient ischaemic attacks is presented.

CHAPTER FIVE

Neuropsychological Sequelae of Transient Ischaemic Attacks (TIAs)

5.1 Introduction

A comprehensive literature survey through 1997 yielded numerous articles on cerebral transient ischaemic attacks. Most of these, however, focus on the medical issues associated with this vascular disorder. The selection of articles for this review will therefore be guided by two aspects of the aims stated in Chapter 1. In the first instance, only those studies reporting on the neuropsychological sequelae of transient ischaemic attacks will be reviewed. Secondly, only those studies reporting on those transient ischaemic attacks involving the carotid arterial system will be included in this review.

Studies investigating the neuropsychological effects of transient ischaemic attacks generally employ two major types of research designs. One type involves the examination of those patients who have not undergone any form of vascular surgery, specifically endarterectomy and superior temporal artery-to-middle cerebral artery anastomoses, surgical techniques used to reduce the risk of suffering a full-blown stroke. These studies appear to broadly hypothesize that there are neuropsychological sequelae that persist beyond the resolution of neurological symptoms.

The second type of study involves the assessment of those patients who have undergone vascular surgery in a typical pre-test post-test design. In this type of study, transient ischaemic attack patients are given neuropsychological tests before and after the endarterectomy or superior temporal artery-to-middle cerebral artery anastomosis procedures. The reasoning behind this methodology is that any changes in neuropsychological performances may be attributed to the assumed restoration of brain blood flow, which appears to be the specific purpose of these vascular reconstructive procedures. Additionally, neuropsychological measures have been indirectly used as an outcome index of the efficacy of these surgical interventions.

It would appear that the rationale underlying both types of research design is to show that transient ischaemic attacks are accompanied by neuropsychological deficits which, in turn, are related to interruptions in cerebral blood flow. The studies employing the different research strategies will be reviewed separately since they involve different methodological issues, the critique of which will serve for clarification purposes.

5.2 Studies of Transient Ischaemic Attack Patients who have not undergone Vascular Surgery

A comprehensive survey of the literature, conducted for the period of January 1980 through to 1997, reveals that few studies reporting neuropsychological data fell within this methodological domain. One possible reason for this is that endarterectomy is now considered a routine procedure prescribed for transient ischaemic attack patients who meet certain criteria. The following presentation is based on a chronological review of those studies reporting the neuropsychological findings in those transient ischaemic attack patients who had not undergone vascular surgery.

In one study employing the nonsurgical research design conducted in the state of Ohio, U.S.A, Delaney, Wallace, and Egelko (1980) studied 15 male patients who had suffered transient ischaemic attacks of the carotid distribution. Of these, 12 had left and three had right carotid artery involvement. The patients were free of a history of previous stroke or other neurological insult, revealed no alcohol abuse nor evidence of psychiatric illness, and were all less than 70 years of age. A control group, matched for age, education and an IQ estimate at the time of testing, and without a history of transient ischaemic attacks, was selected from patient relatives, non-neurological patients and hospital workers.

The experimental group (the transient ischaemic attack patients) was given a series of tests within two to five days after the resolution of neurological symptoms. The neuropsychological battery included the Halstead-Reitan Neuropsychological Test Battery, the Wechsler Memory Scale, the Wechsler Adult Intelligence Scale, the Lafayette Grooved Pegboard, the Rennick Visual Search test and the H-Word test of Verbal Fluency. The performance of the transient ischaemic attack group was then compared to the normative data for these tests in an effort to identify deficits in performances. These comparisons revealed significantly poorer experimental group performances on the Wechsler Memory Scale, the Lafayette Grooved Pegboard, the H-Word test of Verbal Fluency, as well as on the Trail Making Test (Forms A and B), the Category, and the Tactual Performance Tests of the Halstead-Reitan Neuropsychological Battery. These tests, which revealed significant differences when compared to the norms, were then administered to the control group for further comparisons.

The transient ischaemic attack group revealed a significantly poorer performance than the control group on the overall computed Halstead-Reitan Impairment Index ($t = 4{,}55$, $p \leq 0.001$), which was computed on the basis of all the tests administered. Although individual statistical tests of differences were not performed on each of the tests, the mean scores of the experimental group were consistently lower than the control group and thereby interpreted as showing a deficient performance.

Although the study by Delaney et al. (1980) yields important information, suggesting impaired general memory performances, poor motor dexterity, lowered verbal performances and poor planning among transient ischaemic attack patients, several methodological shortcomings become apparent. One of the main features of the transient ischaemic attack is the resolution time of neurological symptoms. This study reports that all of the patients had recovered completely from their neurological symptoms within 24 hours, but neither individual nor average resolution times were reported. A correlation of resolution time with neuropsychological performance would have provided a better understanding of the underlying dynamics of transient ischaemic attacks and their sequelae. Treating the resolution time of 20 minutes and that of 20 hours homogeneously, which is quite acceptable according to the definition of transient ischaemic attacks, gives the erroneous impression that the underlying pathology and outcome of all these patients may be similar.

The finding that the transient ischaemic attack group had a significantly poorer Halstead-Reitan Impairment Index than the controls may be subject to interpretations alternate to those proposed in the study. Although no tests of significance of difference were performed on the pairs of scores (experimental versus control), it is possible that individual tests could have had variable contributions to the overall Impairment Index. Analyzing individual pairs of means (experimental versus control) could help delineate the individual contributions of tests, as well as suggest the comparative level of performance of the different domains of functions being measured. This latter analysis would also contribute to our knowledge regarding the differential recovery of functions after such episodes of cerebral ischaemic attacks. Some literature suggesting such variability in the recovery of neuropsychological function has been reported. For example. Finlayson (1990) and Tupper (1991) reported that problem-solving ability showed the poorest recovery among a group of stroke patients tested one to twelve months after the episode.

In addition, research suggests that there are several non-neurological factors which may influence performance on neuropsychological tests. For example, Martin and Franzen (1989) found in their study on normal subjects that even under mild levels of anxiety, neuropsychological test performance declined. In the study by Delaney et al. (1980), no attempt was made report on the possible effects of anxiety on neuropsychological test performance, and it is likely that among subjects who are assessed within five days of symptom resolution, anxiety among patients may persist thereby forming an extraneous variable in this study. Thus, it is possible that optimal performances, as is often assumed in neuropsychological testing, were not elicited in the experimental group. It is therefore also difficult to ascertain to what extent the poorer performances of the experimental group were due to psychological reactions to the ischaemic event, or to the attack itself and its underlying neuropathological processes. Thus an analysis of the interaction of these variables may provide some answers to the effects of transient ischaemic attacks on neuropsychological functioning.

Dull, Brown, Adams, Shatz, Diaz and Ausman (1982) reported the neuropsychological test profiles of a sample of ischaemic stroke patients drawn from a population of cerebrovascular patients at a clinic in Michigan, U.S.A. Dull et al. (1982) studied the pre-operative neuropsychological performance of subgroups of transient ischaemic attack, reversible ischaemic neurologic deficit (RIND), and stroke patients who were being prepared for varying types of vascular surgery. These subgroups were defined on a temporal basis of symptom presentation of less than 24 hours, between one and seven days, and longer than seven days, respectively.

Individual neuropsychological scores and Average Impairment Ratings were computed from the administration of the following tests: Grip test, Rennick's Visual Search, H Words, the Grooved Pegboard, the Digit Symbol subtest of the Wechsler Adult Intelligence Scale, Seashore Rhythm Test, Speech-Sounds Perception Test, the Finger Tapping Test and the Trail Making Test (Part B).

A one-way analysis of variance comparing the Impairment Ratings of the transient ischaemic attack, reversible ischaemic neurologic deficit and stroke groups revealed a significant difference ($F\ (2,37) = 20.17,\ p \leq 0.01$), with the performance ratings of the former two groups indistinguishable from each other. The authors used this statistical finding to collapse the transient ischaemic attack and reversible ischaemic neurological deficit groups into a single category called the less impaired ischaemic group for further analyses.

The patients in this study were then categorized according to the type of surgery that would be performed on them. Four groups were thus derived--14 patients in the superior temporal artery-to-middle cerebral artery bypass, 18 in the carotid endarterectomy, eight in the posterior fossa surgery group, and 18 transient ischaemic attack and reversible ischaemic neurologic deficit patients who did not undergo any surgery. These groups were reportedly comparable in terms of age, education and premorbid IQ, A four-way analysis of variance revealed no significant differences in the Average Impairment Ratings of the four groups.

However, individual t-test comparisons revealed that the value of the Average Impairment Index of the superior temporal artery-to-middle cerebral artery group was significantly poorer than that of the carotid endarterectomy group ($t\ (30) = 2.07,\ p \leq 0.05$). On the other hand, the posterior fossa group did not perform significantly different from the combined superior temporal artery-to-middle cerebral artery and carotid endarterectomy groups.

The Dull et al. (1982) study yields an important finding in that neuropsychological performance was found to be directly related to the duration of the longest ischemic attack. Thus, an important implication for transient ischaemic attacks is that the duration of neurological symptom presentation is an important variable that warrants investigation with respect to its relationship to neuropsychological performance. However, the obvious methodological issue that emerges from an analysis of this study is that an inadequate sample size has been investigated, particularly in view of the multiplicity of subgroups defined at various stages of analysis. For example, it is not clear how many subjects were transient ischaemic attack and reversible ischaemic neurologic deficit patients, respectively. It may well be that the lack of appropriate subgroup sizes in statistical analyses resulted in spuriously significant differences (Kirk, 1982).

It is surprising also to find that there is no discrimination between left and right hemisphere involvement patients in statistical analyses. The authors note that of the 18 patients who were classified as carotid endarterectomy patients, seven had bilateral, six right-, and five left- hemisphere involvement. All these patients were treated homogeneously in analyses which could possibly explain the failure of the transient ischaemic attack-reversible ischaemic neurologic deficit difference reaching statistical significance.

Coupled with this issue is the tendency to analyze the neuropsychological data in terms of overall performances as indicated in the Average Impairment Ratings rather than individual test comparisons. While such values are useful in conveying general neuropsychological status

(Hom, 1991), analysis of individual subtest or test performances may yield data concerning specific abilities, for example, abstract reasoning (Lezak, 1995; Walsh, 1987).

Despite the methodological issues related to the derivation of experimental groups and data analyses, some important findings are nevertheless forthcoming in this study. Neurobehavioural summary scores correlated strongly with the duration of the ischaemic episode. For example, stroke patients (who presumably had the longest ischaemic duration) had scores in the moderately impaired range, with transient ischaemic attack and reversible ischaemic neurological deficit patients usually showing only mild neuropsychological impairment. Also, patients with cerebral infarction had longer lasting symptoms than those with transient ischaemia. Thus, the study underscores the importance of estimating the duration of symptom presentation in studies of cerebral transient ischaemic attacks.

Bornstein (1983) investigated the relationship of age and education to neuropsychological performance in a sample of patients who were to undergo carotid endarterectomy following transient ischaemic attacks at a stroke clinic in Ohio, U.S.A. Thirty eight male and 17 female patients with an overall mean education level of 10.1 years and a mean age of 62.2 years were included in the study sample. At the time of assessment, 25 were alleged to have presented with transient ischaemic attacks while 30 had suffered completed strokes.

The neuropsychological battery employed in this study comprised the Wechsler Adult Intelligence Scale, the Halstead-Reitan Neuropsychological Battery, the Wide Range Achievement Test, the Wechsler Memory Scale, Grip Strength, the Knox Cube Test, several subtests of the Klove-Matthews Motor Steadiness Battery and the Reitan-Klove Sensory

Perceptual Examination. All subjects were given the neuropsychological battery one to two days prior to surgery.

With respect to intellectual-academic measures, statistical analyses revealed significant positive relationships between age and Performance IQ ($r = 0.34$, $p \leq 0.05$) and the Picture Completion subtest ($r = 0.22$, $p \leq 0.05$) of the WAIS. Significant correlations were found between education and all the intellectual-academic tests and subtests (with the exception of the Block Design, Object Assembly, Visual Reproduction and Associate Learning subtests).

Bornstein (1983) noted that no significant correlations were obtained between age and performance on most neuropsychological tests. Significant correlation values were however obtained between age and right Tactual Performance ($r = 0.32$, $p \leq 0.01$), left Grooved Pegboard ($r = -0.23$, $p \leq 0.05$) and right Static Steadiness ($r = 0.29$, $p \leq 0.01$) performances. The negative findings with respect to the left Grooved Pegboard performances suggest a decrease in this test of motor dexterity with increasing age.

The findings of this study are difficult to interpret with respect to the neuropsychological sequelae of transient ischaemic attacks since the stroke and transient ischaemic attack groups were collapsed in statistical analyses. However, the differential relationship of demographic variables such as age and education with performance on certain neuropsychological tests among cerebrovascular disease patients is highlighted as an important source of variability of test scores. In addition, it becomes apparent from this study that not all neuropsychological test scores are influenced by age. This finding may reflect the differential rate of deterioration in the domains of behaviour and therefore underscores the need for systematic analyses of the relationship between age and neuropsychological test performances in different groups of neurological patients. Such analyses may serve to provide information on the role of age in neuropsychological test performances in the presence of varying types of neurological disease, and in the case of the present investigation, transient ischaemic attacks.

Soelberg-Serensen, Marquardsen, Pedersen and Heltberg (1989) studied a mixed group of 201 reversible ischaemic attack subjects, comprising subgroups of 147 transient ischaemic attack and 54 reversible ischaemic neurologic deficit patients at a cerebrovascular clinic in Sweden. The subjects were selected from a four-year span, and detailed histories with respect to the risk of stroke, episodes of myocardial infarction, as well as incidence of hypertension and diabetes mellitus were obtained.

On the basis of an interview it was determined that in the group as a whole psychomotor slowing, general asthenia, fatigue, emotional instability, depression or anxiety, an increased need for sleep and impaired memory were common complaints. The authors reported that these complaints were reported more commonly among patients who had suffered a stroke during the study period, and in 50 per cent of those who had suffered only a reversible ischaemic attack.

The importance of this study relates to the findings with regard to age and the medical risk factors of hypertension and diabetes in cerebrovascular diseases. The findings of the report suggest that patients below 60 years of age may be less likely to suffer strokes related to hypertension and diabetes mellitus. In addition, the study highlights the importance of subjectively reported symptoms which raises the question of whether these symptoms are neuropsychological sequelae per se or reactions to the cerebrovascular disease. Whichever of these explanations is more tenable, it appears that these sequelae may form part of the complex of neuropsychological symptoms post-stroke. Furthermore, the prevalence of these symptoms raises the additional possibility of their potential influence on neuropsychological test performances.

One major shortcoming of this study is that the authors have treated all patients with a symptom resolution period up to seventy-two hours homogeneously. In effect, a broadened resolution period for defining transient ischaemic attacks appears to have been adopted without any apparent motivation. Furthermore, despite the known cerebral variations in carotid and vertebrobasilar distributions, patients with these differing vascular involvements were treated as a single group. Several authorities (Lishman, 1987; Bigler, Yeo and Turkheimer, 1988) suggest that the functional anterior-posterior organization of human brain has important implications for neuropsychological assessment. It is difficult to ascertain the relative contributions of this vascular dichotomy to the overall performances of this study group.

Also, there is no attempt to differentiate between left and right hemisphere patients despite the evidence of the asymmetrical functioning of the brain (Puente and McCaffrey, 1992; Lezak, 1995). Thus, this study fails to adhere to accepted diagnostic guidelines for transient ischaemic attacks, and issues relating to the distribution of psychological functions within the brain. Despite these limitations, the findings in this study make an important contribution in isolating hypertension as an important variable in the study of neuropsychological functioning in patients who have suffered transient ischaemic attacks. In addition, sex appears to form an important variable and the interaction of sex and age appears to be a worthwhile research question among transient ischaemic attack patients.

Bradvik, Sonesson and Holtas (1989) studied the neuropsychological functioning of right hemisphere transient ischaemic attack in Swedish patients who showed no evidence of carotid artery stenosis. A four-group design was employed in which samples of transient ischaemic attack, house painters and liver cirrhosis patients formed the experimental subjects, and a fourth group of healthy subjects comprised the controls. The transient ischaemic attack group was comprised of two men and eight women who had suffered one to four episodes of right hemisphere transient ischaemic attack. The mean age of this group was 62 years (range of 42 to 70 years) and they were all right handed without a history of previous cerebral dysfunction. Eight patients were found to have middle cerebral artery involvement on the basis of clinical presentation, while the authors were undecided on whether the remaining two candidates had carotid and/or vertebrobasilar artery involvement. The neurological examination was performed an average of 3.5 months after the last ischaemic event. The electroencephalogram was found to be normal in all subjects while the computed tomogram findings were also reported to be normal in four subjects, with the exception of one patient who revealed a widening of the right parietal sulcus. The computed tomogram findings of the remaining subjects in this group were not reported. Neuropsychological testing was performed an average of 14 months (range of 2 to 44 months) following the most recent transient ischaemic attack.

Ten house painters, who were matched with the transient ischaemic attack group for age and education were randomly selected from a group of house painters with or without symptoms of toxic encephalopathy. These subjects were reported to have no other central nervous system disorders. Ten patients with biopsy-verified cirrhosis (five cases of which were of alcohol origin), were randomly selected from a clinic. At the time of the neuropsychological testing, it was reported that all these subjects were in a stable condition.

Ten volunteer subjects (five men and five women) constituted the control group. None of these subjects had a history nor clinical findings indicating central nervous system dysfunction or arterial vascular disease and all were reported to have normal electroencephalogram recordings and computed tomogram scans.

Eight neuropsychological tests (constituting the battery) were administered to all the subjects in this study. The eight neuropsychological tests were reported to measure four psychological dimensions. Two tests measured verbal performance--a Swedish standard verbal intelligence scale and the Cronholm-Molander Paired Associates test measuring verbal short-term memory. Three tests were used to measure speed of perceptual and logical processing and/or reviewing ability and flexibility--these being a Swedish test for perceptual speed, the WAIS Digit Symbol subtest and a modified version of the Reitan Trail Making Test. Spatial ability was measured using the Block Design from the WAIS, the Graham-Kendall Memory-for-Designs (MFD) test and the Benton Visual Retention Test (BVRT). In addition, mean simple serial reaction times were recorded in response to a small light flashed at irregular intervals of 16 times per minute for ten minutes. Intraindividual analysis of the transient ischaemic attack group indicated that the verbal intellectual scores were within or above average in nine of the patients, with one patient scoring below average. Speed of perceptual processing was reported to be disturbed (i.e., the scores on the relevant tests were found to be below the reference norms) for five subjects. Spatial ability was reported to be impaired in eight patients, with three subjects showing disturbance of spatial organization and visual construction and seven patients evidencing impaired spatial learning and memory.

The authors summarized the intergroup analysis using the ANOVA and Duncan's post-hoc comparisons test. Transient ischaemic attack patients and painters performed significantly better than cirrhotic patients on the verbal intelligence scale, while the control and transient ischaemic attack groups performed significantly better than the painters on the verbal short-term memory scale.

With respect to the perceptual tests, the performances of the control and the transient ischaemic attack patients test were found to be significantly better than the painters only on the Digit Symbol Test. On the spatial tests, the controls and the painters scored significantly better than the cirrhotic group on the Block Design, while the controls performed significantly better than the transient ischaemic attack and cirrhotic group on the number of correct reproductions on the Benton Visual Retention Test and the Memory-for-Designs test.

The findings that the mean scores of the transient ischaemic attack group were significantly lower than the controls on the Benton Visual Retention and Memory-for-Designs Tests were interpreted as indicating visuospatial dysfunction. However, no explanation for the insignificant differences in the spatial test scores between the transient ischaemic attack and cirrhotic patients are advanced by the authors. It is also interesting to note that the transient ischaemic attack and control groups did not differ on the Digit Symbol Test and serial reaction time performances. These findings suggest that not only do right hemisphere transient ischaemic attack patients suffer speed processing deficits related to spatial tasks, but such deficits are also demonstrable in patients with liver cirrhosis--a condition with no apparent cerebrovascular involvement but systemic changes in the chemistry of blood.

One shortcoming of the study by Bradvik et al. (1989) is that too few subjects were studied in each group, thus constraining generalizability of the findings. In addition, F values were not reported for the ANOVA computation, making reported statistical findings difficult to interpret. However, an important contribution of this study is the finding that even in the absence of significant carotid stenosis, impairment in circumscribed areas of neuropsychological functioning may be found.

In a subsequent study by the same group, Bradvik, Dravins, Holtas, Rosen, and Ingvar (1990) studied a mixed neurological group of Swedish patients (experimentals) which included a sample of transient ischaemic attack subjects with respect to their ability to process the prosodic qualities of speech. Fourteen subjects with a mean age of 53.9 years (range of 28 to 69 years) formed the group that showed computed tomogram evidence of a right hemisphere infarct. All of these patients were assessed an average of 14.4. months after their initial neurological examination which yielded the diagnosis of a right cerebral infarct, and these patients presented with varying neurological deficits at the time of neuropsychological assessment.

The transient ischaemic attack group was comprised of seven subjects with a mean age of 61.4 years (range of 41 to 70 years). The interval between the initial neurological diagnosis and the neuropsychological assessment was 5.5. months (range of 3 to 17 months). These patients were reported to have a history of one to three ischaemic attacks with uniform transient symptoms related to the right hemisphere. None of these subjects were reported to show haemodynamically significant stenosis (determined through angiography) in any of the cerebral blood vessels. The subjects in the transient ischaemic attack group were free of any persisting neurologic deficit and all had reported a clear right handedness bias on a modified version of the Edinburgh Handedness Inventory.

The authors reported that twenty-one subjects (thirteen male and eight female), matched with the experimentals for age at the time of neuropsychological testing, were drawn from the population register in correspondence to each patient in the infarct and transient ischaemic attack groups to comprise the control group. None of the control subjects had a history of cerebral dysfunction.

Three tests, adapted for the Swedish language, were administered to the subjects to measure the ability to perceive and express prosodic qualities of speech. The first part measured the ability to perceive and identify pairs of lexical and syntactic items distinguished by prosodic cues. In the second part of the test, the ability to perceive emotional qualities of speech was measured. The third part of the test measured voice quality and the ability to produce and express prosodic qualities of speech.

The mean values on each of the three tests were reported for each of the infarct, transient ischaemic attack and normal groups. On the basis of a multivariate test of significance, for which no specific F values were reported, no differences between the three groups on any of the three measures were reported.

The authors interpreted the failure to find significant differences between the groups on the tests of prosody as suggesting that their tests may not have been sensitive enough to detect prosodic difficulties, particularly in the transient ischaemic attack and infarct groups. It is important to note that aprosodia has not formed a dependent variable in previous studies on transient ischaemic attack patients. The focus on this variable appears to derive from studies on stroke patients (Gordon, Hibbard, Egelko, Diller, Shaver, Lieberman and Ragnarsson, 1985) which reported that right hemisphere lesions resulted in different specific types of aprosody which depended on the location of the lesion within the right hemisphere.

The study by Bradvik et al. (1990), despite reporting no significant differences among the study groups, reveals several confounding variables which could account for the findings. Firstly, the timing of the assessment appears to form an important variable in this study. Two transient ischaemic attack subjects were administered the tests of aprosodia within three days after the ischaemic attack, while others in this group were evaluated after seven months. This factor regarding the timing of assessment invokes the possible role of an additional variable related to the recovery of function after cerebral ischaemia. On the basis of the data provided, it is impossible to determine to what extent the timing of assessment influenced the overall performances since such analyses are lacking in this study.

In addition, the transient ischaemic attack group included subjects with a varying number of transient ischaemic attacks, ranging from one to three. It is likely that those subjects who had three transient ischaemic attacks would suffer more lasting symptoms as opposed to those with a history of one transient ischaemic attack. An important contribution of this study is nevertheless found in its focus on a specific area of neuropsychological functioning, i.e., the prosody of language. The study is also based on studies suggesting the anatomical localization of this function in the right hemisphere (Ross, 1988). In adopting this view, the study seems to suggest that analyzing test performances relating to specific domains of behaviour (rather than global neuropsychological ratings based on batteries) may be more productive with regard to investigations on neuropsychological tests after a transient ischaemic attack.

5.2.1 Evaluation and Concluding Comments on Studies using Transient Ischaemic Attack Patients who have not undergone Vascular Surgery

An overall evaluation of the studies reviewed in the preceding section will be presented. The major rationale underlying the use of patients who have not undergone endarterectomy or superior temporal artery-to-middle cerebral artery anastomosis is to investigate whether these individuals suffer lasting neuropsychological impairments related to the disruption of blood supply.

Several methodological inconsistencies, peculiar to this research paradigm, make comparability of the results of the studies difficult. Firstly, there appears to be no consistency in the timing of the neuropsychological assessments. For example, in their study, Delaney et al. (1983) administered the neuropsychological test battery within five days following the resolution of neurological symptoms. Dull et al. (1982) do not report the timing of their neuropsychological assessments, while Soelberg-Serensen et al. (1989) selected a sample from a four-year span of patients. Bradvik et al. (1989) on the other hand, use a assessment timing period of three to seventeen months. Apart from making comparability of findings difficult, this methodological shortcoming is in violation of two significant findings in the neuropsychological literature.

The one relates to the reported differential recovery rates of neuropsychological functioning in the different domains of behaviour, which in turn may be related to the time taken for the remission of neurological symptoms in transient ischaemic attacks. The single most important criterion for the diagnosis of transient ischaemic attacks is the time taken for the remission of neurological symptoms. It would seem appropriate to investigate the relationship between the time taken for the resolution of neurological symptoms of transient ischaemic attacks and neuropsychological performance on various tests.

Damasio (1991) noted that aphasia, for example, presents in different levels of severity, as well as different forms from the time of the cerebrovascular insult. Reitan and Wolfson (1993) reported that the recovery of visuo-spatial and motor functions follow a differential path, each reaching a plateau at varying points on the recovery curve. Thus, neuropsychological performance one week after the onset of the cerebrovascular disease may be different from that occurring six months or a year later. It becomes obvious that the samples used in the different studies reflected differing levels of recovery following the onset of the transient ischaemic attack.

The second issue relating to the timing of the assessment is the finding that psychological reactions to the cerebral dysfunctioning may influence performance on neuropsychological tests. As stated previously, Martin and Franzen (1989) reported that mild levels of anxiety were associated with significantly lowered performances on certain tests. The tests reported to be susceptible to the influence of anxiety in their study included the Randt Memory Scale (Acquisition, Recall and Overall Index measures) and the Knox Cube Tapping Test (specifically the index of Knox Surprise Misses).

Newman and Silverstein (1987) reported that depression, which may co-exist with anxiety in the early post-stroke phase, is correlated with a failure to resume premorbid social activities. Depression has been related to motivation which, in turn, has been shown to influence performance on neuropsychological tests (Golden, 1981; Lezak, 1995). Also, it is difficult to establish whether any of the patient samples in any of the studies reviewed were receiving any form of therapy. This confounds decisions regarding the relative contributions of spontaneous recovery and therapy to overall recovery as measured on neuropsychological tests (Meier and Strauman, 1991).

Thus, it becomes obvious that there is a lack of uniformity regarding the timing of the neuropsychological assessment, neither is there any apparent underlying rationale for adopting a particular time schedule for assessment. Findings have not been linked to the time-frame within which the assessments were conducted.

Second, there appear to be inconsistencies in the neuropsychological test batteries employed in the various studies. Delaney et al. (1980) base their findings on the Halstead-Reitan Impairment Index, using the Wechsler Adult Intelligence Scale score to control for IQ, while the battery of Dull et al. (1982) comprised only some of the (unspecified) tests of the Halstead-Reitan Battery. Under such varying test conditions, the meaning and implications of such neuropsychological findings become even less clear when they are considered in the light of other variables such as the timing of assessment.

Related to the issue of test battery composition is the matter of data treatment in the analysis of group differences. Statistical analysis appears to be limited to the level of comparing overall performances reflected in the Impairment Index (Delaney et al., 1980; Dull et al., 1982). The result of such data analyses is that variations on individual test performances do not become apparent. Several authors (Lezak, 1995; Walsh, 1987; Bigler et al., 1988) note that individual test performance analyses reflect functioning in different ability areas. For example, performances on the Trail Making Test (Part B) are purported to reflect planning, mental flexibility and visuomotor speed. Thus, statistical analyses on overall impairment index scores should be supplemented by those performed on individual tests to reveal trends in different skill areas.

In addition to methodological inconsistencies, an obvious shortcoming in the design of the studies reviewed is the conceptualisation and broad treatment of data. Careful documentation of the features of transient ischaemic attacks relating in particular the arterial territory and hemispheric involvement, as well as resolution time, is required. Furthermore, documentation of the underlying aetiology of the transient ischaemic attack may assist in partialling out the effects of risk factors such as hypertension, diabetes, stenosis and cardiac-related problems. This may provide a basis for the prediction of neuropsychological outcome which appears to be the major aim of studies falling under this research paradigm.

Despite the methodological difficulties associated with neuropsychological studies on transient ischaemic attack patients who have not undergone vascular surgery, several important findings have been derived from these investigations. The cumulative findings suggest that there may be persisting memory difficulties, poor fine motor skills, impaired verbal and planning abilities in the first week after the resolution of neurological symptoms in this group of patients (Delaney et al., 1980). The importance of relating neuropsychological test performance to the duration of the ischaemic attack was suggested by the findings of the Dull et al. (1982), study supporting the view that neuropsychological abilities may have varying levels of recovery after a cerebral transient ischaemic attack.

The role of varying rates of recovery also appears to be suggested in the study of Soelberg-Serensen et al. (1989) who reported that several difficulties relating to psychomotor slowing, emotional stability and impaired memory may persist up to four years after the transient ischaemic attack. The Soelberg-Serensen et al. (1989) report was also important in suggesting the differential role of diabetes and hypertension in male and female transient ischaemic attack patients.

The role of demographic variables in neuropsychological test performance has been highlighted in some studies. For example, Bornstein's (1983) report suggests that age and education may have a differential relationship with performance on neuropsychological tests. The Bradvik et al. (1989; 1990) studies suggested that cerebral laterality forms an important independent variable in further investigations on transient ischaemic attack patients. They also found that speed of information processing was compromised in these subjects.

Next, studies comparing the pre- and post-test neuropsychological performances of patients who have undergone carotid endarterectomy and superior temporal artery-to-middle cerebral artery anastomosis types of surgeries will be reviewed.

5.3 Pre- and Post-Test Endarterectomy and Superior Temporal Artery-to-Middle Cerebral Artery Anastomosis Studies of Transient Ischaemic Attack Patients

The literature search for the period January 1980 to 1997 yielded several studies reporting the neuropsychological sequelae of transient ischaemic attack patients undergoing surgery. These studies were conducted on patients who had undergone vascular reconstructive surgery (superior temporal artery-to-middle cerebral artery anastomosis) or carotid endarterectomy. The major thrust of the studies appear to relate changes in neuropsychological performance to the surgical restoration of adequate cerebral blood flow. This line of research has been appealing because, with the greater deployment of these surgical techniques in the treatment of transient ischaemic attack patients, it is presumed that there will be a concomitant increase in associated neuropsychological studies. For the purposes of this review, only those superior temporal artery-to-middle cerebral artery anastomosis and carotid endarterectomy studies reporting neuropsychological sequelae will be considered. For the additional purpose of gaining some impression on the direction of research using this methodological process, these studies will be presented in chronological order.

Hemmingsen, Mejsholm, Boysen and Engell (1982) administered neuropsychological tests to 25 Danish patients (8 women and seventeen men) who underwent carotid endarterectomy surgery for internal carotid artery stenosis. The 13 right hemisphere patients were comprised of seven transient ischaemic attack, one syncope, three transient ischaemic attack and subsequent stroke, and two minor stroke disorders. The 12 left hemisphere patient group consisted of six transient ischaemic attack, two transient ischaemic attack and stroke, and four minor stroke subjects. Neuropsychological testing was performed one week before surgery, and repeated at one to two weeks, as well as eight months, post-operatively.

The authors described their neuropsychological test battery to include the Word Pairs, Story Recall and Visual Gestalts tests (learning and memory), Facial Recognition, the Trail Making test (Forms A and B), the Word Fluency and Digit Span tests (perception and attention), and the Similarities and Block Design subtests of the Wechsler Adult Intelligence Scale. The results revealed that the mean values on all tests for the entire group were below the appropriate norms, although the significance of these differences were not indicated. At one to two weeks post-operatively, there was reportedly a statistical worsening of performances on Word Pairs (reproduction), Visual Gestalts (reproduction) and Story Recall. At eight months post-operatively, performance improved on all tests compared to pre-operative levels although only the difference in scores on Story Recall, Visual Gestalts, Digit Span, Similarities and Block Design tests reached statistical significance. Again, no significance levels were reported.

The transient ischaemic attack group showed a significantly greater improvement on Visual Gestalt (reproduction), Block Design and Story Recall when compared to the minor stroke group at eight months, post-operatively. The left hemisphere group showed significant improvement in mean test values on the Word Pairs, Trail Making (Part B) and Story Recall tests. The right hemisphere group showed statistically significant post-operative values on the Visual Gestalts, Block Design and Digit Span tests. These results suggest that improvement in neuropsychological functioning is related to the side of surgical intervention. The findings in this study are important in documenting the changes in several dimensions of neuropsychological functioning. However, the effect of certain extraneous variables on neuropsychological test performances remain unaccounted for in this study. For example, nearly one-third of the sample was made up of females. No attempt has been made to separate the effects of sex on neuropsychological test performance, a phenomenon that is well documented (Matthews, 1992). Since research evidence suggests that females are less lateralized than males regarding the cerebral organization of psychological functions, it is possible that the homogeneous treatment of the group in terms of sex may account for the failure of certain test scores to reach significance, for example, test of Facial Recognition (Matthews, 1992).

Another factor confounding the findings is the treatment of lateralized patients with differing diagnostic labels homogeneously. For example, the right hemisphere group consisted of transient ischaemic attack, syncope, as well as minor stroke patients. Cerebrovascular diseases entail varying neuropathological processes which may differentially affect neuropsychological processes. Thus, treating the subjects with varying types and severity of cerebrovascular disorders as a single group limit the findings of the study with respect to lateralized effects on a broad group of such disorders.

Parker, Granberg, Nichols, Jones and Hewett (1983) studied the effects of symptomatic carotid artery disease on neuropsychological performance in a sample of White American patients in Denver, Colorado, U. S. A. Fifty-one male and two female patients were divided into three study groups. Twenty patients comprised the carotid endarterectomy group who received surgical intervention. Sixteen patients who showed evidence of symptomatic artery disease but either declined or did not form candidates for surgery comprised the second group. Seventeen patients comprised a third group of general surgical controls who had surgery described as being unrelated to cerebral functioning, although the specific surgery type was not specified. The groups did not differ significantly in age or educational level. The carotid artery group who underwent endarterectomy was reportedly not significantly different from the group that did not have this surgical procedure on Full Scale Wechsler Adult Intelligence Scale Scores, although no statistical values were reported.

Both carotid artery disease groups were comparable in terms of percentage of individuals exhibiting severe carotid artery stenosis, and with the lateralized representation of this phenomenon. All groups were given the Halstead-Reitan Neuropsychological Battery, the Wechsler Adult Intelligence Scale, the Wechsler Memory Scale (1975 Russell version), the Sickness Impact Profile and the Profile of Mood States. Pre-surgery assessments for both carotid groups were conducted one week after arteriograms were performed on the subjects. The control group was assessed one week before their surgery. All post-test assessments were conducted six months after surgery by a psychometrist who was reported to be "blind" regarding their group in 69 per cent of the examinations they conducted, suggesting that the psychometrist was unaware of the group affiliation (surgical, non-surgical or control) of the subjects. In the remaining 31 per cent of examinations, the psychometrist was aware of the group status of the subjects.

The Average Impairment Rating of the control group was reported to be significantly lower than those of both the surgical and non-surgical carotid artery disease groups, respectively, (F (2,45) = 5.03, $p \leq 0.05$), while the two carotid groups did not differ significantly from each other on this measure. However, all groups showed a significant intra-group post-test lowering of Average Impairment scores (F (1,45) = 16.48, $p \leq 0.001$).

The control group had significantly higher pre-test Verbal $F(2,45) = 3.34$, $p \leq 0.05$), Performance ($F(2,45) = 6.11$, $p \leq 0.05$) and Full Scale Wechsler Adult Intelligence Scale ($F(2,45) = 5.55$, $p \leq 0.01$) scores than the carotid artery groups, although the carotid groups themselves did not differ significantly on these measures. All three groups reported significant within-group differences between pre-test and post-test performances on Performance ($F(1,45)= 19.43$, $p \leq 0.001$) and Full Scale IQ scores only ($F(1,45) = 11.78$, $p \leq 0.01$).

Semantic memory measures revealed no group effects although significant within group pre-test to post-test score improvements were found for the short term ($F(1,45) = 6.44$, $p \leq 0.05$) and the half-hour (delayed) recall scores ($F(1,45) = 6.94$, $p \leq 0.05$). On figural memory measures, the groups did not differ significantly, although the within-group pre-test to post-test differences for half-hour recall scores that showed an improvement for all groups was found to be significant ($F(1,45) = 5.12$, $p \leq 0.05$). The Sickness Impact Scale scores indicated that the controls reported a significantly lower post-test disability score than the two carotid artery disease groups

($\underline{F}(2,45) = 8.62$, $\underline{p} \leq 0.001$), although no pre-test to post-test improvement was noted across the groups. The controls also showed significantly more vigour and less fatigue than both carotid artery disease groups on the post-test Mood States scale scores ($\underline{F}(2,45) = 7.61$, $\underline{p} \leq 0.01$).

Parker et al. (1983) reported that their findings suggest that carotid endarterectomy had no positive effects on the neuropsychological functioning and quality of life (as measured by the instruments used in this report) when compared to a control (no surgery) condition. Although this study shows an improvement with regard to some of the issues raised in the Hemmingsen et al. (1982) report, several methodological shortcomings persist which limit the extent of the findings. The authors have controlled for the timing of assessment after the arteriogram procedure, yet there is no documentation of the resolution times for neurological symptoms. It is possible that varying resolution times could reflect differing levels of underlying pathology, thus contributing to the failure to find any significant increases in group mean performances. All groups studied showed improvement on the Impairment Index, suggesting practice effects may have influenced performances on the tests comprising the test battery. In addition, all groups improved their scores when these were compared with their pre-test level of performances. Although the study reports equivalent representation of lateralized transient ischaemic attack attacks in the sample, this variable is not entered into data analyses. Some brain functions are generally considered to have asymmetrical organization, for example, language skills are largely left hemisphere mediated and visuospatial skills are right hemisphere based, as noted before. In the present study, all the patients are treated homogeneously with no attempt to distinguish between left and right hemisphere involvement groups, making interpretation of findings difficult.

The use of the Halstead-Reitan Neuropsychological Test Battery requires clarification with regard to several issues. Reitan and Wolfson (1993) indicate that the composition of this battery may vary across laboratories in accordance to the preference of individual investigators. In addition to failing to describe the test composition of this battery, Parker et al. (1983) analyze the battery results only in terms of the Average Impairment Index. In addition, there is no indication as to which specific tests in the battery were entered into the derivation of the Average Impairment Index. The finding that the surgical groups showed a post-test increase on this dependent variable offers little information on the relative contributions of individual tests to these findings. It is possible that some of the tests in the battery may have been differentially sensitive to the neuropsychological changes that accompany damage to specific areas of the brain, as may be the case in carotid artery disease.

Thus, while this study strongly suggests generalized neuropsychological impairment, it is difficult to determine which areas of neuropsychological functioning had been compromised or preserved. The findings that there were equal gains in test scores across all the groups (including the controls) raises the suspicion of the effects of test-retest and associated practice effects. Thus, the Parker et al. (1983) study is important in elucidating the potential confounding influences of of the variables of practice effects, examiner bias and time delay between initial and follow-up assessment. Failure to document other critical variables and treatment of the data as outlined above limit the value of the findings.

Brinkman, Braun, Ganji, Morrell and Jacobs (1984) studied the pre- and post-operative neuropsychological performances of a group of 14 male Norwegian patients who had a history of transient ischaemic attacks or a small stroke. Twelve patients had unilateral internal carotid artery occlusion and two had bilateral stenosis of the same vessel. Somatosensory evoked potential (SSEP) recordings were conducted during the operation to monitor cerebral ischaemia due to the surgical procedure. The authors indicate that this measure appears to be related to cerebral blood flow. Neuropsychological testing was conducted within a period of two days prior to the operation, and then four to nine days post-operatively. The neuropsychological test battery that was employed was comprised of the Wechsler Adult Intelligence Scale, Russell's Revised Wechsler Memory Scale, Buschke's Selective Reminding Procedure, the Trail Making Test, and the Reitan Sensory-Perceptual Examination.

The authors found that there were no significant changes in the pre- to post-operative neuropsychological test data in the group as a whole. Further analyses revealed that reductions in somatosensory evoked potential amplitudes (reported in 11 patients) were associated with a decrement in post-operative neuropsychological performance. Three other patients who had evidence of cerebral ischaemia, however, showed greater neuropsychological improvement, post-operatively. It was reported that patients who had ischaemic episodes within one week after the operation tended to perform better on neuropsychological tests, post-operatively.

Several methodological shortcomings become evident from an analysis of this report. In the first instance, age, education, socioeconomic status and occupation on neuropsychological test performance were not controlled in this study. The influence of age and education on neuropsychological test performances has been reported by Bornstein (1983).

A second issue derives from the failure to employ a control group. Awaiting surgery is an anxiety-provoking situation and no data regarding this variable is forthcoming in the study. The deployment of an appropriate control group in this study would have minimized the effects of anxiety and other illess-related psychological variables on neuropsychological test performance (Tarter, Van Thiel and Edwards, 1988).

Furthermore, the group was treated homogeneously despite the variability in the side of carotid occlusion or stenosis, as well as the degree of stenosis. The failure of the study to elicit any pre-test to post-operative test score differences could also be attributed to the short interval between pre- and post-testing and the use of a limited number of neuropsychological tests.

Nielsen, Hojer-Pederson, Gulliksen, Haase and Enevoldsen (1986) reported the neuropsychological scores of 12 transient ischaemic attack patients who underwent superior temporal artery to middle cerebral artery bypass surgery. Widespread variability in the disease features of this group was reported. Eleven subjects were right-handed; before the operation, six had three or more ischaemic episodes, one had 2 and five had only 1 such attack. Computerized tomography showed cerebral infarction in six patients together with a range of slight, moderate diffuse, and/or regional cortical atrophy. A control group matched for sex, age and educational level, and without a positive neurological or psychiatric history was selected for comparison.

The neuropsychological battery used in this study comprised the Information, Arithmetic, Digit Span, Similarities, Block Design and Picture Arrangement subtests of the Wechsler Adult Intelligence Scale, the Trail Making Test (A and B), the Symbol Digit Modalities test, Fifteen Words Learning test, Immediate Story Recall, Face Recall and Visual Gestalt tests. The battery of tests was administered an average of seven days pre-operatively, and an average of 99 days, post-operatively.

Post-operatively, the transient ischaemic attack group performed significantly better on the Trail Making Test (on both forms A and B), Symbol Digit Modalities and the Face Recall tests. The pre-operative performance of the transient ischaemic attack group was significantly worse than the control group on Information, Arithmetic, Symbol Digit Modalities and the Visual Gestalts (Immediate recall and learning). The post-operative performance of the experimental (transient ischaemic attack) group was significantly poorer than that of the controls on the Information and Arithmetic, but significantly better on Face Recall. No statistical values were reported in this study.

The findings in this study were based on a small group of subjects who demonstrated some variability in their disease profiles. The finding that all subjects had evidence of varying degrees of cerebral atrophy is a confounding factor. The computed tomogram findings indicating infarcted areas may be related to the number of transient ischaemic attacks suffered by the patients (Levy and Werdelin, 1988), and there was little attempt to relate this variable to neuropsychological performance. There is evidence that cerebral atrophy is associated with histories of degenerative brain conditions such as Alzheimer's Disease (Bigler et al., 1988), a variable which was not excluded in this study.

Also, the finding that the performance of the control group on the Face Recall Test was significantly poorer than that of the experimentals, post-operatively, is difficult to interpret. This finding may be related to the hemispheric integrity of the patients, which was not reported in this study. Alternatively, the test-retest reliability of the test itself, an issue related to the effects of practice on performance on this test, may account for these findings. The report however shows the importance of establishing the presence of computed tomogram infarcts in transient ischaemic attack patients, and the investigation of the relationship of this variable to neuropsychological test performance.

Extending the findings of previous researchers regarding the effects of lateralized cerebral surgery on test performance, Hemmingsen, Mejsholm, Vorstrup, Lester, Engell and Boysen (1986) investigated the neuropsychological functioning of a group of 31 transient ischaemic attack patients in Sweden. The experimental sample consisted of 17 left (ten female, seven male) and 14 right (four female, ten male) hemisphere subjects who were submitted for carotid endarterectomy. The neuropsychological test battery comprised the Visual Gestalts, Word Pairs and Story Recall tests which measured learning and delayed memory skills. The Digit Span and Digit Symbol subtests from the Wechsler Adult Intelligence Scale, together with the Trail Making Test (Forms A and B) were reported to constitute measures of attention.

A control group matched for age, sex, and type of employment, comprised a sample of patients undergoing vascular surgery for atherosclerosis in the lower extremities. The test battery was administered to both the experimental and control groups one to two weeks prior to the operation, and three to five months, post-operatively.

The post-operative performance of the left hemisphere group was significantly better on Word Pairs (learning and reproduction), Story Recall (immediate), and the Trail Making Tests (both A and B). The right hemisphere group performed significantly better after surgery on the Visual Gestalts (both learning and reproduction) and the Trail Making test (Form B). The control group showed no significant improvement on any of the tests administered.

The results in the Hemmingsen et al. (1986) provide strong evidence for the effect of restored cerebral blood flow particularly from the view that there were no reported neuropsychological test score gains in the control group. Other factors may explain the improvement in these scores in the experimental group. One such explanation relates to patient expectations which form an important source of variance in neuropsychological test performance based in the clinical trials model (Bornstein, 1991; Rourke, Costa, and Ciccheti, 1991). Two-thirds of the transient ischaemic attack group were reported to be comprised of skilled and professional workers. This suggests that there may be a SES factor related to the neuropsychological findings obtained (Ardilla, Rosselli and Ostrosky-Solis, 1992). It is likely that skilled professionals were cognizant of the possible neuropsychological effects of such surgical techniques which in turn may have shaped their expectations. Such expectations could affect the level of motivation, particularly after a successful operation, and thus their performances on neuropsychological tests. Anticipating no such effects after surgery on their lower limbs, the control group, despite having similar employment status', may have indifferent expectations regarding outcome and thus a lower motivation to perform optimally on the neuropsychological battery.

Lezak (1995) notes that on certain tests, for example, the Trail Making test (Forms A and B), it is difficult to conclude whether slow performances are due to neuropsychological factors or to poor motivation. Allen, Lewis, Eyman, and Coyne (1989) further note that patient collaboration is crucial to optimum neuropsychological performance and therefore needs to be systematically documented during assessment. The authors emphasize that patient collaboration in the testing process is a key factor mediating neuropsychological test validity.

Perhaps support for this argument is provided by an examination of the pre-operative median scores for Word Pairs (learning) of the left and right hemisphere and control groups respectively, these being 22, 16, and 22 reported in the Hemmingsen et al. (1986) study. The authors report that this test reflected one of the strongest gains in neuropsychological performance among the left hemisphere patients. Since, on inspection, there are no significant differences between the left hemisphere and control groups, improvement of these scores in the left hemisphere group is difficult to interpret. However, it may be possible that the improved left hemisphere performance reflects a superior premorbid ability level on this skill among the subjects of this group, perhaps related to their occupational standing since two-thirds of the transient ischaemic attack group were reported to be skilled professionals.

Despite these interpretative difficulties, the study is important in demonstrating the importance of treating left and right hemisphere transient ischaemic attack patients independently in analyses of their neuropsychological profiles.

Greiffenstein, Brinkman, Jacobs and Braun (1988) investigated the pre- and post-operative neuropsychological performances of 15 left and 15 right carotid endarterectomy patients in Denmark. In the right hemisphere group there were five patients with strokes only, eight with transient ischaemic attacks only, and two with both strokes and transient ischaemic attacks. The left hemisphere group comprised six patients with stroke, seven with transient ischaemic attacks, and two with both strokes and transient ischaemic attacks. The neuropsychological battery consisted of the Wechsler Adult Intelligence Scale (Revised), the Trail Making test (Forms A and B), the Finger Oscillation Test, Digit Symbol Substitution test and the Buschke Selective Reminding Procedure (total recall).

A control group, reported to be matched for age, educational level and Full Scale IQ score on the Wechsler Adult Intelligence Scale-Revised, was selected from general surgery candidates. Pre- and post-surgery scores were obtained for the experimental group, while two measures prior to surgery were obtained for the controls due to delays in their operations.

Only the right endarterectomy group showed significant post-operative test score gains, this being with respect to Performance IQ scores ($t = -3.88$, df = 7, $p \leq 0.05$). The scores on the Trail Making (Forms A and B), the Tapping (Right and Left hands) and Digit Symbol tests were converted to a speed/concentration composite score. The difference between the pre- and post-test neuropsychological performances was found to be significant for the right carotid endarterectomy group showing a significantly larger post-surgical improvement on this index ($t = 1.73$, df = 28, $p \leq 0.05$). This group also showed a significantly better post-endarterectomy score on the total Recall measure on the Buschke Selective Reminding Procedure ($t = 2.11$, df = 14, $p \leq 0.05$).

Some of the findings of this study are in concert with those of previous reports. The finding that the right hemisphere showed post-surgical improvement on nonverbal tasks partially support the findings of Hemmingsen et al. (1986).

While the data are useful in identifying improvement in some skill areas, it would be more meaningful to interpret the scores on the Wechsler Adult Intelligence Scale-Revised on a subtest basis since such analyses suggest patterns of performance associated with different skill areas. An example of this is the Similarities subtest which is reported to be one of the best predictors of left hemisphere disease (Lezak, 1995).

Another observation that may be contributory to the overall findings was that three of the left hemisphere subjects were reported to be mild to moderately aphasic. No details are presented regarding the type of aphasia nor the severity of the disorder. It is therefore not possible to determine to what extent the aphasia contributed to the overall poorer post-surgical performance of the left hemisphere group. Furthermore, the diagnosis of aphasia reflects a more stable disability, perhaps reflecting a more severe ischaemic process, even possibly multiple events or infarcts.

Clearly, this study has attempted to reduce the effects of practice on test performance by using a control group who were also tested twice in the research design. Moreover, the finding that the right carotid endarterectomy group performed better on timed tasks suggests the involvement of an attention factor rather than problem solving skills per se, which requires further investigation.

Baird, Ausman, Diaz, Dujovny, Adams and Shatz (1988) reported on the mean Impairment Ratings of different groups of surgical patients at a cerebrovascular disease clinic in Michigan, U.S.A. Six patient groups were followed, viz., a carotid endarterectomy, superior temporal artery to middle cerebral artery anastomoses, multiple revascularization, vertebrobasilar, spinal complaints, and a cerebrovascular group that did not undergo surgery. The pertinent study groups and time variables investigated in this study are illustrated in Table 1.

Table 1.

Characteristics of Study Groups in the Baird et al. (1988) Investigation

Group Number	Study Group	Mean duration (days) between pre- and post- operative testing (Range values in parentheses)
1	Carotid Endarterectomy	5, 201 (160-259)
2	Superior temporal artery to middle cerebral artery anastomosis	5, 201 (160-259)
3	Verterbrobasilar artery	5, 201 (160-259)
4	Multiple revascularization	5, 246 (173-363)
5	Spinal complaints	5, 246 (173-363)
6	Nonsurgical cerebrovascular	5, 246 (173-363)

As indicated in Table 1, the average time interval between pre- and post-operative neuropsychological assessment was five days (range from 0 - 45 days) and 201 days (range from 160 - 259), respectively, for the carotid endarterectomy, superior temporal to middle cerebral artery and vertebrobasilar artery groups; the mean times for these assessments were five days (range was 2 - 8 days) and 246 days (range was 173 - 363), respectively, for the multiple revascularization group, the spinal complaints and the cerebrovascular comparison groups. All the study groups were reported to be comparable for age, gender and race, and the spinal complaints group revealed a significantly higher number of years of education and a higher premorbid IQ estimate.

The authors derived a mean impairment rating as an index of cognitive, perceptual and motor functioning. This rating was derived from scores on the Token Test, the Wechsler Digit Symbol subtest, the Trail Making Test (Part B), the Finger Tapping Test, the Foot Tapping Test, the Static Steadiness Test, the Sensory Perceptual Exam rating and the Grip Strength Test. The Sickness Impact percent summary score, based on the subject's endorsement of statements describing dysfunction in 12 domains of daily life, was used as a general life-quality index of adaptive functioning.

The cerebrovascular comparison group obtained a significantly lower mean impairment rating than the equally-weighted, combined impairment rating of the carotid endarterectomy, superior temporal artery to middle cerebral artery and multiple revascularization groups. referred to as the combined surgical groups (t (48) = 2.23, $p \leq 0.05$). The spinal complaints group obtained a significantly lower mean impairment rating than the combined surgical groups at baseline assessment (t (43) = 3.13, $p \leq 0.003$), and at six-month follow-up assessments (t (2.83 = $p \leq 0.007$). No significant differences were found between the superior temporal artery to middle cerebral artery, multiple revascularization and the vertebrobasilar revascularization groups on post-test adaptive functioning scores.

The findings of the Baird et al. (1988) study fail to provide any evidence of differential neurobehavioural gains in groups of patients who underwent cerebral revascularization versus those who were considered for surgery but did not receive such intervention. In fact, surgery patients tended to have poorer outcome scores than the non-surgery or spinal groups. The findings in this study raises questions regarding the clinical efficacy of vascular surgery, particularly with reference to neuropsychological functioning which have probably contributed to the current uncertainty about the psychological benefits of this surgical procedure (Alexandrova, Gibson, Norris and Maggisano, 1996).

A closer analysis reveals that several methodological issues could account for the findings in this study. The index of neuropsychological functioning was based on a composite score of various tests. No attempt was made to analyze the individual variations of scores across these tests which could reveal fine grain changes in performance and hence domains of neuropsychological functioning (Walsh, 1987; Lezak, 1995). Also, the battery does not include tests of conceptual thinking or memory, thereby providing a restricted range of assessed neuropsychological abilities. The small sample sizes in each group could also prevent the statistical detection of systematic changes in performances (Kirk, 1982). There is also wide variation in the timing of pre- (baseline) and post-surgical neuropsychological assessments, which could confound the findings obtained in this study. Despite these methodological difficulties, the study is important in alerting researchers to the potentially confounding influences of intraoperative variables which are often difficult to document. Somatosensory evoked potential recording thus appears to provide an effective and sensitive method of monitoring the effects of intraoperative ischaemia on neuropsychological test performances and needs to be documented and explored more systematically in studies on transient ischaemic attack patients undergoing surgery.

Casey, Ferguson, Kimura and Hachinski (1989) studied the effects of carotid endarterectomy on neuropsychological performance in a group of American transient ischaemic attack patients resident in the state Ohio. Twelve patients comprised each of three groups--two experimental groups of left and right carotid endarterectomy patients, respectively, and a third group of transient ischaemic attack patients with symptomatic evidence of the disease who did not undergo the operation. All subjects were free of neurological symptoms and did not reveal focal abnormalities on computed tomogram scanning. Six males and six females comprised the samples in each study group. A neuropsychological test battery, comprising the Wechsler Adult Intelligence Scale, the Wechsler Memory Scale, the Modified Knox Cubes Test, the Finger Tapping test, the Two-Point Discrimination Test and the Visual Search Test, was administered to the subjects twice to yield pre-test and post-test scores on these tests.

Pre-surgery testing of the endarterectomy subjects was completed an average of 2.6 days (SD = 3.6) prior to surgery. Correspondingly, the control group was assessed an average of 1.8 (S.D.= 3.8) days after initial hospitalization. The average post-test time was eight weeks following baseline assessment for all groups.

To control for practice effects, the authors stated that post-operative assessments were performed by using alternate forms of all the neuropsychological tests, with the exception of one test which was not specified in the report. Well-trained psychometrists and graduate students were paid to perform all assessments. Demographic and associated analyses of the subjects revealed no significant differences in age, years of education, follow-up interval, or baseline measures of psychometric intelligence or memory across the three groups. All the groups showed a significant improvement on Verbal IQ ($F(1,33) = 6.07$, $p \leq 0.05$), Performance IQ

($\underline{F}(1,33) = 45.40$, $\underline{p} \leq 0.05$), Full Scale IQ ($\underline{F}(1,33) = \underline{30.65}$, $\underline{p} \leq 0.05$), and Memory Quotient ($\underline{F}(1,33) = \underline{p} \leq 0.05$). No significant group effect of Groups x Trials interaction were reported. With respect to lateralized findings, the only significant post-test performance was the lowering of the time taken to perform on the Visual Search Test, specifically in the left visual field. This statistically significant finding was reported across the three groups ($\underline{F}(1,33) = 5.66$, $\underline{p} \leq 0.05$).

Casey et al. (1989) interpreted their findings to suggest that carotid endarterectomy does not improve neuropsychological functioning in patients. The results of their study are compelling despite several possible extraneous explanations for the findings. One major issue relates to the diagnostic criteria employed for transient ischaemic attacks which do not appear to be clearly defined in this study. It is presumed that the authors adhered to the 24-hour limit for the resolution of symptoms, yet it is entirely possible that the diagnosis was based on different time criteria, e.g., 72-hour resolution period, as has been adopted by other investigators (Soelberg-Serensen et al., 1989).

Another issue relates to the use of computed tomography to exclude focal abnormalities. From the data given in the study, it is not clear when these CT procedures where conducted. Levy and Werdelin (1988) and Waxman and Toole (1984) noted that sufficient time after the resolution of the neurological symptoms of a transient ischaemic attack should be allowed before a computed tomogram scan is performed so that the lesion can form (Waxman and Toole, 1984). Thus, this variable does not appear to be stringently controlled and it is therefore unascertainable to what extent the presence of infarcts may have influenced neuropsychological test performances.

Also, the description of the possible underlying pathology of the control symptomatic transient ischaemic group may offer some alternate explanation for the findings derived in the Casey et al. (1989) study. Two of the control patients were reportedly considered to have evidence of carotid artery stenosis (the significance of which was not reported), four were suspected to have stenosis, while three patients were considered to have a cardio-embolic aetiology. The causes of the transient ischaemic attacks in three cases were unknown. Thus, the failure of the control subjects to show improvement may be due, in part, to the performances of the six candidates with evidence of carotid artery stenosis. The inclusion of patients with heart disease (which made up at least 25 per cent of the control sample) raises other methodological problems. There is strong evidence that patients with coronary heart disease (which presumably led to the cardio-embolic related transient ischaemic attack) manifest a high degree of neuroticism, anxiety, depression and intrapunitive hostility (Haynes and Czajkowski, 1993). Apart from forming an extraneous variable, the inclusion of patients with heart disease suggests that personality factors may have influenced the neuropsychological performances of transient ischaemic attack patients, particularly among those with cardiogenic emboli-induced transient ischaemic attacks. It is also difficult to ascertain what effect the patients with unknown aetiologies may have had on the neuropsychological performance in the control group. It is likely that a failure to advance an explanation for their symptoms would have raised feelings of anxiety among these patients. It is not known to what extent these variables were a moderating or aggravating influence in the recovery of the control patients.

Another criticism of the control group is that while great care was taken to differentiate between the left and right endarterectomy groups, no data are forthcoming regarding the hemispheric involvement among control patients. This makes comparison difficult since one major aim of this study was to report on the hemispheric effects of carotid endarterectomy on neuropsychological functioning. Another major methodological shortcoming of this study is the small sample sizes that have been used, which raises suspicion about the validity of using a parametric statistical technique, viz., analysis of variance (repeated measures), in testing for significant differences (Kirk, 1982).

The issues raised primarily question the adequacy of the control group. To add to this uncertainty is the finding, on inspection, that there was a greater increase in the time score for the Visual Search Task (right visual field) for the control group (thereby suggesting a poorer performance) than for the endarterectomy groups on the second assessment. Although this finding was not significant, this difference was not reported and raises suspicion about the practice effects on this test. A survey of available handbooks on psychometric data (Spreen and Strauss, 1991; Anderson, 1994; Lezak, 1995) does not reveal such data for the Visual Search Test.

The use of several graduate students and psychometricians to gather data raises another serious methodological question. When several psychological investigators are involved in the elicitation of data, it is standard practice to compute and report inter-rater reliability coefficient values as a measure of consistency regarding the adoption of test administration procedures (Franzen, 1989).. These data have not been reported in this study, neither is there any indication of how many investigators were used. The major contribution of this study is that it points to the potential influence of practice effects on neuropsychological test performance. It becomes apparent that several medical, methodological and psychological issues are unresolved in this study which limit the validity and generalizability of the findings.

Mononen, Lepojarvi and Kallanranta (1990) compared the neuropsychological test performances of a sample of 30 transient ischaemic attack patients with those of a group of 16 patients who revealed evidence of cerebral infarction drawn from a cerebrovascular disease clinic in Oslo, Norway. Eleven of the transient ischaemic attack patients reportedly showed lateralized symptoms (although this variable was not specified), and two had bilateral involvement. Of the remaining subjects in this group, widespread variability in their neurological findings was evident and their affiliation to the transient ischaemic attack group was based on the following criteria: ten ipsilateral and one bilateral case of monocular blindness, one case of retinal infarction and five brainstem transient ischaemic attacks. The symptoms were classified as severe in 41 per cent (over three transient ischaemic attacks per week), moderate in 20.7 per cent (over 2 transient ischaemic attacks per week) and as mild in other cases. Fifteen of the 16 patients in the cerebral infarction group had infarcts in the region of the middle cerebral artery region, while the other revealed evidence of an anterior cerebral artery region infarct. Sixty-seven per cent of the infarcts were found to occur in the six-month period prior to the operation, while the age of the infarct was not specified in the remaining subjects. The infarctions were classified as mild in seven cases and moderate in nine cases. The neuropsychological tests selected for the battery were reportedly aimed at assessing lateralized cognitive functions. Verbal tests consisted of the following: the Word Fluency Test (presumably the FAS test) which was scored on the basis of the number of S and A words given in sixty seconds; the Stroop Colour Word test which was scored as time in seconds; Serial learning which scored the total number of words remembered on six successive trials; Digit Span, scored as the combined number of digits repeated forwards and backwards.

The visual tests comprised the following: the short form of an unspecified, facial recognition test, scored as the number of correct matches; a visual memory test scoring the number of correct design recognitions; the Cronholm recognition of concrete pictures, reportedly scored as the number of correct-incorrect recognitions. The same neuropsychologist conducted the preoperative assessments one to three days prior to surgery. Two postoperative neuropsychological assessments were performed at two weeks and two months, respectively, on both groups. The same forms were used for all the tests in the postoperative assessments.

No significant differences were found between the groups on preoperative neuropsychological test performance. The analyses that were performed related to within-group performances at the various test intervals. At two weeks, postoperatively, the transient ischaemic attack group performed significantly better on the Stroop Colour Word, Word Fluency, verbal learning and visual memory tests. Such upward trends in performance were observed at two months only on the Word Fluency, Stroop Colour Word and verbal learning tests, although the statistical significance of these differences were not reported.

The transient ischaemic attack group was then differentiated into groups of 12 left hemisphere and 18 right hemisphere patient groups, comparable for age and education. The left hemisphere group were then found to have significantly lower preoperative mean scores on the Digit Span and the Stroop Colour Word tests, respectively. The left hemisphere group showed significantly improved postoperative performances on the Stroop Colour Word and Serial learning tests at two weeks and two months, respectively.

The right hemisphere group performed significantly better at two weeks, postoperatively, on the Word Fluency, Serial learning, Visual memory and Recognition of Concrete Pictures tests, with only the latter three tests showing significant improvement at two months, together with an improved performance on the Stroop Colour Word test. The infarcted group showed a significantly improved performances at two weeks and two months respectively, only on the Serial Learning test, and at two months only on the Visual memory test.

The findings of the Mononen et al. (1990) study generally support those of previous studies in that there are differential gains in the scores on neuropsychological tests. Clearly, this study is an improvement on earlier studies (for example those of Greiffenstein et al. (1988) and Baird et al. (1988)), particularly with respect to equalizing practice effects across the study groups. Thus, the main findings of this study relate to the effects of carotid endarterectomy on neuropsychological functioning in a mixed group of transient ischaemic attack patients in comparison to those with cerebral infarcts. In keeping with this overall trend of findings, the transient ischaemic attack group showed a more consistent improvement on postoperative neuropsychological test performance when compared to the infarcted group.

Within the transient ischaemic attack group, findings with respect to left and right hemisphere patient subgroups seem to substantiate the left hemisphere-right hemisphere, verbal-nonverbal dichotomy. According to Mapou and Spector (1995), poorer scores on the Stroop Colour Word test are generally found in left frontal lobe damage than for other neurological or control groups. However, the finding that there was an improvement in the post-test Stroop test scores of the right hemisphere group, although this was a delayed effect, raises other possible explanations. Firstly, from a neuropsychometric perspective, it is possible that this finding may be related to a general delayed recovery in right frontal lobe functioning, while the recovery of function in simple verbal skills reached a maximum earlier on, i.e., at two weeks. Alternatively, the results may suggest that the right hemisphere contributes to performance on the Stroop since the test also involves the processing of visual information (Golden 1981).

Second, the lack of clearly defined characteristics regarding the degree of stenosis in the transient ischaemic attack group may have accounted for some of the findings obtained on the Stroop test. It is unclear from the report whether the left and right hemisphere groups showed evidence of unilateral or bilateral stenosis, and whether the patients in these study groups had involvement of the carotid or vertebrobasilar artery circulation, or both. The lack of information regarding these variables limits the interpretation of data obtained in this study, particularly with regard to the laterality effects on Stroop test performance.

The findings in the Mononen et al. (1990) study suggest that there is a delay in recovery of verbal processing speed. However, certain methodological problems that persist raise queries regarding these findings. Firstly, the transient ischaemic attack group appears to be comprised of patients with varying hemispheric involvement, and laterality for data analyses is seemingly based on the side of surgical intervention. Thus, the degree of carotid stenosis is not reported and cannot be determined from the data provided. It is also difficult to establish whether there was bilateral stenosis and if surgical priority was given to the side of greater stenosis. The possible involvement of bilateral stenosis in mediating neuropsychological test scores may account for the findings obtained on the Stroop test.

In addition, brainstem transient ischaemic attacks were included with those of carotid origin in the data analyses. Thus, it is difficult to establish the relative contributions of carotid artery and vertebrobasilar artery patient performances to the overall neuropsychological test findings.

Second, the transient ischaemic attack group reveals widespread variability with respect to the severity of the ischaemic attack, defined on the basis of the frequency of such attacks over a given period. The arbitrary discrimination of groups in severe, moderate and mild suggests that there may also be accompanying variability in the symptom resolution time across patients, yet this information is lacking.

Third, the finding that steady increases were reported on the Stroop Colour Word, the Serial Learning and Word Fluency tests on both the transient ischaemic attack and infarct groups, as well as across left and right hemisphere transient ischaemic attack groups, raises the issue of the possible influence of practice effects. Spreen and Strauss (1991) reported significant practice effects on the Stroop Colour Word test (at the 0.001 level) among college students, although no data are reported for neurological groups. The finding that both left and right hemisphere groups improved on Stroop Colour Word Test performance scores suggest improved mental flexibility, as indicated by factor analytic studies (Regard, 1981). Although desRosiers and Kavanagh (1987) reported a retest reliability coefficient value of 0.88 after 19 to 42 days in adults on the Word Fluency test, the increase in performance among right hemisphere patients as well as in the infarcted groups raises the possibility of practice effects on these scores. This argument is supported in the Mononen et al. (1990) study since it was reported that the same forms of the respective tests were used on repeat assessments.

Benke, Neussl and Aichner (1991) studied the neuropsychological sequelae of asymptomatic carotid artery stenosis in a sample of 20 subjects which was comprised of 12 men and 8 women in a cerebrovascular disease clinic in Finland. None of the subjects showed evidence of a transient ischaemic attacks per se, but on routine neurological check-ups allegedly reported complaints like headache, dizziness or vertigo. Routine CT in eight subjects' scans revealed either normal findings or a "slight degree of cortical/subcortical atrophy but no focal pathology" (p. 378). The average degree of stenosis of the internal carotid artery was reported to be "moderate and predominantly unilateral" (p. 379) but no values were reported for this variable. Six subjects were found to reveal bilateral carotid flow reduction.

A control group of 23 subjects was selected from unpaid volunteers who were chosen from patient relatives and non-neurological medical patients, matched for age and formal education. The authors report that risk factors (hypertension, heart and arterial occlusive disease, overweight, smoking, diabetes mellitus, hyperlipidaemia) were significantly higher in the patient group (Wilcoxon's test statistic = 2.67, $p \leq 0.007$). Several neuropsychological measures were obtained from the subjects. These included a word fluency score derived from the generation of names of animals, items beginning with a letter, or items in a supermarket. In a lexical decision task subjects had to report the digit flashed on a screen correctly and had to decide whether the presented strings were words or nonsense words. In this test, recognition accuracy was recorded and the final net score was obtained by subtracting all errors from correct decisions.

Immediate recall of a word list of semantically unrelated words constituted a verbal learning test. To test verbal concept formation and deductive reasoning abilities, a paradigm comparing the relationship of word pairs was designed. Subjects had to recognize the logical relationship of two words and, in a following step, to decide whether a second pair of words was related in an analogous way as the first couple. The Block Design subtest of the WAIS was used to measure visuoperceptive and visuoconstructive functions.

The authors reported that the patient sample performed significantly poorer than the controls on Word Fluency, Lexical Decision and Block Design ($p \leq 0.05$). Using the Bonferroni correction and adjusting the significance level to 1% revealed significantly poorer performances in the patient sample on Word Fluency, Verbal Analogies and Block Design. A Spearman r correlation value between degree of unilateral (left or right) stenosis and any of the neuropsychological test scores revealed no significant findings.

The findings of significant domain-specific neuropsychological impairment in the presence of moderate stenosis is an important finding. The lack of any significant findings regarding hemisphere involvement and neuropsychological impairment may be due to the inadequate sample size. In addition, the failure to find a significant correlation between degree of stenosis and neuropsychological test performance may be due to a combination of the small sample size as well as the use of a nonparametric test which is not sensitive to these small changes (Kirk, 1982). However, the findings of this study are important in that neuropsychological sequelae in less than severe carotid artery stenosis disease and in the absence of neurological symptoms are reported. Another important finding of this study is that there are differential sequelae with respect to the domains of neuropsychological functioning. An additional possible finding is that the neuropsychological sequelae in carotid artery disease are varied, implying alternatively or jointly that the neuropsychological functions measured are multidimensional and subserved by different brain regions or that the cerebrovascular disease is diffuse and not specific to the carotid system.

In a long-term study of the efficacy of carotid endarterectomy, Sirkka, Salenius, Portin and Nummenmaa (1992) compared the neuropsychological test performances of a surgical and nonsurgical group of carotid artery disease patients in a study conducted in Oslo, Norway. Eighteen subjects comprised the non-surgical group. Of these, 14 were TIA and four were stroke patients. Six of the patients had stenosis of the right carotid artery, six with left carotid stenosis and six with bilateral stenosis. The mean time interval between commencement of non-operative treatment and neuropsychological assessment was 11 years.

Forty-four subjects, 31 TIA, 8 stroke and 5 asymptomatic carotid artery stenosis cases, comprised the surgical group. Of these, 25 underwent right and 19 left carotid reconstruction, with 9 needing bilateral endarterectomy . The mean time interval between operation and neuropsychological assessment was 8 years, which was significantly shorter than that of the non-surgical group. Both patient groups had a mean age of 66 years. In addition, a control group was selected from a "normal group of subjects" (p. 59) matching the patients samples for age, sex and education.

On the basis of a personal interview and a questionnaire, the surgical and non-surgical patients were reported not to differ significantly. Interestingly, the stroke patients who did not form surgical candidates estimated their physical condition to be significantly better relative to those undergoing surgery ($p \leq 0.05$). Those subjects who were operated on more than once reported a quality of life significantly poorer than both those operated on once ($p \leq 0.05$), and those who had not undergone surgery ($p \leq 0.05$). Although 17% of the total sample reported fear of paralysis or stroke, there was no difference in their general attitude toward their illness when the surgical and non-surgical groups were compared.

To assess neuropsychological functioning, the Digit Span, Stroop, Kim Visual Memory Test, Benton Visual Retention Test, Rey Osterrieth Complex Figure Test, Verbal Associative Memory Test, Digit Symbol, Block Design, and Similarities were administered to all subjects. Few significant findings were reported by the authors. The control group performed significantly better in the following instances: on the Stroop Colour Word test, naming the colours of words when compared to those undergoing one operation ($p \leq 0.05$); on the Kim version of delayed visual memory compared to the twice-operated patients ($p \leq 0.05$); on Block Design compared to non- and once-operated patients ($p \leq 0.05$); and on Similarities compared to the non-operated ($p \leq 0.05$) and twice-operated ($p \leq 0.05$) groups, respectively.

The findings of this study suggest that the restoration of blood flow in endarterectomy procedures appears to have differential effects on the neuropsychological functioning of patients, being associated with improvement in some domains while no improvement is documented in others. The study demonstrates the possible influence of other surgery-related variables (such as the number of operations) which warrant study in the investigation of the clinical effects of carotid endarterectomy on neuropsychological functioning. What is most interesting in this study is that no significant differences on neuropsychological test performances were obtained when the endarterectomy group was compared to the medical treatment (non-surgical group). These findings serve to underscore the continuing debate about efficacy regarding the long-term cognitive and behavioural benefits of endarterectomy (Taghavy and Hamer, 1995). Clearly, there are several surgical variables that may influence neuropsychological outcome, amongst others intraoperative ischaemia, degree of stenosis, patency or availability of anastomostic connections, number of operations required, laterality of stenosis and presence of cerebral infarcts.

In a study conducted in a Finnish cerebrovascular disease clinic, Primavera, Novello and Stara (1993) compared the quantified electroencephalographic (qEEG) records of 13 subjects each with experiences of TIAs and transient global amnesia (TGA), respectively, with a third group of normal subjects matched for age and sex and a completely negative history of neurologic and /or psychiatric disorder. The TGA group (6 men and 7 women, mean age = 69.9, SD = 6.5) was diagnosed using the criteria of Caplan (1985) and qEEG investigations were performed within one week after the onset of the TGA attack. The TIA group (6 men and 7 women, mean age = 65.1, SD = 6) involved only those patients with involvement of the left hemisphere. The qEEG recordings were also performed within one week after the TIA episode.

The overall findings of this study suggested that the TGA group showed a significant reduction of the value of beta 2 power in the posterior and central divisions, both in the left and right locations, when compared to the TIA group ($p \leq 0.05$), with the right parietal location showing a significant difference in this value ($p \leq 0.01$). The TGA group showed a reduction of beta 1 power in frontal, central and parietal locations when compared to the normal group, with the greatest level of statistical difference related to a reduction of alpha power in the left temporal location. Of particular interest was the finding that the TIA group did not differ from the normal group on any of the qEEG measures.

The findings of this study appear to be inconsistent with the neuropsychological findings of the studies reviewed. It appears from the results that there are no electrophysiological changes in the TIA when compared to the normal subjects. However, the lack of significant differences may be due to several characteristics of the TIA group which are not documented in the study. For example, several questions with respect to the duration of symptom presentation, whether either or both carotid and vertebrobasilar circulations were involved, the degree of stenosis and the presence of infarcts remain unanswered. Thus, while the TIA group appears to be similar to the normal subjects on specified qEEG variables, the implications for neuropsychological functioning is undeterminable from this study. Thus, this study serves to underscore the continuing difficulty in isolating neuropsychological sequelae in TIA patients, emphasizing the need for further study in this patient population.

In a more recent study employing both electrophysiological and psychometric measures of attention and memory, Taghavy and Hamer (1995) studied a group of 28 patients (21 males and 7 females, mean age = 68.3 years, SD = 8.1), with a mean degree of unilateral stenosis of the carotid arteries of 85% (SD = 5.8). Two patient groups were derived from this pool of subjects.. In one group there were 11 males and 4 females with asymptomatic internal carotid artery stenosis. The mean age of this group was 70.7 years (SD = 6.3) and the mean degree of unilateral (left or right) stenosis was 84% (SD = 5.4). In the second group, described as symptomatic or the TIA group, there were 10 males and 3 females, with a mean age of 65.5 years (SD = 9.3) and mean unilateral (left or right) degree of stenosis of 86.2% (SD = 6.2). The authors report that there was an incidence of 54% of controlled hypertension in the TIA group and 53% in the asymptomatic group. A lower incidence of diabetes was found in the experimental groups--38% for TIA group and 40% for asymptomatic group. A control group of 15 subjects, matched with the experimental subjects for age and sex, was comprised of paid volunteers without a history of neurological disease or vascular insufficiency.

Two types of dependent variables were measured in the experimental and control groups. Using visual evoked potentials as one measure, the P300 complex was measured when two different kinds of randomly presented checkerboard patterns, A and B, were presented. Both A and B stimuli consisted of presentation durations of 120 milliseconds each, with a flash rate of 1.0 Hz on a grey background. Stimulus B constituted the task-relevant or target stimuli and these were presented at a ratio of 1:4 in reference to stimulus A. The task of the subjects was to keep a silent running count of the infrequent B stimuli. During the presentation of the A (frequent) stimuli, both P1 (defined as the first positive peak around 90 milliseconds in the A potentials) and N1 (defined as the negative potential subsequent to P1 around 115 milliseconds) were measured. During the presentation of the target (B) stimuli, N250 (defined as the immediately preceding negative peak to P300) and P300 (reflecting task processing potential), were also measured. In addition to these measures, conventional pattern reversal visual evoked potentials (PVEPs) were recorded binocularly in all subjects after a period of rest.

Twenty-six of the experimental and all of the control subjects were also administered a German-based psychometric cognitive performance test. The test consisted of nine subtests: naming objects, immediate recall, naming numerals, arranging blocks, replacing blocks, counting symbols, reversal naming, delayed recall, and recognition memory.

In their analyses, the authors found that the asymptomatic and TIA groups did not differ on any of the measured parameters and thus these two groups were collapsed for further comparisons to the controls. With regard to latencies, in general the N250 latencies (considered to be related to stimulus discrimination and evaluation by Taghavy and Kugler, 1988) both ipsilateral ($F(2.6,100.2) = 6.18$; $p \leq 0.0007$) and contralateral ($F(2.7,103.8) = 3.55$, $p \leq 0.022$) to the stenoses were significantly prolonged in the occipital, temporal, parietal and central regions in the experimentals when compared to the controls . In contrast, only the P300 latency at the occipital site showed significant prolongation in the patient group when compared to the controls. In this case, t-test analyses revealed that the respective ipsilateral and contralateral P300 latency values were significantly prolonged when compared to these values for the controls ($p \leq 0.05$), but there were no significant lateralized findings.

With regard to amplitude values, only N250 amplitude value at the central site was found to be significantly reduced ($p \leq 0.05$) in the patient group, and no laterality findings were obtained. On the other hand, P300 amplitudes derived over hemispheres ipsilateral ($F(2.6,102.2) = 3.66$, $p \leq 0.014$) and contralateral to the internal carotid artery stenosis ($F(2.2, 90.1) = 3.18$, $p \leq 0.044$) were significantly reduced in the patient sample when compared to the controls. These significant findings were obtained in the temporal ($p \leq 0.01$), parietal and central ($p \leq 0.05$) regions. No significant findings were obtained with respect to P1, N1 and conventional PVEP measures. In addition, the authors collapsed the total patient sample into carotid stenosis with diabetes and/or hypertension. In all measured parameters, no significant differences were obtained on subsequent analyses.

With regard to the psychometric findings, the cognitive performance scores of the two patient groups did not differ significantly, but were reported to indicate a "slight cognitive disorder for both patient groups" (p. 171) when compared to the norm values in the respective test manual. On the other hand, the patient sample performed significantly worse than the controls on the cognitive performance test ($t = 5.21$, $p \leq 0.001$). In addition, strong linear correlations were found between cognitive performance raw scores and N250 and P300 latencies, with the N250 showing generally higher correlation values. These findings imply that the longer the latency values, the higher the cognitive performance test scores and the more impaired the test performance. No significant differences between the cognitive performance test scores of patients with carotid stenosis and/or diabetes and hypertension were reported.

The Taghavy and Hamer (1995) study appears to be the only reported investigation of P300 potentials, internal carotid artery stenosis and TIA that was retrieved in this literature search. These authors argue that since the P300 is independent of the person's motivation, the measure reflects task processing abilities and therefore represents a real endogenous potential. The study strongly suggests that in comparison to subjects with no reports of neurological or vascular disease, patients with internal carotid artery stenosis (those without associated symptomatology and those with TIAs) are impaired in both the discrimination of stimuli (N250 showed lengthening of latencies and reduced amplitudes at central sites) and the capacity to handle information (P300 revealed significantly reduced amplitude and prolonged latency at occipital sites). The additional findings of significantly poorer cognitive performance scores in the patient sample tends to support the finding of reduced cognitive efficiency. However, a shortcoming in respect of this finding is that the cognitive test that was administered may be considered a global cognitive screen with little information of the relative level of functioning in the different areas of cognitive functioning. As indicated previously, nine different subtests, including but not limited to tests of naming, immediate recall and recognition memory, formed the test battery. Thus it is difficult to establish which areas of cognitive functioning have been disrupted in the patient sample.

Another important finding is the suggestion that the hemisphere contralateral to the stenosis may be compromised in cerebral functioning. One implication of this finding is that even unilateral TIA atherosclerosis is a diffuse process and may affect the general cerebral vasculature. Thus the presence of atherosclerosis in other regions of the cerebral vasculature may offer an alternate or extended explanation for the neuropsychological test findings. As suggested by the findings of the Mononen et al. (1990) study, the results obtained on some neuropsychological tests (for example, the Stroop test) suggest that stenosis may be bilateral, implicating the involvement of both hemispheres in the performance of these tests.

Thus it seems that while the measurement of cerebral evoked potentials offers a useful, objective way of examining cognitive sequelae in the presence of TIAs the technique requires sophistication with regard to equipment, laboratory specifications and expertise. The study however is important in suggesting that even in the absence of CT infarcts or neurological symptoms, the presence of internal carotid artery stenosis, as well as TIAs is associated with changes in neuronal functioning which may be associated with cognitive deficits.

Next, an overall evaluation of these studies will be undertaken to establish their contribution to the body of research on the neuropsychological sequelae of transient ischaemic attacks.

5.3.1. Evaluation of Endarterectomy Studies investigating the Effects of Cerebral Transient Ischaemic Attacks on Neuropsychological Functioning

The preceding review of the endarterectomy studies investigating the effects of transient ischaemic attacks on neuropsychological functioning entails several methodological issues which are peculiar to this type of research design. These methodological issues may be viewed as two broad types--medical and psychological.

With respect to medical issues, inherent in the selection of subjects are problems related to the criteria adopted for selection which appears to impact the overall findings derived in these studies. In the studies of Hemmingsen et al. (1982), Brinkman et al. (1984) and Mononen et al. (1990), the selection of transient ischaemic attack subjects included those with varying symptom presentation, pathologies, hemispheric involvement as well as with respect to the presence of cerebral infarcts. The variability in the selection criteria suggests a lack of consistency in the application of this variable as well as an inconsistent use of computed tomogram data, with a result that heterogeneous cerebrovascular samples constituted study groups. As a result, study samples of carefully defined subgroups of cerebrovascular diseases tended to be small in number for robust statistical findings to be generated.

Alternatively, when sample sizes were adequate for computing statistical data, the study groups were collapsed (Dull et al.,1982) with the result that neuropsychological sequelae with respect to transient ischaemic attacks were not clear or indistinguishable from other ischaemic cerebrovascular disease groups.

Related to this issue is the presence of other critical variables, related to the surgical procedure, which appear to influence neuropsychological findings. The report of Brinkman et al. (1984), which indicated that post-operative changes in neuropsychological test performances may be related to intraoperative ischaemia, is demonstrative of one such issue. Although the risk of intraoperative ischaemia is obviously minimized in the surgical procedures adopted, it is clear that studies employing this type of design need to document this variable more consistently than has been the case in the studies reviewed. An alternative method of excluding the presence of intraoperative-related cerebral infarcts may be to perform post-operative computed tomogram imaging findings. The importance of documenting such data is underscored by the findings that such infarcts often remain asymptomatic in these patients. Obvious constraints for the adoption of this procedure is that postoperative computed tomography is largely impractical and prohibitively costly, in addition to posing a medical risk to the patient. Recent studies have made attempts to investigate the risk for further TIAs in those patients undergoing carotid endarterectomy.

Another medically-related issue pertains to the documentation of risk variables in surgical patients. One important criterion for selection to undergo endarterectomy is based primarily on the degree of carotid artery stenosis. The value of documenting the contribution of this variable to the understanding of the neuropsychological sequelae of transient ischaemic attacks has been documented in several studies.

For example, Diener, Hamster and Seboldt (1984) studied 33 patients with relevant stenosis (or occlusion) of extracranial arteries carrying a variety of diagnoses. They found that, as a group, these patients showed more cognitive compromise than control subjects who had been matched for age and level of education. These authors found that neuropsychological deficits were present even in those subjects in whom the stenosis had not been associated with symptoms. The documented difficulties included impairments in memory, deficits in attention under stress, and difficulties in visual-motor integration.

Similarly, Naugle, Bridgers and Delaney (1986) reported that haemodynamically significant stenosis entails subtle neuropsychological compromise in the areas of attention/immediate recall of verbal input, delayed recall of both verbal prose and visual stimuli, fine manual dexterity of both dominant hands, and the performance of complex tasks of visual-spatial reasoning. In view of recent reports (Norris and Zhu, 1992) that cerebral infarction may be found in up to 70 per cent of subjects with clinically silent stenosis, in addition to its reported statistical interaction with infarction in effecting neuropsychological test performances, the studies reviewed have not investigated these issues in transient ischaemic attacks. Similarly, hypertension is reported to be a risk variable (particularly in male patients and those female patients over 60 years of age (Soelberg-Serensen et al., 1989), and its influence on neuropsychological test performance needs to be documented more closely. Mazzucchi, Mutte, Poletti, Pavanetti, Novanrini and Parma (1986) reported that subjects with uncomplicated essential hypertension obtained significantly poorer scores on tests of memory and visuomotor skills when compared to normotensive controls. In another study, Elias, Robbins, Shulz, Streeten and Elias (1987) found interactive effects of education and hypertension in the scores of differences between hypertensive and normotensive groups of subjects. No significant differences were found in the Average Impairment index scores of hypertensive subjects who had a high educational level when they were compared with normotensive groups. In contrast, hypertensive subjects in the low education group exhibited poorer Average Impairment index scores when a similar comparison was performed. In addition, the low educated hypertensive group performed significantly more poorly on the Categories and the Tactual Performance (both memory and localization) tests.

None of the studies reviewed herein have documented blood pressure readings, nor attempted to interpret its influence on neuropsychological test performances. It becomes clear that hypotheses exploring the predictive role of carotid stenosis and hypertension in the neuropsychological test scores of transient ischaemic attack patients need to be investigated using multiple regression analytical techniques.

With respect to psychological variables, the first issue of methodological concern relates to the identification of those areas of psychological function relevant for study in transient ischaemic attacks. Most studies have tended to use a preselected, but varying or unspecified test battery, most often the Halstead-Reitan neuropsychological test battery. Those studies using this instrument tended to report Average Impairment Ratings as the only dependent variable. Hom and Reitan (1990) indicated that, apart from the Average Impairment Index reflecting overall brain functioning, the following indices may also be derived: attention and concentration from the scores on the Speech-Sounds Perception, the Seashore Rhythm test and the Trail Making (Part A) tests; abstraction from scores on the Category, Tactual Performance (total time) and Trail Making (Part B) tests; incidental memory from scores on the Tactual Performance test (memory and localization scores); and motor based on the dominant and non-dominant scores on the Finger Oscillation test.

None of the studies reviewed which used the Halstead-Reitan test battery applied their analyses to the data in this manner. This argument may be extended to the relative disadvantage of reporting global scores such as Average Impairment indices. In the study of transient ischaemic attacks, there is strong indication for employing measures or data analytic techniques that allow for the assessment of functioning in specific domains of behaviour (see chapter three). This reasoning is based on two principles of brain-behaviour relationship studies. Firstly, the pathogenesis of transient ischaemic attacks suggests that there is more likely to be disruption of blood flow to specific neural regions, for example, those regions supplied by the anterior and middle cerebral arteries. Thus, in the presence of dynamic circulatory changes, psychological functions associated with distributed neural networks involving specific domains of behaviour are likely to be affected. Thus, investigating domains of psychological function will more likely uncover specific components of neuropsychological deficits, providing greater yield than those studies investigating and reporting the overall functional integrity of the brain, as indicated by the Average Impairment Index scores of the Halstead-Reitan test battery.

Secondly, in terms of accepted definitional guidelines, transient ischaemic attacks are accompanied by little or no evidence of cerebral infarcts as determined by current neuroimaging techniques available. The existence of those cerebrovascular disease cases with symptom resolution times of less than twenty-four hours, but with evidence of cerebral infarcts, presents a classification challenge. Thus, it may be useful to study those transient ischaemic attack patients with and without cerebral infarcts to contribute to this problem of classification. In addition to contributing to this classification difficulty, comparison of these subgroups of transient ischaemic attack patients may also be of clinical value in delineating and documenting the extent and probable location of brain dysfunction in transient ischaemic attack patients using relevant psychometric tests. Only one study under review in this section appears to attempt this form of data analysis (Mononen et al., 1990). However, these authors do not relate their findings to the issue of classification as suggested in the foregoing argument. An associated factor is that of degree of stenosis, with degree of stenosis forming an important variable in the study of TIA as suggested in the studies of (Diener et al., 1984; Hemmingsen et al., 1986). Recent studies (Taghavy and Hamer, 1995) have emphasized the need to discriminate between symptomatic TIA patients and those with asymptomatic carotid artery stenosis in the eivaluation of neuropsychological sequelae.

The second psychological issue of methodological concern pertains to the necessity for repeat testing in endarterectomy studies. Inherent in this methodological process is an expressed need for those tests with demonstrable reliability which permits repeated measurement over a period of time. An obvious methodological concern which arises in this instance is the potential influence of practice effects on psychological test performance. In general, the literature suggests that two strategies have been employed to circumvent the problem of practice effects.

In the first instance, some studies have used alternate forms of tests, a strategy used in only one documented study, that of Parker et al., (1989). Consequently, Parker et al. (1989) provided strong support for practice effects, emphasizing that this variable may account for many of the significantly improved post-test neuropsychological performances among endarterectomy subjects. One major constraint to using alternate forms of tests is the reported lack of such psychometric material for most neuropsychological tests, particularly those relevant for clinical populations (Lezak, 1995; Spreen and Strauss, 1991; Crawford, Parker and McKinlay, 1992).

The second attempt to overcome practice effects in test performance relates to the interpretive use of the same forms of the tests in both the comparison or control groups (for example, in the Mononen et al., 1990 report). In this study, the demonstration of superior test scores post-test, is attributed to the ability of control subjects to benefit from practice as opposed to those who fail to show significant post-test improvements in scores. Alternatively, assessment scores obtained early in the postictal period may be compared with those derived at a later period to establish the recovery profiles in specific areas of functioning.

Using this interpretation, Mononen et al.(1990) attributed the worse early performance of the infarct group to slower learning in these patients as opposed to the transient ischaemic patients who showed greater early post-operative gains in performance. This strategy is appropriate for between groups analysis as has been the case in the study reviewed. However, Mononen et al. (1990) do not discriminate between the transient ischaemic attack patients with varying symptom resolution times, hemisphere involvement or the presence of various risk factors.

Therefore, similar procedures may be used in left and right transient ischaemic attack patients with arbitrarily-defined shorter and longer neurological symptom resolution times. Such designs may yield information on whether processes, similar to those purported to explain findings in the infarcted group in the Mononen et al. (1990) study, may also be applicable to those transient ischaemic attack patients with longer resolution times but with no evidence of infarction.

A third psychological issue relates to the expectations of patients to perform better on neuropsychological tests after endarterectomy, which poses a powerful confounding variable in the interpretation of results. This is a difficult variable to control in cerebrovascular disease patients undergoing surgery since there will be expectations of improved performance prevalent in this sample of patients. Moreover, this variable has ethical and moral weighting since endarterectomy patients are more likely to perceive that the surgical intervention would promote quality of life and reduce the prospects of a stroke. Tentative findings have reported the perceptions of patients regarding the outcome of such surgical interventions

A fourth methodological issue related to the endarterectomy design is the timing of assessment. Hemmingsen et al. (1982) performed pre- and post-operative assessments at one week before surgery, and post-operatively one-to-two weeks and eight months, respectively. In the Parker et al. (1983) study, no information is given on the timing of the pre-operative assessments, while the postoperative assessment was performed at six months. Similarly, Dull et al. (1982) did not report the test-time parameters related to their assessment procedures. Brinkman et al. (1984) completed the pre- and post-operative assessments within two days and in a period of four to nine days, respectively. It thus appears that there is a serious lack of consistency across the studies reviewed with respect to the timing of assessment. When viewed in the context of variable neuropsychological test usage, comparability of findings is severely hampered.

An associated variable that has not been documented in endarterectomy studies is the emotional state of the subject at the time of test administration. The effects of even mild anxiety on certain test performances were reported by Martin and Franzen (1989). None of the endarterectomy studies reviewed reported the emotional state of the subjects they tested. Soelberg-Serensen et al. (1989) found that fifty per cent of the reversible ischaemic attack patients in their sample reported experiences of psychomotor slowing, general aesthenia, fatigue, emotional instability, depression or anxiety. Thus, the prevalence and potential influence of these affective variables on neuropsychological test performances have not been systematically documented in studies of transient ischaemic attack. In addition, the differential influences of affective variables on left and right hemisphere transient ischaemic attacks patients neuropsychological outcome requires further exploration, together with the interaction of other variables such as resolution time of symptoms. Moreover, the question of whether such affective symptoms were directly related to cerebral infarcts were not explored in previous studies.

A final methodological issue in endarterectomy studies relates to assumptions adopted for statistical analyses. Rourke, Costa and Ciccheti (1991) note that in group comparison designs of the type used in endarterectomy clinical trials, large groups of subjects should be used to reduce between-subject variability. In addition, random assignment of subjects to groups under investigation for the clinical efficacy of intervention strategies is essential for accurate assessment of treatment effectiveness.

The studies surveyed suggest that, in an effort to adhere to the requirements for careful selection of subjects and equating the several demographic and biographical variables influencing psychological test performance, large sample groups and randomization were often neglected principles of study design.

It becomes apparent from this discussion that the clinical trials-type design researching the question of post-operative neuropsychological changes is confronted with a plethora of medical, psychological and statistical demands of methodological rigour. It also becomes evident that the criteria of clinical trials designs are difficult to satisfy. Therefore, the use of endarterectomy designs is constrained in generating substantial empirical information regarding the neuropsychological sequelae of transient ischaemic attacks. It is possibly for this reason that there is a relative dearth of neuropsychological studies on endarterectomy patients in recent years, particularly post-1990.

On the other hand, TIA patients who have not undergone some form of vascular surgery, but who have been placed on varying forms of medical prophylactic therapy, are relatively poorly investigated. In principle, these patients are more accessible and offer a potent source of information regarding the investigation of neuropsychological sequelae of transient ischaemic attacks.

It is partially for these reasons that the present study was undertaken on samples of transient ischaemic attack patients who had not undergone any form of vascular surgery treatment for the disorder. The methodological process adopted to investigate the hypotheses outlined in chapter one of this study is presented next in Chapter 6.

CHAPTER SIX

Method

6.1 Introduction

The present investigation was aimed at studying the neuropsychological sequelae in transient ischaemic attacks involving the carotid arterial system. As indicated in Chapters 1 and 2, the anterior (carotid) and posterior (vertebrobasilar) vascular systems perfuse different regions of the brain, with little overlap. However, while these systems remain anatomically independent, they communicate with each other in the system of vessels provided through the circle of Willis. Research evidence suggests that the majority of transient ischaemic attacks (TIAs) are associated with the carotid system (Norris, 1991) and thus form the focus of interest in this study.

In order to investigate the hypotheses posited in Chapter 1 systematically, a series of methodological steps was followed.

6.2 Subjects

The nature of this study dictated that a highly select sample of subjects was required to investigate the aims and hypotheses presented in Chapter 1. South African provincial hospitals within the province of Kwazulu-Natal formed the setting where patients were selected for the study. A copy of the study proposal was sent to the superintendents of King Edward VIII and Addington Hospitals seeking permission for the study from the relevant authorities. Once permission was granted in each case, contact was made with the Heads of Department of Neurology and Vascular Surgery since it was likely that patients would form part of the intake in these units, and a copy of the proposal was made available to these respective individuals. Contact was then made with the registrars in these respective departments. Registrars are medical doctors who undertake postgraduate studies for specialist training in various disciplines of health care. The researcher initiated discussions around the study proposal which informed the heads of department and registrars of the specific needs of the researcher with regard to the TIA patients.

Over a 30-month period, the subjects selected for this study were randomly drawn from the vascular and neurological units of two hospitals located within the city of Durban, South Africa--the King Edward VIII Hospital and the Addington Hospital. In keeping with the aims of the study, two experimental groups, a left TIA and a right TIA group were randomly selected. A third control group was selected from a pool of hospitalized general medical and surgery patients who had conditions unrelated to the central nervous or cardiac systems. Forty left TIA, forty right TIA and forty general medical control subjects comprised the final study sample.

Several criteria were used for the selection of the subjects. Firstly, all subjects included in the sample were Indian South Africans. Second, all experimental subjects were diagnosed with TIA clinically and through neurological work-up by certified neurologists or physicians. The left and right TIA groups comprised patients who were determined to have suffered the respective lateralised ischaemic event based on clinical presentation and angiographic study of the carotid arterial system. The controls were all diagnosed with varying medical conditions in the categories of orthopaedic injuries in the peripheral limbs, as well as inguinal hernia and gastrointestinal disorders. All patients were under the care of specialist medical practitioners in the respective medical and surgical specialties.

Third, all subjects in the study were free from any disorder that required psychiatric or psychological intervention. Fourth, in an attempt to control the influence of sex and age, all subjects were male and fell in the age range 50 to 60 years.

6.3 Instruments

Two major categories of psychological instruments were employed in this study.

6.3.1 Biographical Inventory (Appendix A).

A biographical inventory was designed to elicit basic demographic and illness-related information. The name, date of birth, educational level, family size, total family income and occupation formed the basic demographic features of this questionnaire. Information relating to the several health risk factors was also elicited from the subjects. The health-risk information recorded for each subject concerned the prevalence of cigarette smoking, alcohol consumption, presence of heart disease (which was corroborated from health charts) and medications taken at the time of the study. Although an attempt was made to establish the quantity and frequency of both cigarette smoking and alcohol consumption in the patients, these data were vague in terms of the information elicited from the subjects. The majority of the subjects tended to be too speculative in this information and it was difficult to even establish categories of quantities or frequencies of smoking or alcohol consumption with any degree of consistency or accuracy. Despite the absence of these data in the current study, their relevance as risk factors in transient ischaemic attacks is acknowledged. Patients with reports of psychological or psychiatric disorders were excluded from the sample. In addition, data regarding the degree of carotid stenosis as determined by cerebral angiography and the presence of brain infarcts as recorded by CT were documented from the charts for each subject in the TIA group.

6.3.2 Psychological Test Battery.

A battery of neuropsychological tests was compiled on the basis of two major guiding principles. In the first instance, the literature review in Chapter 5 yielded findings that suggested the sensitivity of certain neuropsychological tests to neuropsychological dysfunction in the presence of TIAs.

Second, the review of the vasculature of the brain and the distribution patterns of the internal carotid system in Chapter 2 as well as the neuroanatomical-cognitive model in Chapter 3 provided a useful guideline in selecting those tests that would be sensitive in elucidating dysfunctions in selected neurocognitive domains. Thus, the following tests were selected to constitute the neuropsychological battery employed in the study.

6.3.2.1 WAIS-R Digit Span Test. Several measures of the varying components of the function of attention were employed to elucidate the functioning of attention at different levels. In terms of Lezak's (1995) classification, short-term memory storage capacity is an important component of the attention complex. Lezak (1995) identified two aspects of short-term memory capacity--processing speed and short-term capacity. The Digit Span Test (Forward, Backward and Total Score) was used as a basic measure of capacity or span of immediate verbal recall (Lezak, 1995). The underlying assumption of this test is that attentional capacity is measured by exposing the subject to increasingly larger amounts of information with instructions to indicate how much of the stimulus was immediately taken in by the subject repeating what was heard.

In this instance the Digit Span test used was the format described in the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981). Both Digits Forward and Digits Backward consisted of seven pairs of random number sequences that the examiner reads aloud at a rate of one digit per second.

In most studies on TIA included in this review, Digits Total score has been found to be significantly lower when compared to control groups. Although Digit Span Backward has been reported to be more sensitive to brain damage that Digit Span Forward, neither of these independent scores has been reported to be a reliable indicator of laterality (Black, 1986). However, it has been suggested (Anderson, 1994; Lezak, 1995) that Digit Forwards and Digits Backward may involve independent neurocognitive mechanisms for adequate functioning and therefore should be analyzed separately. Thus in an effort to further analyze the verbal attention and immediate verbal span of the subject groups, the scores for Digits Forward and Digits Backward, as well as Digits Total (sum of Digits Forward and Digits Backward) were examined in independent statistical analyses.

6.3.2.2. Paced Auditory Serial Addition Test (PASAT). The PASAT is considered a measure of sustained attention (Spreen and Strauss, 1991) and freedom from distraction (Deary, Langan, Hepburn and Frier, 1991) as well as rate of information processing (Gronwall and Wrightson, 1977). The studies reviewed in Chapter 5 suggest that this test had not been previously deployed in investigations on the neuropsychological sequelae of TIAs. The test used in the present study was the form of Gronwall and Wrightson (1977) as reported in Spreen and Strauss (1991). All levels of the PASAT, i.e., 2.4, 2.0, 1.6 and 1.2 seconds, respectively, were administered.

The PASAT's split-half reliability has been reported as 0.96 (Egan, 1988) implying that the test has high internal consistency. Mixed results of the relationship between certain demographic variables and performance on the PASAT have been reported. Gronwall and Wrightson (1977) found small correlations with arithmetic ability (0.28) and general intelligence (0.28) and Egan (1988) reported that in healthy people the PASAT showed a modest correlation (0.68) with general intelligence and numerical ability. Britain, LaMarche, Reeder, Roth and Boll (1991) on the other hand reported a significant effect for age and IQ, but none for education and race.

Norms for age groups 16-19, 20-29, 30-39, 40-49, 50-59 and 60-69 years have been provided by Stuss, Stethem and Poirer (1987). The general findings of these norms suggested that the faster the rate of presentation, the worse the performance regardless of age. Although the norms also suggested a decline in performance with age, the correlation between age and performance on the PASAT was not significant (Stuss, Stethem and Pelchat, 1988). However, a significant correlation with education was found with those normal subjects in higher educational levels showing better performance (Stuss, Stethem and Poirer, 1987).

With respect to neurological groups, the PASAT appears to be most widely studied in patients with postconcussion types of injuries (Gronwall and Sampson, 1974; Stuss, Stethem, Hugenholtz and Richard, 1989). Both groups of investigators reported that the PASAT test scores of postconcussion patients in general returns to normal levels within 30 to 90 days. Leininger, Gramling, Farrell et al. (1990) noted, on the other hand, that while many patients who have suffered mild concussions performed normally within 30 to 60 days after injury, others continue to lag behind the performance level of the control group. From these findings, there appears to be a general tendency to employ the PASAT as an index of the efficiency of information processing (Anderson, 1994; Lezak, 1995)

The extensive studies of Gronwall (1974), Gronwall and Wrightson (1977) and Stuss et al. (1987; 1988) have not provided any information on the differential performances of their study samples on the varying levels of presentation of the PASAT, i.e., 2.4, 2.0, 1.6 and 1.2 seconds.

It appears that the underlying assumption of these studies is that all four levels of increasing speed of presentation are accompanied by a concomitant decrease in performance.

6.3.2.3 Trails A and B. The Trail Making test consists of two parts--Part A and Part B. Although both Parts A and B are considered to be a measure of visual scanning with a motor component (Shum, McFarland and Bain, 1990), variations in the format of these tests have differing implications for the neuropsychological functions that are being assessed. In Trail Making Test (Part A), the subject must draw lines to connect consecutively numbered circles, 1 through 25. The subject is urged to connect the circles quickly without the lifting the pencil from the paper and the performance is timed in seconds.

In Trail Making (Part B), the subject is required to connect the same number of consecutively numbered circles (1 to 13) and letters of the alphabet (A to L), alternating sequentially between number and letter. In the performance of both Parts A and B, the subject's performance is monitored and corrected.

In general, reported reliability coefficients are found to vary, with most values reported to be above 0.60, but several values ranging between 0.80 and 0.90 (Spreen and Strauss, 1991). Lezak (1983) reported reliability coefficient of concordance values of 0.98 for Part A and 0.67 for Part B. Snow, Tierney, Zorzitto, Fisher and Reid (1988) reported a one-year retest reliability of 0.64 for Part A, and 0.72 for Part B in 100 older subjects with a mean age of 67 years. Dodrill and Troupin (1975) reported 6- to 12-month reliability values for epileptics which ranged between 0.67 and 0.89 for Part A, and between 0.30 and 0.87 for Part B.

Normative studies on Trails A and Trails B show that performance times increase significantly with each succeeding age decade (Stuss et al., 1987). In another study comparing age-related performances, the average education level of control subjects in the 45 and older age group was almost 15 years while that of the 15-44 year old age group was about 10.5 years.
No significant age effect was found in this study, but a significant education effect was reported (Boll and Reitan, 1973). Similar reports of the effects of education (those with ten years of education or less had a lower performance) were reported by Bornstein and Suga (1988).

Thus both Trails A and Trails B have been reported to be useful measures of brain damage in neurological patients, with Part B showing greater sensitivity to brain damage (Spreen and Strauss, 1991; Lezak, 1995).

6.3.2.4 Rey Auditory Verbal Learning Test (RAVLT). The RAVLT was administered as a measure of several dimensions of verbal memory--immediate memory span, delayed memory and recognition memory (Spreen and Strauss, 1991). The list of words reflected in Spreen and Strauss (1991) as constituting the RAVLT was used as the experimental measure in the present study. To measure immediate word span recall, the list of 15 words was administered in five consecutive trials of presentation and recall. The number of words recalled were noted in each case. After the fifth trial and a series of interpolated tasks, the subject is asked to recall as many words as possible from the list--this constituting the sixth trial. Then a recognition list consisting of 50 words (Spreen and Strauss, 1991) is administered and the subject is required to recognize those words which appeared on the list. Research studies indicate that over one-year intervals, the test has been reported to have a modest test-retest reliability, with correlations of about 0.55 (Snow, Tierney, Zorzitto, Fisher and Reid, 1989). Small, but significant improvements (on average, one to two words per trial) can be expected on successive administrations of the same form of the RAVLT (Crawford. Stewart and Moore, 1989; Lezak, 1983).

A review of the major sources describing neuropsychological tests (Spreen and Strauss, 1991; Anderson, 1994; Lezak, 1995) did not yield any data regarding validity studies on the RAVLT. However, factor analytic studies (McCartney-Filgate and Vriezen, 1988) indicate that the learning measures (Trials V and recognition) correlate significantly with other learning measures with values ranging between 0.50 and 0.65. In the study by McCartney-Filgate and Vriezen (1988), the authors reported that trial 1 (the supraspan measure) probably reflects a large attentional component since negligible correlations (0,17 to -0.13) were reported with other learning measures.

6.3.2.5 Controlled Oral Word Association Test (COWAT). This test was originally called the Verbal Associative Fluency Test. The COWAT forms an important measure in neuropsychological assessment, particularly of neurological patients, since this measure may provide an index of verbal production (Anderson, 1994; Lezak, 1995). The COWAT requires that the subject generate as many words as possible that begin with a given letter of the alphabet, excluding proper nouns, numbers, and the same word with a different suffix, within 60 seconds (Lezak, 1995). Review of the test compendiums (Spreen and Strauss, 1991; Anderson, 1994) suggests that the most extensively used letters in the COWAT have been F, A and S.

Interscorer reliability for the COWAT has been reported as near perfect and one year test-retest reliability in normal, older adults has been reported as 0.70 (Snow et al., 1989). Concurrent validity has been reported by Coelho (1984), and correlation values with age has been found to be -0.19, and with education, 0.32 in the study by Yeudall, Fromm, Reddon and Stefanyk (1986). Spreen and Strauss (1991) reported that while mean scores for less well-educated older subjects slowly decline from the a 50-54 year high (which at a mean value of 41.52 does not differ from younger groups nor from their better educated peers), mean values remain about the same for those with 13+ years of schooling until the 75+ years at which time the mean scores drop by an apparently nonsignificant amount.

6.3.2.6 Wisconsin Card Sorting Test (WCST). The WCST is considered a test of concept formation, and has been more specifically described as a test of "abstract behaviour and shift of set" (Lezak, 1995, p. 621). This test consists of 128 cards, divided into two packs with 64 in each. Each card has one to four symbols--triangle, star, cross, circle in varying colours of red, green, yellow or blue. No two cards have identical stimuli. The patient's task is to place the cards, one by one, under four stimulus cards--one red triangle, two green stars, three yellow crosses and four blue circles. This process must be undertaken according to a principle that the patient must deduce from the pattern of the examiner's verabl responses to the patient's placement of cards.

According to Lezak (1995), the WCST appears to have first earned its reputation as a measure of frontal dysfunction in the studies of Milner (1963). Spreen and Strauss (1991) note however, that data regarding test-retest, split-half or other forms of reliability are currently unavailable although Axelrod, Goldman and Woodward (1992) reported satisfactory interrater reliability values. O'Donnell, MacGregor, Dabrowski & Oestreicher (1994) reported that principal component and factor analytic findings on the category scores of community dwelling adults indicate that the WCST loaded strongly on a conceptual factor. The validity of this finding has been supported by suggestions that this neuropsychological test may be sensitive to lesions in the dorsolateral frontal cortex in comparison to lesions in the orbitofrontal cortex or posterior brain areas (Milner, 1963). In contrast, Anderson, Damasio, Jones, and Tranel (1991) found no significant differences in the WCST performances of subjects with frontal versus nonfrontal brain damage.

6.3.2.7 Block Design. The Block Design Test of the WAIS-R is a timed measure of visuoconstructive function (Wechsler, 1981). The subject is presented with four or nine red and white blocks, depending on the stimulus item of the test. Each block has two white sides, two red sides, and two half-red and two half-white sides with the colours divided along the diagonal. The task is to use the blocks to construct replicas of four-block constructions in the case of six items, and nine-block constructions in the case of three items.

WAIS-R Block Design split-half reliability coefficients given in the WAIS-R (Wechsler, 1981) manual are reported to range between 0.83 to 0.89. One year test-retest reliability values were given by Snow et al. (1989) as 0.84 in a sample of patients with more than 13 years of education and a mean age of 67 (SD = 7.7). Factor analytic studies demonstrate high loadings on the perceptual organization factor regardless of the number of factors derived, the age or the neuropsychological status of the subjects (Ryan and Schneider, 1986; Zillmer, Waechtler, Harris and Kahn, 1992).

Lezak (1995) reports that Block Design scores tend to be lower in the presence of any kind of brain damage, with characteristically posterior lesions being associated with more impaired performances.

6.3.2.8 Rey-Osterrieth Complex Figure Test. The Rey-Osterrieth Complex Figure Test is a measure of visual-spatial planning and visual memory (immediate and delayed). The test was originally devised by Rey (1941; translated by Corwin and Bylsma, 1993) to investigate both visual memory and perceptual organization functioning.

The subject is first instructed to copy or reproduce the figure, exactly. The copy performance of the subject is scored according to 18 elements of the design, using the system described by Lezak (1995). As reported by Spreen and Strauss (1991), there is little variation in the mean copy scores of normal adults ranging in age from 30 to 70+ years. The strict scoring system has provided a high interrater reliability (above 0.95, according to Spreen and Strauss, 1991). A factor analytic study of a large battery of neuropsychological tests placed the copy trial among tests requiring reasoning and planning (Baser and Ruff, 1987).

6.4 Procedure

Initially, the researcher made personal contact with several registrars in the Departments of Neurology and Vascular Surgery. These personnel were already in possession of the study proposal and thus aware of the type of patients that were sought for the investigation. The study involved TIA patients who were not surgery candidates but instead were managed through prophylactic medical therapy. The registrars were therefore requested to identify these patients from the records of the departments, who also met the following additional criteria over the previous six months.

1. Male patients between 50 and 60 years of age were selected for the sample.

2. The patient must have suffered a lateralized (left or right) TIA according to the classification criteria of Toole (1991).

3. The TIA patient had CT scan information regarding the presence of infarcts.

4. The TIA patient had angiographic data showing significant stenosis with a classification of the degree of stenosis as being mild (less than 50%), moderate (50 to 75%) or

high (75 to 99 %). For the most part, this classification system of stenosis was found difficult to adopt by the registrars in view of the angiographic technology available in these departments at the time of the study. Despite these difficulties, the registrars were asked to attempt approximations of the degree of stenosis in order to establish whether a patient had mild, moderate or severe stenosis.

A total of twenty patients, thirteen left TIA and seven right TIA, met the criteria specified in the schedule. These patients were then contacted telephonically by both the registrars and the researcher and were informed that at their following monthly appointment, the researcher and the Heads of either the Vascular or Neurology Units would approach them regarding the research project. This process led to five subjects (two left and three right TIA) declining to be interviewed and were subsequently excluded from further involvement in the study. The remaining 15 subjects were willing to participate in the interview during which time the patients were solicited for participation in the study. While the complete anonymity of the patients was guaranteed, the patients were also assured of their freedom of choice to terminate their involvement in the study at any stage without any compromise in their continued health care by their respective units or other health departments at the hospitals. These 15 subjects gave their consent to participate in the study and were informed that they were included in the pool of subjects from which a random sample would be drawn.

In order to complete the sample size and to acquire at least 40 left and 40 right TIA subjects, the researcher then contacted the registrars of the Vascular and Neurology Units on a weekly basis to establish whether further subjects meeting the selection criteria had been identified. Over the following eighteen months, the registrars collaborating in the study identified a total of 80 subjects who met the selection criteria. Of these, 37 were established to have suffered right TIAs, and 43 left TIAs. Once a patient was identified as meeting the selection criteria, the researcher was introduced to the patient through the registrar and/or head of the unit. The patients were explained the nature of the study in a manner similar to that conducted in the selection of the initial fifteen subjects. The patient was requested to participate in the study with the proviso that he would be free to terminate his involvement in the study at any stage without any prejudice to his continued care. In addition, it was emphasized that no immediate benefits would derive from the study and that once completed, the results of the investigation would be made known to the subject. Complete anonymity regarding all information about the patient that was recorded, was guaranteed to all subjects. Permission was sought from the subjects to extract data regarding medical risk factors, degree of stenosis and CT findings from the chart of the patient.

Once written permission for inclusion into the study was established with the patient, further permission was sought to contact the patient at his home for administration of the psychological tests at a time and location convenient to the subject within the following three months. The patient was informed that this psychological testing would only take place if the patient was selected for the study. This selection process resulted in a total pool of subjects of 95 subjects who met the criteria for selection in the study.

The complement of 95 patients which constituted the total pool of TIA subjects were made up of 41 right TIA and 54 left TIA patients, respectively. The names of the left TIA patients were written on pieces of paper and 40 subjects were randomly drawn using the fishbowl technique of selection. Once drawn, these patients were informed telephonically of their selection into the study. Those left TIA patients not selected into the final sample were also informed telephonically of their nonselection. All 41 right TIA patients were included in the final sample.

At this point it was decided to select the control sample from general medical patients. to control for general illness and short-term hospitalization factors. The Heads of Departments of General Medicine and General Surgery were contacted through the Departments of Neurology and Vascular Surgery. The study protocol was discussed with these individuals and permission for the study elicited from the relevant persons in these departments. From a register of patients under treatment in the Departments of General Medicine and General Surgery, a sample of forty male patients aged between 50 and 60 years, was randomly selected for inclusion into the control group. These patients were contacted in the wards by the researcher, a process facilitated through the Heads of the General Medical and Surgical Units. Once the nature of the study was explained to these patients, 12 declined to participate and were excluded from further study.

A group of 12 patients (50 to 60 years of age) was then again randomly selected through the registrars of these units and contact made with regard to the study. After being briefed on the study by the head of the General Surgical and/or Medical Units, all 12 patients were willing to participate in the study and signed the consent forms and the agreement to allow for the extraction of relevant information from their charts with the permission of the head of the unit. The 40 subjects comprising the controls were made up of the following patient types:--15 orthopaedic patients with injuries to the lower limbs which required surgery, 12 inguinal hernia patients (seven of whom required surgery) and thirteen patients who had undergone gallstone removal. Basic information regarding the names of these patients, telephone numbers and addresses were extracted from their charts. The subjects were informed that contact would be made with them over the following three months to establish the time and place for psychological testing.

Once the entire sample of 120 patients was selected, the names and telephone numbers of all subjects were written on slips of paper. The slips of paper were then drawn from a total pool to ensure randomness of patient selection for testing purposes. Since the subject was assessed on the basis of their random selection from the total pool of subjects, little knowledge of the subjects' status as left or right TIA or control patient was available prior to the psychological testing. The researcher felt that despite the objective nature of the psychological tests administered, the procedure adopted for psychological testing would prevent any further bias that may be forthcoming in psychological testing.

Telephonic contact was made with each subject in accordance with their random selection from the pool of subjects. In the case of 57 patients, the subject's home was the test venue. In the remaining cases, the University of Durban Westville, Durban, South Africa, was the test venue.

Four subjects were tested each day--two in the morning and two in the afternoon. Each test session lasted one-and-a-half to two hours. Testing took about four months to complete in view of several cancelled appointments. In the initial stages of the testing procedure, the subjects were given the biographical questionnaire which elicited relevant demographic and personal health information. The neuropsychological tests described in this chapter were administered according the instructions in their respective manuals. In some cases, for example, the Rey Auditory Verbal Learning Test, the instructions of Spreen and Strauss (1991) were used.

6.4.1 Data Analyses. The raw biographical and test data for each subject was separated into the three study groups--left TIA, right TIA and control groups. These data subjects were then entered into the SAS data capture schedule in consecutive form, in their respective groups (first left TIA, then right TIA, and finally control). This format was advised by the computer analyst in view of the statistical analyses that were to be performed.

The data were entered in varying forms, the format being dependent on the level of the data (categorical or interval/ratio) that was elicited. Age was entered as the number of years and education was determined as the combined number of years of formal education (school, college, university) undertaken by the subject. Per capita income was derived by dividing the total family income by the number of members in each household. In this way, the raw data for age, education and per capita income were respectively entered into the SAS spreadsheet.

Several categories of data were nominal in nature and numerical values were assigned in accordance with the categories. For example, the following categories were obtained for nominal level data--marital status (1 = single, 2 = married, 3 = divorced, 4 = widowed), consumption of alcohol (1 = yes, 2 = no), presence of previous heart complaints (1 = yes, 2 = no), presence of diabetes or hypertension (1 = yes, 2 = no) and previous psychological or psychiatric illness (1 = yes, 2 = no). With respect to the question of previous psychological or psychiatric illness, these were categorized as 1 = Anxiety, 2 = Depression, 3 = both, 4 = none, 5 = other. Degree of stenosis in the case of the experimental subjects was coded as 1 = mild stenosis, 2 = moderate stenosis, 3 = severe stenosis. All psychological tests yielded quantitative data and these were entered in the form recommended in the respective manuals or by the authors from whom the test was derived (for example, the Rey Auditory Verbal Learning Test as presented by Spreen and Strauss, 1991).

The review of literature on transient ischaemic attacks (and cerebrovascular diseases in general) indicates that it is extremely difficult to carry out a group comparison study (experimental versus control) in a reasonable period of time because of the variability in the demographic and disease profiles of such patients. As indicated in Chapter 6, the methodology adopted in this study was based on the aims and the hypotheses outlined in Chapter 1. One possible way to accomplish this was to design a study in which a group of transient ischaemic attack patients (experimental group) are compared to a control group, with these groups falling in the same age decade. Age forms a critical variable in performance on neuropsychological tests and is relatively easy to control in the comparison group particularly when age is defined in terms of age decade. However, the selection of subjects within a defined age range (which in the present study was 50 to 60 years) does not exclude the possibility of obtaining significant differences between the groups under investigation since age is measured in years. Thus, the investigation of the age, education and SES amongst the left and right transient ischaemic attack and control groups comprised the initial aims of this study as indicated in Chapter 1.

Furthermore, in order to systematically investigate the aims and hypotheses stated in Chapter 1, several types of regression and mulitvariate tests of difference were computed. The results obtained from these analyses are presented in Chapter 7.

CHAPTER SEVEN

Results

In the introduction to this study (Chapter 1) and the literature review (Chapter 5), it was suggested that several variables influenced the effect of transient ischaemic attacks on neuropsychological functioning. Transient ischaemic attacks occur in the context of several medical variables (for example, hypertension, diabetes). In addition, several neurological variables have been identified as being part of the transient ischaemic attacks clinical presentation. Critical variables influencing neuropsychological test scores include degree of stenosis, laterality, number of transient ischaemic attacks, duration of symptoms, presence of heart disease and the presence of psychiatric conditions. Moreover, pertinent demographic variables such as age, education and SES form important factors that influence neuropsychological test performance.

In this chapter, the results are presented in accordance with the hypotheses stated in Chapter 1. The results obtained are then discussed in relation to these hypotheses in Chapter 8.

7.1 Demographic Analyses

7.1.1 Age.

A one-way ANOVA was used to statistically compare the mean ages of the left and right transient ischaemic attack (experimental) and general medical (control) groups. The results obtained are reflected in Table 2.

Table 2

Analysis of Variance for Age (in Years) of Left TIA, Right TIA and Control Groups

Source	df	F
Age	2,117	7.33**

Note. In Table 2, $^{**}p \leq 0.01$

The results in Table 2 suggest that the left and right transient ischaemic attack (experimental) and general medical (control) groups differed significantly on age. To establish which groups differed significantly from one another on age, the Tukey post-hoc test was computed. The results obtained are reflected in Table 3.

Table 3

Tukey Test for Age (Years) Comparison between Left TIA, Right TIA and Control Groups

Groups compared	Mean Age in Years	Absolute difference in mean age
Left TIA vs control	55.80 vs 53.85	1.95*
Right TIA vs control	55.85 vs 53.85	2.00*
Left TIA vs Right TIA	55.80 vs 55.85	0.05

$^{*}p \leq 0.05$

The results in Table 3 suggest the following.

1. The left TIA group had a significantly higher mean age than the control group.

2. The right TIA group had a significantly higher mean age than the control group.

3. There was no significant difference in the mean ages between the left and right TIA groups.

7.1.2 Income.

Income levels are generally considered to reflect an index of socio-economic status. Per capita income is considered to be a more accurate index of socio-economic status since this computation is based on total family income and family size (Hollingshead, 1968). In the analysis of income levels, it was decided to use per capita income since this would reflect the socio-economic levels of the subjects participating in the study. The results from the one-way ANOVA comparing per capita family income are reflected in Table 4.

Table 4

Analysis of Variance for Per Capita Family Income (in South African Rands) of Left and Right TIA and Control Groups

Source	df	F
Per Capita Income	2,117	26.79***

****$p \leq 0.001$

The Tukey Studentized Range (HSD) test was computed to determine which groups differed significantly on per capita income. The results are shown in Table 5.

Table 5

Tukey's Test for Per Capita Income Comparing Left TIA, Right TIA and Control Groups

Groups compared	Per Capita Income in Rands	Absolute difference in Per Capita Income
Left TIA vs control	386.28 vs 236.13	150.15*
Right TIA vs control	259.05 vs 236.13	22.92
Left TIA vs Right TIA	386.28 vs 259.05	127.23*

*$p \leq 0.05$

The following conclusions may be drawn from the results in Table 5.

1. The left TIA group had a significantly higher-mean per capita income than the control group.

2. The mean per capita income of the left TIA group was significantly higher than that of the right TIA group.

3. There was no significant difference in the per capita income of the right TIA and control groups.

7.1.3 Education.

Education was determined by establishing the number of years of formal education completed by the subjects. A one-way ANOVA was computed to compare the mean number of years of education of the three groups. These results are shown in Table 6.

Table 6

Analysis of Variance for Education (in Years) comparing the Left TIA. Right TIA and Control Groups

Source	*df*	*F*
Education	2,117	3.91*

*$p \leq 0.05$

The Tukey Studentized Range (HSD) Test was then computed to establish which groups differed significantly.

Table 7

Tukey Test Comparing Left and Right TIA and Control Groups on Mean Number of Years of Education

Groups compared	Mean Education in Years	Absolute difference in Mean Education
Left TIA vs control	11.725 vs 11.825	0,100
Right TIA vs control	10.800 vs 11.825	1.025*
Left TIA vs Right TIA	11.725 vs 10.80	0.925*

Note. In Table 7, *$p \leq 0.05$

The following conclusions may be drawn from the findings in Table 7.

1. The control group had a significantly higher mean number of years of education than the right TIA group.

2. The left TIA group had a significantly higher mean number of years of education than the right TIA group, a finding which probably explained the higher per capita income of the former group.

3. The left TIA and control groups did not differ significantly on the mean number of years of education.

7.1.4 Overall Summary of Findings on Age, Education and Per Capita Income

Table 8 graphically represents the relative positions of each study group with respect to the findings of analyses on age, education and per capita income. Groups that occupy the same level within the table do not have statistically different mean values for that variable. Groups higher up in the table have statistically higher mean values on the variable.

Table 8

Relative Placing of Left TIA, Right TIA and Control Groups regarding Age, Education and Per Capita Income

Variables	Age	Education	Per Capita Income
Groups	Left TIA/RightTIA	Left TIA/Control	Left TIA
	Control	Right TIA	Right TIA/Control

Table 8 suggests the following general conclusions:

1. Overall, the left TIA group was significantly older, had a higher level of education and a higher per capita income.

2. The right TIA group was similar to the left TIA group only in mean age, and similar to the control in mean per capita income.

3. The right TIA group had significantly lower mean number of years of education than both the left TIA and control groups, respectively.

The significant differences among the left TIA, right TIA and control groups with regard to age, per capita income and education suggest that these groups were not comparable on these variables. Although an attempt was made to match the groups on age by selecting patients and controls from the same age decade, statistical analyses suggested that the transient ischaemic attack group were significantly older than the controls. Therefore it seems important to consider these significant findings in further analyses.

7.2 Regression Analyses for Pertinent Variables Predicting Neuropsychological Test Performance

In order to study the effects of transient ischaemic attacks in neuropsychological functioning, it becomes apparent from factor analytic studies (Chapter 3) that several factors may influence subjects' neuropsychological test performances. These factor analytic findings are reflective of the multidimensional nature of neuropsychological tests (Anderson, 1994; Lezak, 1995). Therefore, one approach to investigating the effects of transient ischaemic attacks on neuropsychological test performance was to conduct a regression analysis in which the relative contributions of important factors to test performance may be determined. Once these factors were identified, the experimental and control groups were then compared on these variables to determine if there was a significant difference between these groups. This statistical strategy was adopted in the present study in which two separate stepwise regression analyses were computed for the transient ischaemic attack and control groups, respectively, to determine which factors contributed to the test performances of the respective groups. The results obtained for the transient ischaemic attack and control groups for the different dependent variables are reflected in the following tables.

7.2.1 Regression Analyses on Test Scores obtained from Transient Ischaemic Attack Group

7.2.1.1 Stepwise Regression Analyses on Digit Span Test Scores.

The findings of the stepwise regression analyses on Digit Span Test were analysed in terms of Digit Span Forward, Digit Span Backward and Digit Span Total scores as suggested by Anderson (1994) and Lezak (1995). These results are reflected in Tables 9, 10 and 11.

Table 9

Summary of Stepwise Regression Analysis for Variables Predicting Performance on Digits Forward in the TIA Group (n = 80)

	Variable	Partial R^2	Model R^2	F
Step 1				
	Stenosis	0.2885	0.2885	31.6314***
Step 2				
	Laterality	0.1273	0.4158	16.7825*

Note. In Table 9, $^{***}p \leq 0.001$

$^{*}p \leq 0.05$

The findings in Table 9 indicate that two factors, stenosis and laterality contributed significantly to the variance of Digit Span Forward scores in the transient ischaemic attack group. Of these, degree of stenosis made a significant contribution of about 29 % and laterality about 13%.

Table 10

Summary of Stepwise Regression Analysis for Variables Predicting Performance on Digits Backward in the TIA Group (n = 80)

Variable	Partial R^2	Model R^2	F
Step I			
Stenosis	0.3748	0.3748	46.7666***

***$p \leq 0.001$

The findings in Table 10 indicate the stenosis was the only variable that entered the model, thus contributing significantly (about 37 %) to the performance in Digits Backward test in the transient ischaemic attack group.

Table 11

Summary of Stepwise Regression Analysis for Variables Predicting Performance on Digits Total in the TIA Group (n = 80)

	Variable	Partial R^2	Model R^2	F
Step 1				
	Stenosis	0.4092	0.4092	54.0232***
Step 2				
	Laterality	0.0374	0.4466	5.2020*

*$p \leq 0.05$

***$p \leq 0.001$

The findings in Table 11 indicate that stenosis formed a significant variable, contributing to the variance of scores on Digit Span Total, predicting about 41 % of the variance of scores. Laterality made a less significant contribution to this variance (about 3.7 %).

Next, the findings from the regression analyses performed on the PASAT test scores are presented.

7.2.1.2 Stepwise Regression Analyses on PASAT Test Scores

The PASAT was given to the subjects at the varying time intervals of stimulus presentation, i.e., 2.4, 2.0, 1.6 and 1.2 second intervals. Regression analyses were performed on the scores obtained from these independent test administrations and the findings are reflected in Tables 12, 13, 14 and 15.

Table 12

Summary of Stepwise Regression Analysis for Variables Predicting Performance on PASAT Scores (2.4. second) in the TIA Group (n = 80)

	Variable	Partial R^2	Model R^2	F
Step 1				
	Stenosis	0.2695	0.2695	28.7785***
Step 2				
	Laterality	0.0963	0.3658	11.6884**
Step 3				
	Age	0.0317	0.3975	4.1500*

*$p \leq 0.05$

**$p \leq 0.01$

***$p \leq 0.001$

As indicated in Table 12, degree of stenosis made the highest contribution (about 27%) to the scores on the PASAT (2.4. second presentation), although laterality (9%) and age (3%) made significant contributions to the variance of test scores.

Table 13

Summary of Stepwise Regression Analysis for Variables Predicting Performance on PASAT Scores (2.0 second) in the TIA Group (n = 80)

	Variable	Partial R^2	Model R^2	F
Step 1				
	Stenosis	0.2630	0.2630	27.8384***
Step 2				
	Laterality	0.0955	0.3588	6.3527*

*$p \leq 0.05$

***$p \leq 0.001$

Stenosis contributed significantly (about 26 %) to the variance of scores on the PASAT (2.0 second presentation), with laterality also contributing less significantly (about 10%) to the variance of test scores.

Table 14

Summary of Stepwise Regression Analysis for Variables Predicting Performance on PASAT Scores (1.6 second) in the TIA Group (n = 80)

Variable	Partial R^2	Model R^2	F
Step 1			
Stenosis	0.2630	0.2630	27.8384***
Step 2			
Laterality	0.1291	0.3921	16.3527*

*$p \leq 0.05$

***$p \leq 0.001$

As indicated in Table 14, stenosis contributed significantly (about 26 %) to the variance of the scores on PASAT (1.6 second presentation), while laterality contributed less significantly (about 13 %) to the variance of scores on this test.

Table 15

Summary of Stepwise Regression Analysis for Variables Predicting Performance on PASAT Scores (1.2 second) in the TIA Group (n = 80)

	Variable	Partial R^2	Model R^2	F
Step 1				
	Stenosis	0.2663	0.2663	28.3100***
Step 2				
	Laterality	0.0862	0.3525	10.2512*

*$p \leq 0.05$

***$p \leq 0.001$

As indicated in Table 15, stenosis contributed most significantly (about 27 %) to the variance of scores on PASAT (1.2 second presentation), with laterality contributing less significantly (about 9 %).

Next, the findings obtained from regression analyses performed on Trails A and Trails B test scores are presented.

7.2.1.3 Stepwise Regression Analyses on Trails A and Trails B Scores.

The regression analyses performed on Trails A and Trails B are presented sequentially in this section in order to provide some comparison of the findings.

Table 16

Summary of Stepwise Regression Analysis for Variables Predicting Performance on Trails A in the TIA Group (n = 80)

	Variable	Partial R^2	Model R^2	F
Step 1				
	Stenosis	0.1225	0.1225	10.8867**

**$p \leq 0.01$

The results in Table 16 suggest that stenosis contributed significantly to the variance of scores on Trails A (about 12%).

Table 17

Summary of Stepwise Regression Analysis for Variables Predicting Performance on Trails B in the TIA Group ($n = 80$)

	Variable	Partial R^2	Model R^2	F
Step I				
	Stenosis	0.5342	0.5342	89.4625***
Step 2				
	Education	0.0617	0.5959	11.7625*

*$p \leq 0.05$

***$p \leq 0.001$

As is evident in Table 17, stenosis was a significant contributor to the variance of scores on Trails B (about 53 %) and education was also found to be significant (about 6 %).

Next, the results of the regression analyses performed on the Block Design Test are presented.

7.2.1.4 Stepwise Regression Analyses on Block Design Test Scores.

Table 18

Summary Table of Stepwise Regression Analysis for Variables Predicting Performance on Block Design in The TIA Group (n = 80)

Variable	Partial R^2	Model R^2	F
Step 1			
Laterality	0.1474	0.1474	13.4855**

$^{**}p \leq 0.01$

The results in Table 18 suggest that stenosis contributed significantly to the variance of scores on Block Design (about 15 %).

Next, the findings of the regression analyses performed on the Verbal Fluency test are presented.

7.2.1.5 Stepwise Regression Analyses on Verbal Fluency Test Scores.

Table 19

Summary of Stepwise Regression Analysis for Variables Predicting Performance on Verbal Fluency in the TIA Group ($n = 80$)

	Variable	Partial R^2	Model R^2	F
Step 1				
	Laterality	0.2504	0.2504	26.0518***

***$p \leq 0.001$

The results in Table 19 suggest that laterality contributed significantly to the variance of scores on the Verbal Fluency Test (about 25 %).

Next, the findings from regression analyses performed on the Rey Auditory Verbal Learning test scores are presented.

7.2.1.6 Stepwise Regression Analyses on the Rey Auditory Verbal Learning Test Scores.

Independent regression analyses were performed for each trial of the Rey Auditory Verbal Learning Test given to the subjects. Only trial 1 showed significant findings and these results are reflected in Table 20.

Table 20

Summary of Stepwise Regression Analysis for Variables Predicting Performance on the Rey Auditory Verbal Learning test (Trial 1) in the TIA Group (n = 80)

Variable	Partial R^2	Model R^2	F
Step 1			
Laterality	0.2070	0.2070	20.3631**

**$p \leq 0.01$

Laterality formed a significant predictor variable contributing about 21 % to the variance of scores on trial 1 of the Rey Auditory Verbal Learning Test in the transient ischaemic attack group.

Next, the findings obtained from the regression analyses performed on the test scores in the control group are presented.

7.2.2 Stepwise Regression Analyses on Scores Obtained from Control Group

In an effort to establish which factors contributed significantly to the variance of scores in the control group, stepwise regression analyses were performed. Inspection of these results indicated that education emerged as the only predictor variable of neuropsychological test scores, and these findings were obtained on selected tests, that is, on the Digit Span and PASAT tests. These results are reflected in Tables 21 to 27.

7.2.2.1. Stepwise Regression Analyses on Digits Forward Scores.

Table 21

Summary of Stepwise Regression Analyses for Variables Predicting Performance on Digits Forward Scores in the Control Group (n = 40)

	Variable	Partial R^2	Model R^2	F
Step 1				
	Education	0.3068	0.3068	16.8213**

** $p \leq 0.01$

Education formed a significant predictor of performance on Digits Forward, accounting for about 30 % of the variance of scores on this test.

7.2.2.2. Stepwise Regression Analyses on Digits Backward Test Scores.

Table 22

Summary of Stepwise Regression Analyses for Variables Predicting Performance on Digits Backward Scores in the Control Group ($n = 40$)

	Variable	Partial R^2	Model R^2	F
Step 1				
	Education	0.1783	0.1783	8.2455**

**$p \leq 0.01$

Education formed a significant predictor of performance on Digits Backward, accounting for about 18 % of the variance of scores on this test.

7.2.2.3. Stepwise Regression Analyses on Digits Total Scores.

Table 23

Summary of Stepwise Regression Analyses for Variables Predicting Performance on Digits Total Scores in the Control Group (n = 40)

Variable	Partial R^2	Model R^2	F
Step I			
Education	0.3751	0.3751	22.8122**

**$p \leq 0.01$

Education formed a significant predictor of performance on Digits Total, accounting for about 37 % of the variance of scores on this test.

7.2.2.4. Stepwise Regression Analyses on PASAT Test Scores.

Table 24

Summary of Stepwise Regression Analyses for Variables Predicting Performance on PASAT Scores (2.4 second) in the Control Group (n = 40)

	Variable	Partial R^2	Model R^2	F
Step 1				
	Education	0.2928	0.2928	15.7293**

$^{**}p \leq 0.01$

Education formed a significant predictor of performance on the PASAT (2.4 second presentation), accounting for about 29 % of the variance of scores on this test.

Table 25

Summary of Stepwise Regression Analyses for Variables Predicting Performance on PASAT Test Scores (2.0 second) in the Control Group (n = 40)

Variable	Partial R^2	Model R^2	F
Step 1			
Education	0.2235	0.2235	10.9404**

**$p \leq 0.01$

Education formed a significant predictor of performance on the PASAT (2.0 second presentation), accounting for about 22 % of the variance of scores on this test.

Table 26

Summary of Stepwise Regression Analyses for Variables Predicting Performance on PASAT Test Scores (1.6 second) in the Control Group (n = 40)

	Variable	Partial R^2	Model R^2	F
Step I				
	Education	0.1943	0.1943	9.1667**

$^{**}p \leq 0.01$

From Table 26 it can be ascertained that education formed a significant predictor variable of performance on the PASAT (1.6 second presentation), accounting for about 19% of the variance on these test scores.

Table 27

Summary of Stepwise Regression Analyses for Variables Predicting Performance on PASAT Test Scores (1.2 second) in the Control Group (n = 40)

	Variable	Partial R^2	Model R^2	F
Step 1				
	Education	0.1481	0.1481	6.61**

$^{**}p \leq 0.01$

The results in Table 27 indicate that education formed a significant predictor of performance on the PASAT (1.2 second presentation), accounting for about 15 % of the variance of scores on this test.

The overall findings obtained in Tables 21 to 27 indicate that education formed the only significant predictor of neuropsychological test performance in the control group, and this finding was obtained on the Digit Span and PASAT tests.

7.3 Summary of Stepwise Regression Analyses on Test Performances in the Transient Ischaemic Attack and Control Groups

A survey of the results in Tables 9 to 20 indicate that consistently two significant predictors of performance on Digits Forward, Digits Backward, Digits Total, PASAT (all levels of presentation), Trails A and Trails B, Block Design, Verbal Fluency and Rey Auditory Verbal Learning Test (trial 1) were identifiable in the transient ischaemic attack group. Laterality made significant contributions to the variance of scores on Digits Forward, Digits Total, and PASAT (all levels), Block Design, Verbal Fluency and Rey Auditory Verbal Learning Test (trial 1). The contribution of laterality to the variance of scores on these tests ranged from 3 % on Digit Span Total to 25 % on the Verbal Fluency test.

Stenosis made significant contributions to the variance of scores on all tests, showing significant results with the exception of Block Design, Verbal Fluency and Rey Auditory Verbal Learning Test (trial 1). The contribution of stenosis to the variance of scores on these tests ranged from 12 % on Trails A to 53 % on Trails B.

Two demographic variables also formed significant predictors of performance on isolated tests. Age and education made significant contributions of about 3 % to the variance on PASAT (2.4 seconds) and 6 % on Trails B test scores, respectively.

Next, the neuropsychological test scores obtained in the left and right transient ischaemic attack and control groups were compared in statistical tests of difference.

7.4 Comparison of Neuropsychological Test Performance across Left and Right Transient Ischaemic Attack and Control Groups

The results obtained from the regression analyses indicated that stenosis and laterality formed the most important predictor variables of neuropsychological test performance in the transient ischaemic attack group, with age and education contributing to the variance of scores on PASAT (2.4 seconds) and Trails B. In the control group, education was the only predictor of neuropsychological test scores. Using these findings as a basis to test for differences in neuropsychological test performances across the left TIA, right TIA and control groups, a MANOVA design was employed entering stenosis, laterality, age and education as classification variables. When differences between groups classified on these variables were obtained, the Tukey HSD post-hoc test was used to determine which groups differed on those neuropsychological test scores that showed significant findings. This post-hoc test has been suggested by Keppel (1973) and SAS (1989). Only significant results are reflected in Tables 28 and 29.

Table 28

Summary Table of MANOVA Findings from comparison of Left TIA, Right TIA and Control Groups for Neuropsychological Test Scores

Source	df	Neuropsychological Test	F
Laterality	2	Digits Forward	29.50***
Laterality	2	Digits Backward	79.91***
Laterality	2	Digits Total	55.98***
Laterality	2	PASAT: 2.4 second	27.06***
Laterality	2	PASAT: 2.0 second	27.39***
Laterality	2	PASAT: 1.6 second	26.23***
Laterality	2	PASAT: 1.2 second	37.82***
Laterality	2	Trails A	23.33***
Laterality	2	Trails B	63.79***
Age	10	Trails B	3.12**
Laterality	2	Rey Auditory Verbal Learning: Trial 1	10.58***
Laterality	2	Block Design	22.20***
Age	10	Block Design	2.30*
Laterality	2	Verbal Fluency	16.24***

***$p \leq 0.001$

**$p \leq 0.01$

*$p \leq 0.05$

From the results in Table 28, it becomes apparent that two variables yielded significant effects in these analyses. Laterality significantly influenced performance on Digits Forward, Digits Backward, Digits Total, PASAT (all levels of the test), Trails A, Trails B, Rey Auditory Verbal Learning Test (trial 1), Block Design and Verbal Fluency.

Age formed a significant variable for performance on Trails B and Block Design. No other variables entered the MANOVA model and no significant interaction effects between age and laterality were obtained.

Since laterality formed a significant effect, the left and right transient ischaemic attack and control groups were compared on the Tukey test. Significant findings are shown in Table 29.

Table 29

Summary Table of Tukey Test Findings Comparing Left TIA (n = 40), Right TIA (n = 40) and Control Groups (n = 40) on Neuropsychological Test Performance

Neuropsychological Test	Groups Compared	Mean Difference
Digits Forward	Left TIA vs Right TIA	9.95 - 11.425*
	Left TIA vs Control	9.95 - 11.925*
Digits Backward	Left TIA vs Control	5.275 - 7.675*
	Right TIA vs Control	5.450 - 7.675*
Digits Total	Left TIA vs Right TIA	15.225 - 16.875*
	Left TIA vs Control	15.275 - 19.600*
	Right TIA vs Control	16.875 - 19.600*
PASAT: 2.4 second	Left TIA vs Right TIA	31.5 - 35.7*
	Left TIA vs Control	31.5 - 37.2*
PASAT: 2.0 second	Left TIA vs Right TIA	27.55 - 31.8*
	Left TIA vs Control	27.55 - 34.075*
	Right TIA vs Control	31.8 - 34.075*

Table 29 (continued)

Neuropsychological Test	Groups Compared	Mean Difference
PASAT: 1.6 second	Left TIA vs Right TIA	20.700 - 25.725*
	Left TIA vs Control	20.700 - 26.450*
PASAT: 1.2 second	Left TIA vs Right TIA	13.90 - 19.05*
	Left TIA vs Control	13.90 - 21.00*
Trails A	Left TIA vs Control	39.350 - 33.575*
	Right TIA vs Control	37.450 - 33.575*
Trails B	Left TIA vs Right TIA	123.20 - 112.20*
	Left TIA vs Control	123.20 - 82.95*
	Right TIA vs Control	112.20 - 82.95*
Rey Auditory Verbal Learning: Trial I	Left TIA vs Right TIA	6.475 - 5.625*
	Left TIA vs Control	6.475 - 5.975*
Block Design	Left TIA vs Right TIA	30.75 - 28.25*
	Left TIA vs Control	30.75 - 26.925*

Table 29 (continued)

Neuropsychological Test	Groups Compared	Mean Difference
Verbal Fluency	Left TIA vs Right TIA	31.150 - 26.425*
	Left TIA vs Control	31.150 - 28.350*

*$p \leq 0.05$

The following conclusions may be drawn from the results in Table 29.

1. The left transient ischaemic attack group performed significantly poorer than the right transient attack and control groups, respectively on: Digits Forward, Digits Total, PASAT (all levels), Trails B, Rey Auditory Verbal Learning Test (trial 1), Block Design and the Verbal Fluency tests.

2. The right transient ischaemic attack group performed significantly poorer than the controls on Digits Forward, Digits Backward, PASAT (2.0 seconds), Trails A and Trails B.

The results obtained in Tables 2 to 29 are discussed in Chapter 8 in terms of the hypotheses presented in Chapter 1.

CHAPTER EIGHT

Discussion of Hypotheses relating to Demographic Variables

8.1 Introduction

Tables 1 to 28 in Chapter 7 reveal the statistical findings of demographic and predictor variable analyses in the transient ischaemic attack and control groups. These results are discussed in terms of the hypotheses presented in Chapter 1.

8.2 Hypothesis One

There were no significant differences in age, education and SES (as indexed by per capita income) between the left and right transient ischaemic attack and control groups.

The findings obtained in Tables 1 to 7 indicate that there were significant differences in age, education and per capita income between the left and right transient ischaemic attack and control groups and therefore Hypothesis 1 is refuted. The results suggest that despite selecting patients in all study groups from the same age decade (that is, 50 to 60 years), the left (Mean = 55.75 years, S.D. = 2.61) and right (55.85, S.D. = 3.07) transient ischaemic attack groups were each significantly older than the control group (Mean = 53.85, S.D. = 2.25). The left and right transient ischaemic attack groups did not themselves differ significantly from each other in age.

These findings suggest that the 50 to 60 year age decade may not necessarily be considered a homogeneous range with regard to the incidence of cerebral transient ischaemic attacks. It seems that within this age decade, there may be cut-off age values above which the likelihood of a transient ischaemic attack increases. Studies have suggested that increasing age is a risk variable for the onset of transient ischaemic attacks (Wolf, Kanel, Cupples and D'Agostino, 1987). Age itself has been associated with atherosclerotic disease, which is considered to be the main underlying aetiological neuropathological process of transient ischaemic attacks. In their study, Wolf et al. (1987) found that the risk for atherothrombotic brain infarction increased with age with the incidence doubling in each successive decade. These authors suggested that the deposition of atheromatous material in the cerebral arterial walls led to a compromise in the arterial lumen with resulting degrees of stenosis and a concomitant reduction in blood supply to the brain.

In addition to the role of age, recent studies tend to report sex differences in these increased risk trends. For example, Toole, Lefkowitz, Chambless, Wijnberg, Paton and Heiss (1996) found that in their study conducted in four states in the U.S.A., transient ischaemic attacks increased with age in males ($\underline{p} \leq 0.02$) but not in females. Furthermore, the mean age of the transient ischaemic attack subjects in other epidemiological studies tended to be higher than that found in the present investigation. In the Toole et al. (1996) study, the mean age of the male patients was 76.93 years while in the study by Sempere, Duarte, Capezas and Claveria (1996) the mean age of a similarly described sample was 70.8 years. In the present study, although the transient ischaemic attack group (left, right and combined samples) was significantly older than the control group, the transient ischaemic attack sample was younger when compared with samples from other studies.

Several authors have argued that transient ischaemic attacks form an important predictor of stroke (Rutherford, 1995; Toole et al., 1996). It seems that, as a predictor variable, transient ischaemic attacks are found at an earlier age in the present study sample. These findings suggest that cerebral atherosclerosis may have an earlier onset in those patients included in the present study sample. Thus, these subtle yet significant differences in the mean age between transient ischaemic attack and general medical control patients are likely to have implications for neuropsychological test scores which are described later in this chapter.

When education was analysed, the left and right transient ischaemic attack groups were distinguishable from each other in that the left transient ischaemic attack group had a significantly higher mean education level than the right transient ischaemic attack group (Mean = 11.72, S.D. = 1.95 and Mean = 10.80, S.D. = 1.81, respectively). The control group had a significantly higher educational level than the right transient ischaemic attack group ($p \leq 0.05$), but did not differ significantly from the left transient ischaemic attack group. Although an extensive epidemiological literature review was not undertaken, the findings that educational levels may be associated with lateralised transient ischaemic attacks have not been reported in the literature reviewed in Chapter 5.

One possible explanation for the educational differences between the left and right transient ischaemic attack patients may be found in studies of the incidence of these cerebrovascular disorders, particularly in those using hospital-based samples. In general, these studies suggest that there is a higher incidence of left hemisphere transient ischaemic attacks in this patient group (Toole et al., 1996). In another study, Dhanaraj (1994) surveyed 115 hospital-based patients with acute thrombotic infarctions over a period of four years. He reported that among the transient ischaemic attack patients, 43% consisted of left and 39% of right hemisphere transient ischaemic attacks.

In the present study, while neither a comprehensive survey nor extensive review of the hospital records was undertaken, it appears that almost twice the number of left transient ischaemic attack patients visited these Neurological and Vascular Surgery Units (Chapter 6). One possible explanation for these findings is that the association of higher educational level and left transient ischaemic attacks may derive from differences in the knowledge base of these patients with regard to further medical management of these disorders. Some studies (for example, Gross (1995) suggest that a higher level of education implies more knowledge regarding personal health, which generally influences health practices.

Indirect support for the role of education in transient ischaemic attacks was provided in the study of Gross (1995) who reported on the management of cerebrovascular diseases. This author found that for those transient ischaemic attack patients with severe stenosis that did not lead to surgical intervention, patient education regarding the identification of symptoms, the need for prompt and continuing medical attention and risk factor modification was effective in preventative care. Gross (1995) further contends that patients who increase their knowledge base by reading on their medical conditions are likely to seek professional help more readily. Since transient ischaemic attacks are reported to be a critical predictor of stroke (Hobson, 1995), it is argued by Gross (1995) that by improving the knowledge base of these patients who are considered at risk for stroke, there is a greater likelihood for these patients to seek specialised medical care as well as to follow medical intervention strategies.

In the present study, the higher mean educational level of the left transient ischaemic attack group is difficult to explain. If the argument advanced by Gross (1995) that patients with higher educational level are likely to follow preventative self care is accepted, then it is expected that the left transient ischaemic attack patients would have undertaken medical therapy such as taking a regular dose of aspirin, which is reported to reduce the frequency of transient ischaemic attacks (Rutherford, 1995). Thus it appears that the higher mean education level of the left transient ischaemic attack group may be a random finding, due perhaps to the small and highly selected hospital sample used in the present investigation.

Significant lateralized differences in the transient ischaemic attack group were also obtained for per capita income. The left transient ischaemic attack group had a significantly higher mean income level (Mean = R374.13, S.D. = 128.03) when compared to the right transient ischaemic attack (Mean = R259.05, S.D. = 83.60) and control (Mean = R236.12, S.D. = 28.26) groups, respectively. Since per capita income was used as an index of SES, these findings suggest that the left transient ischaemic attack group was of higher SES when compared to the right transient ischaemic attack group and the controls, respectively, with the latter groups similar on this variable.

As with educational levels, a brief survey of the epidemiological studies has not yielded information on the income levels of transient ischaemic attack patients nor have there been studies relating SES to lateralised transient ischaemic attacks. The findings that left transient ischaemic attack patients have a higher mean per capita income level may be explained in an argument similar to that advanced for the differences in educational levels. The higher mean income of this group may be associated with the higher mean educational level of this group, and may even reflect the type of occupations of these patients which also provides an index of SES (Williams, Currie, Wright, Elton and Beattie, 1997). In this study, type of occupation was not elicited from the patients thereby limiting the conclusions that may be drawn regarding the role of SES in these cerebrovascular diseases. Thus, the higher per capita income of the left transient ischaemic attack group may be due to sample selection procedures adopted in this study which was based within a hospital setting. The finding of higher income levels in the left transient ischaemic attack group cannot therefore be treated in isolation from the other demographic variables studied.

While not implying the causal nature of any of the demographic variables studied, the following model reflects the influences of age, education and SES obtained in this study.

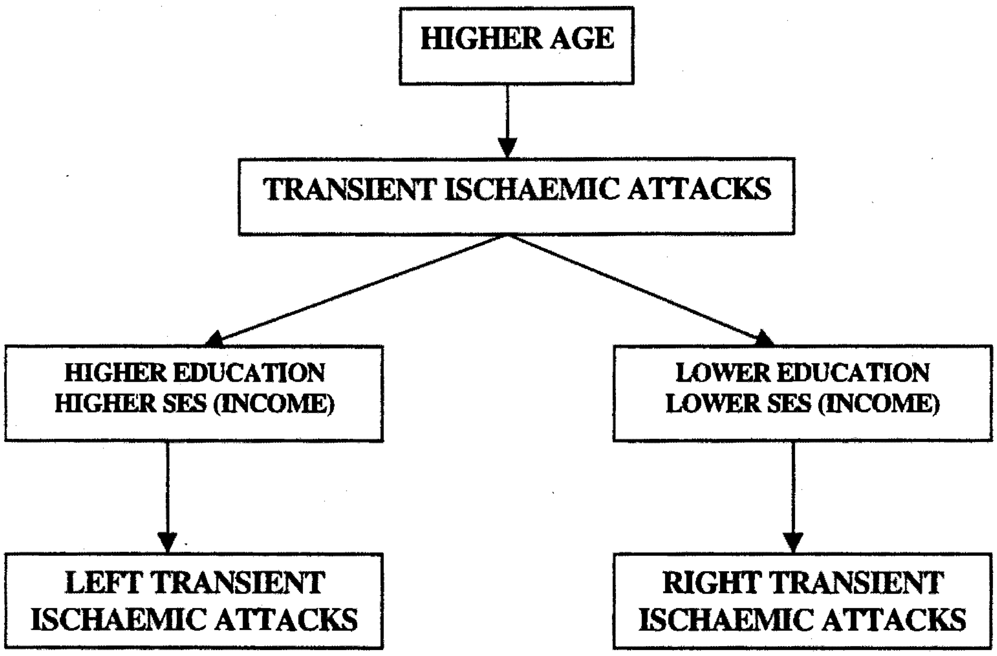


Figure 8. Proposed model showing the influences of age, education and SES in carotid transient ischaemic attacks.

No interaction effects of age, education and per capita income levels were found in the ANOVA analyses. However, an examination of the demographic features of the study groups suggests several pertinent findings. The demographic variables studied appear to characterize the left transient ischaemic attack group in that they were older, had a higher educational level and earned a higher per capita income (higher SES). On the other hand, the right transient ischaemic attack group was similar in age to the left transient ischaemic attack group but had a lower educational level and lower per capita income (lower SES). This complex of pertinent demographic variables describing left and right transient ischaemic attacks has not been previously reported in the studies reviewed in Chapter 5 and may characterize the sample of transient ischaemic attack patients attending specialised hospital units.

These results suggest that despite their similarity in age, the left and right transient ischaemic attack groups may be differentiated on critical demographic variables relating to educational level and SES. However, these findings are derived from a small sample of carefully selected hospital patients and therefore remain to be researched in large-scale epidemiological studies.

Next, in the presence of the obtained demographic similarities and differences and various medical variables elicited in this study, the hypotheses regarding the predictive value of stenosis with regard to neuropsychological test scores in the transient ischaemic attack group are discussed.

8.3 Hypothesis Two

Stenosis did not form a significant predictor of neuropsychological test scores in the combined transient ischaemic attack group.

As reflected in Table 30, stenosis formed a significant contributor to the variance of scores on certain neuropsychological tests in the combined transient ischaemic attack group and thus Hypothesis 2 was refuted.

Table 30

Summary Table of Stenosis as Predictor of Neuropsychological Test Scores in the Transient Ischaemic Attack Group (n = 80)

Neuropsychological Test	% Predicted	F
Digits Forward	28.85	31.63***
Digits Backward	37.48	47.77***
Digits Total	40.92	54.02***
PASAT: 2.4 seconds	26.95	28.78***
PASAT: 2.0 seconds	25.30	25.82***
PASAT: 1.6 seconds	26.30	27.74***
PASAT: 1.2 seconds	26.63	28.31***
Trails A	12.25	10.89***
Trails B	53.42	89.46***

***$p \leq 0.001$

The results in Table 30 revealed differences in the predicted variances on certain neuropsychological test scores in the combined transient ischaemic attack group. The proportion of variance significantly predicted by stenosis ranged from a low value of 12.25% for Trails A ($F = 10.89$, $p \leq 0.001$) to a high of 53.42% for Trails B ($F = 89.46$, $p \leq 0.001$). These findings suggest that neuropsychological functions have a differential sensitivity to stenosis since some test scores were not predicted by this variable while others were predicted to varying degrees. The tests not predicted by stenosis included the Rey Auditory Verbal Learning Test, Block Design, Verbal Fluency and the Wisconsin Card Sorting Test (Perseverative Score).

Two principles may be adopted to explain these findings. Firstly, the results may be interpreted in terms of the psychometric properties of the tests. Second, the findings may be explained according to the proposals presented in Chapter 3 which suggest that the distribution of function in the brain may be viewed in terms of the modular theories of cognitive neuropsychology.

The predictive power of stenosis with regard to neuropsychological test performances may first be examined from a psychometric viewpoint of the tests administered. It becomes apparent that in the transient ischaemic attack group, stenosis was related to scores on certain neuropsychological tests. A closer examination of the results in Table 30 suggests that stenosis was significantly related to those neuropsychological tests associated with circumscribed areas of neurocognitive functioning. Thus, an appropriate approach to interpret these findings would be examine which test performances were predicted by stenosis and what functions are measured by these tests.

In terms of the neurocognitive areas described in Chapter 3, the test scores on Digit Span (Forward, Backward and Total) and the PASAT (all levels) may be viewed as a measurement of attention (Anderson, 1994). All measures of Digit Span and PASAT were significantly predicted by stenosis suggesting that those neuropsychological functions measured by these tests were associated with stenosis. One approach therefore to explain these findings would be to relate a cognitive model of attention to the findings of factor analytic studies of Digit Span and the PASAT.

Attention. as a neuropsychological construct, has been determined to comprise several dimensions which may be assessed using different tests (Cohen, 1993). Summarizing the findings from various factor analytic studies, Anderson (1994) reported that the primary areas of neuropsychological functioning assessed by both Digit Span and PASAT relate to immediate, focussed and divided attention. Kaufman, McLean and Reynolds (1991) found that Digits Forwards measures a cognitive function related to the efficiency of attention which they termed freedom from distractibility.

In the present study, some aspects of attention appear to be significantly predicted by stenosis--focussed attention (Digit Span Forward and Backward), divided attention (Digit Span Backward and the PASAT) and sustained attention (PASAT) (Gronwall and Wrightson, 1977; Spreen and Strauss, 1991; Anderson, 1994).

Attention has been previously reported to be a neuropsychological function that was impaired in carotid transient ischaemic attacks. For example, in the early studies of Diener, Hamster, and Seboldt (1984), it was reported that patients with stenosis in the carotid arteries revealed deficits in attention particularly when the associated tasks were performed under stress. More recently, using evoked potentials, Taghavy and Hamer (1995) reported that N250 and P300 latencies on the presentation of visual stimuli were significantly longer in both symptomatic and asymptomatic transient ischaemic attack patients, with both groups showing significant carotid artery stenosis. In the study sample of Taghavy and Hamer (1995), both left and right transient ischaemic attack groups with evidence of unilateral carotid stenosis were analysed together suggesting that both the left and right hemispheres may have independent roles in focussed attention in the visual modality. These authors concluded that both N250 and P300 provide electrophysiological evidence of the lowered attention-processing capacity of patients with carotid artery stenosis.

In the present study, support for the proposals of Taghavy and Hamer (1995) is provided in that various components of attention proposed by Spreen and Strauss (1991) and Anderson (1994) were influenced by carotid stenosis. However, other dimensions of neuropsychological functioning are also associated with Digit Span and PASAT, for example, these tests are reported to load on immediate verbal memory (Spreen and Strauss, 1991; Von Zomeren and Brouwer, 1987). Thus, the view that both Digit Span and the PASAT are measures of both attention and immediate verbal memory should not be considered inconsistent with each other, but rather that both attention and short-term memory are necessary elements from the viewpoint of information processing.

In support of this argument, Von Zomeren and Brouwer (1992) further proposed that focussed attention and short-term memory cannot be effectively discriminated in practical situations. These authors note that working memory forms an important component of the memory process. Information in working memory is retained for a few seconds and this aspect justifies the use of the term memory. At the same time, the information presents a load on the limited processing capacity of the system, and can therefore also be discussed in terms of attention. Therefore, it may be concluded that in the sample of transient ischaemic attack patients, both left and right unilateral carotid stenoses are associated with scores on neuropsychological tests measuring the various dimensions of attention and immediate verbal memory.

Carotid stenosis also significantly predicted a proportion of the variance on both Trails A and Trails B in the combined transient ischaemic attack sample, although these regression values were discrepant for these tests. With regard to Trails A, although stenosis was the first factor to enter the regression model, only 12.25% of the variance was predicted ($F = 10.89$, $p \leq 0.001$). For Trails B on the other hand, about 53.42% of the variance of scores was predicted ($F = 89.46$, $p \leq 0.001$) suggesting that stenosis accounted for more than half of the variance for performance on this test. These findings suggest that while the neuropsychological functions measured by Trails A and Trails B are influenced by stenosis, these tests are differentially sensitive to this independent variable.

Factor analytic studies by Corrigan and Hinkeldey (1987) suggest that the primary areas of functioning assessed by Trails A include number recognition, visual scanning, visual-spatial functioning and visuomotor co-ordination. According to Reitan and Wolfson (1993), Trails A is considered to be effective in discriminating brain damaged and non-brain damaged groups. However, in the present study, while stenosis formed a significant predictor of performance on Trails A, only a small proportion of the variance of scores was predicted by stenosis. It becomes apparent that factors other than stenosis also made a significant contribution to performance on Trails A.

With regard to Trails B, 53.42% of the score variance of scores was significantly predicted by carotid stenosis in the combined transient ischaemic attack group ($F = 89.46$, $p \leq 0.001$). This finding suggests that Trails B is a more sensitive measure of neuropsychological dysfunction in transient ischaemic attacks since a large proportion of the variance (more than half) was predicted by stenosis. Support for the usefulness of Trails B as a measure of neuropsychological dysfunction has been forthcoming from various studies. Lezak (1995) classifies Trails B as a measure of executive functioning. Stuss (1993) and Anderson (1994) identify shifting cognitive set as the specific characteristic of executive functioning that is measured by Trails B. Corrigan and Hinkeldey (1987) indicate that while number and letter recognition and visual scanning are important functions measured by Trails B, cognitive flexibility is a more critical aspect of executive function assessed by this test.

Von Zomeren and Brouwer (1992) noted that in addition to cognitive flexibility, Trails B also required divided attention since performance on this test depended upon simultaneously changing attention to either symbols or numbers alternatively and sequentially. These authors argued that, as opposed to Trails A in which more sustained attention is required, the performance of Trails B requires sustained and divided attention. Corrigan and Hinkeldey (1987) also note that divided attention may be related to cognitive flexibility since alternate ideas and strategies are entertained. On the basis of these suggestions, it appears therefore that changes in cognitive flexibility (a component of executive functioning according to Kerns and Mateer, 1996) and divided attention may be sensitive to carotid stenosis, both of which are reportedly assessed by Trails B and not by Trails A (Reitan and Wolfson, 1993). The finding that stenosis offered the highest prediction of performance on Trails B when compared to all other tests administered further suggests that performance on this test entails the complex involvement of both sustained and divided attention as well as cognitive flexibility functions that may sensitive to the effects of stenosis.

In summary, the regression analyses performed for the combined transient ischaemic attack group indicate that several dimensions of neuropsychological functions may be predicted by carotid stenosis. On the basis of the findings in this study, it appears that these dimensions relate primarily to attention (focussed, sustained, divided) and cognitive flexibility.

Next, the findings from the stepwise regression analyses for the left and right transient ischaemic attack groups are presented. These analyses were performed to establish whether those functions predicted by stenosis in the combined transient ischaemic attack group could also be predicted independently by stenosis in the left and right transient ischaemic attack groups.

8.4 Hypothesis Three.

Stenosis did not form a significant contributor to the variance of scores in the left and right transient ischaemic attack groups, respectively.

The results of testing Hypothesis 2 indicated that stenosis significantly predicted the variance of scores on tests primarily measuring attention and cognitive flexibility and Hypothesis 3 was therefore rejected. However, the left and right transient ischaemic attack groups were differentiated on education and per capita income suggesting that these variables may influence the predictive ability of stenosis with regard to neuropsychological test scores. Thus, independent stepwise regression analyses performed in these respective study groups revealed similarities and differences in the predictive power of stenosis. Neither education, age nor per capita income (SES) entered the regression model of the left or right transient ischaemic attack groups. The results are shown in Tables 31 and 32.

Table 31

Summary Table of Stenosis as Predictor of Neuropsychological Test Scores in the Left Transient Ischaemic Attack Group (n = 40)

Neuropsychological Test	% Predicted	F
Digits Forward	22.51	11.04*
Digits Backward	40.25	25.60***
Digits Total	35.99	[illegible]1.37***
PASAT: 2.4 seconds	42.98	[illegible]8.64***
PASAT: 2.0 seconds	46.24	[illegible]2.68***
PASAT: 1.6 seconds	58.80	[illegible]4.23***
PASAT: 1.2 seconds	49.40	[illegible]7.09***
Trails A	26.46	[illegible]3.67***
Trails B	64.08	67.80***
WCST: Perseverative Error Score	14.01	6.19*

*$p \leq 0.05$

***$p \leq 0.001$

From Table 31 it becomes apparent that, for the left transient ischaemic attack group, stenosis predicted those neuropsychological test score variances that were obtained for the combined transient ischaemic attack group. In addition, the Wisconsin Card Sort Test Perseverative Error score variance was also predicted by stenosis ($F = 6.19$, $p \leq 0.05$). About 14.01% of the Perseverative Error Score variance was predicted by stenosis.

Different results were obtained for the regression analyses conducted in the right transient ischaemic attack group. Stenosis significantly predicted variance on Digits Forward, Backward and Total, PASAT (2.4 seconds) and Trails B. These results are shown in Table 32.

Table 32

Summary Table of Stenosis as Predictor of Neuropsychological Test Scores in the Right Transient Ischaemic Attack Group (n = 40)

Neuropsychological Test	% Variance Predicted	F
Digits Forward	29.50	15.90***
Digits Backward	36.37	21.72***
Digits Total	40.55	25.92***
PASAT: 2.4 seconds	9.46	4.31*
Trails B	39.16	24.46***

*$p \leq 0.05$

*$p \leq 0.001$

Based on the results reflected in Tables 31 and 32, Hypothesis 3 is refuted since the variances of several tests were significantly predicted by stenosis in the left and right transient ischaemic attack groups. The results suggest that there are both similarities and differences in the implications for neurocognitive functioning in left and right transient ischaemic attack patients. In order to understand these implications, the significance of the regression findings will be considered for each test independently.

Stenosis was associated with Digit Span Test scores (Forward, Backward and Total) in both the left and right transient ischaemic attack groups with regression values approximating each other. These results suggest that the performance of the Digit Span Tests are dependent on both hemispheres and stenosis in either hemisphere predicts the scores on these tests. These findings appear to be consistent with those of Black (1986) who reported that neither Digits Forward nor Digits Backward is a reliable indicator of laterality.

When the percentages of variance predicted by stenosis for Digits Forward, Digits Backward and Digits Total in the left, right and combined transient ischaemic attack groups are compared, little differences in these values become apparent (see Tables 30, 31 and 32). Thus, these results suggest that stenosis does not significantly predict a differential test performance on Digit Span in the left and right transient ischaemic attack groups. It can be concluded from these results that focussed attention (Digits Forward), divided attention (Digits Backward), and immediate verbal memory (Digit Span Total) are therefore similarly influenced by stenosis in either left and right carotid artery.

The results obtained for the PASAT tests are different to those obtained for Digit Span in the left and right transient ischaemic attack groups. In the left hemisphere, stenosis signficantly predicted performance at all levels of the PASAT. Furthermore, there is a significant increase in the percentage of predicted PASAT score variance at all levels of stimulus presentation in the left transient ischaemic attack group when these values are compared to those obtained for the combined transient ischaemic attack group (see Tables 30 and 32). These findings suggest that performance on the PASAT is more likely associated with stenosis in the left hemisphere.

Factor analytic studies have indicated that the PASAT is a measure of sustained attention, immediate verbal memory (Spreen and Strauss, 1991) and divided attention (Van Zomeren and Brouwer, 1987). These functions, in turn, have been linked to the information processing capacity of the individual (Van Zomeren and Brouwer, 1992). Some studies have shown that the PASAT is a measure of complex information processing. For example, in a study on chronic fatigue syndrome patients, the PASAT has been shown to be effective in elucidating information-processing deficiencies. These findings were obtained in chronic fatigue syndrome patients with or without an accompanying diagnosis of depression who were compared to matched controls (Deluca, Johnson, Ellis and Natelson, 1997).

Differences in performances obtained from the various levels of stimulus presentation on the PASAT have been previously reported in the literature. Gronwall (1977) found that the rate of stimuli presentation may be critical to this test administration in eliciting information processing deficits. Gronwall (1977) reported that an inter-stimulus interval of two seconds best discriminates between normal controls and subjects who had sustained mild head injuries. These findings on the PASAT suggest that at different levels of stimulus presentation, varying demands of information processing occur which may relate to varying stages of the disease process under investigation.

In the present study, stenosis significantly predicted the score variances at all levels of stimulus presentation in the left transient ischaemic attack group. These findings suggest that information processing at all levels may present difficulties for these patients. Divided attention forms a critical component of information processing particularly as measured on the PASAT. These results appear to be consistent with the general analytical functioning associated with the left hemisphere (Kolb and Whishaw, 1996).

The findings obtained for the right transient ischaemic attack group (Table 32) were different to those elicited in the left transient ischaemic attack group. Stenosis significantly predicted the PASAT score variance on the 2.4 second presentation in the right transient ischaemic attack group. When compared to the variances predicted in the combined and left transient ischaemic attack groups (Tables 30 and 31, respectively) at the 2.4 second level of stimulus presentation, the predicted variance for the right transient ischaemic attack group was significantly smaller, i.e., 9.46% (F = 9.46, $p \leq 05$). While cerebral lateralising effects on the PASAT have not been previously reported in the literature, the present study suggests that there may be differences in the performances of left and right transient ischaemic attack patients on the PASAT which need to be investigated in further analyses. These differences may arise from the neurocognitive areas of functioning the test measures which appear to be differentially influenced by stenosis in the left and right hemispheres, respectively.

The finding that stenosis predicted performance on the PASAT only at the 2.4 second interval of presentation supports that contention that there may be differences in the rate of information processing between the left and right hemispheres (Van Zomeren and Brouwer, 1992), and this may be particularly noticeable on the PASAT in transient ischaemic attack patients. These findings support the view that transient ischaemic attacks in the left and right hemispheres have different implications for neuropsychological functioning and thus these study groups need to be treated independently.

Further inspection of the results in Table 31 indicate that stenosis predicted 26.46% of the score variance on Trails A in the left transient ischaemic attack group. Stenosis did not predict Trails A score variance in the right transient ischaemic attack group (Table 32). Furthermore, the proportion of Trails A score variance predicted by stenosis in the left transient ischaemic attack group was more than double ($F = 13.67$, $p \leq 0.001$) than that obtained for the combined transient ischaemic attack group. These findings suggest that stenosis of the left carotid artery had a greater association with performance on Trails A than when the groups were collapsed.

While visual scanning and visuo-spatial functioning have been reported to be the main factor structure of Trails A (Corrigan and Hinkeldey, 1987), the role of attention in effectively completing this task has been suggested in other studies. Van Zomeren and Brouwer (1992) noted that although Trails A is primarily a visual search task, it can also be considered a minimally divided attention task as the subject must keep track of numbers while searching for the next circle. Symbol search and recognition are considered language related tasks and are therefore mediated in the left hemisphere. While the role of visual search appears to be an important factor in completing Trails A, attention may also be an important requirement for this test and this appears to be related to the left hemisphere. These results appear to be consistent with the results on the Digit Span and PASAT tests which suggest that deficits in attention appear to be the primary finding associated with transient ischaemic attacks in the left carotid artery.

The findings of the regression analyses on Trails B were different to those obtained for Trails A. Stenosis significantly predicted the score variance on Trails B in both the left and right transient ischaemic attack groups. The variance predicted for the left transient ischaemic attack group was 64.08% ($F = 67.80$, $p \leq 0.001$) and the equivalent valuefor the right transient ischaemic attack group was 39.16% ($F = 24.46$, $p \leq 0.001$). These findings suggest that while stenosis was associated with Trails B scores in both the left and right transient ischaemic attack groups, this association was stronger in the left group.

When the respective predicted variances of scores on Trails B in the left and right transient ischaemic attack groups are compared to the value obtained for the combined transient ischaemic attack group, an interesting finding emerges. The figure obtained for the combined group was 53.42% ($F = 89.46$, $p \leq 0.001$) which was below the corresponding value obtained for the left transient ischaemic attack group (64.08%, $F = 67.80$, $p \leq 0.001$), but higher than that obtained for the right transient ischaemic attack group (39.16%, $F = 24.46$, $p \leq 0.001$). These results suggest that while stenosis in either the left or right hemisphere was associated with scores on Trails B, this association was strongest for the left hemisphere with a greatest proportion of the variance predicted by stenosis.

Factor analytic studies suggest that Trails B loads on several factors that underlie this test --number and letter recognition, visual scanning, visual-spatial functioning and cognitive flexibility (Corrigan and Hinkeldey, 1987; Reitan and Wolfson, 1993). The factor structure for Trails A was reported by Corrigan and Hinkeldey (1987) and Reitan and Wolfson (1993) as comprising number recognition, visual scanning and visual-spatial functioning which appears to be similar to that reported for Trails B. However, the difference in the factor structures of these tests suggests that Trails A does not load on cognitive flexibility, considered to be a component of executive functioning (Anderson, 1994). Therefore the results obtained suggest that cognitive flexibility (as measured on Trails B) is associated with both left and right hemisphere functioning and may represent a function more sensitive to stenosis.

The score variance of one other test was signficantly predicted by stenosis in the left transient ischaemic attack group (Table 31). Although the correlation was low, stenosis signficantly predicted 14.01% of the Wisconsin Card Sorting Test Perseverative Error Score ($F = 6.19$, $p \leq 0.05$). The Wisconsin Card Sort Test Perseverative Error Score entered the regression equation when independent analyses for the left and right transient ischaemic attack groups were conducted suggesting that stenosis in the left carotid artery was associated with this score.

The Perseverative Error Score of the Wisconsin Card Sortiing Test has been considered by certain authorities to be a more reliable index of cerebral impairment (Lezak, 1995). Perseverative Errors on the Wisconsin Card Sorting Test occur when the subject continues to sort the stimuli according to a previously successful principle. According to Cohen (1993), the Perseverative Error score is useful for documenting problems in concept formation, profiting from correction, and conceptual flexibility.

Support for the usefulness of the Wisconsin Card Sorting Test Perseverative Error score has been provided in some studies. Milner (1963) reported the Perseverative Error Score findings obtained on patients undergoing surgery for focal epilepsy. In her study, Milner (1963) found that patients with dorsolateral frontal epilepsy had significantly more perseverative errors than a control group matched for age and Full Scale IQ. She attributed these difficulties to a failure in conceptual flexibility and concept formation among these patients.

There appears to be little consistency between the number of Perseverative Errors and the lateralisation of brain damage. Taylor (1979) reported an association between the number of Perseverative Errors and dorsolateral lesions of the frontal lobes, but found that more patients with left-sided lesions displayed such difficulties after lobectomy than those patients with damage in the right hemisphere. Similar findings were reported by Grafman, Jonas and Salazar (1990) who found that patients with missile wounds to the left anterior area of the brain had a higher number of Perseverative Errors.

Drewe (1974) found a contrasting result in that patients with right frontal damage made more Perseverative Errors than those with left-sided lesions. Similarly, Hermann, Wyler and Ritchie (1988) found a significant association between right temporal lobe seizure foci and increased Perseverative Errors. The study by Martzke, Swan and Varney (1991) found that in a group of 20 head trauma patients whom they alleged had orbitobasal frontal damage on the basis of their anosmia, only eight made more Perseverative Errors than a cut-off score set at the 5th percentile for normal subjects.

A more recent study on the factor structure of the Wisconsin Card Sorting Test was conducted by Greve, Brooks, Crouch, Williams and Rice (1997) among normal university students and a mixed clinical sample. A two-factor model for the combined group was obtained accounting for 91% of the variance with Factor I accounting for 70% of this value. Variables loading on this factor were reported as Total Errors (0.98), Perseverative Errors (0.95) and number of Perseverative Responses (0.93). The cognitive processes associated with scores on Factor I were described as abstract thinking, concept formation and conceptual set shifting.

The variable loading on Factor II was reported as Total Correct (0.74). The cognitive processes underlying Factor II were reported as memory, motivation and attention. The authors concluded that while the component processes associated with each factor may be dissociable, the Wisconsin Card Sorting Test was unable to distinguish among them. They therefore proposed that Factor I represents an "undifferentiated executive function" (p. 284).

Factor analytic studies by Daigneault, Braun, Gilbert and Proulx (1988) suggest that when the Wisconsin Card Sorting Test Perseverative Error scores were analysed, failure to maintain set (0.44) and planning (0.25) showed significant components. While the equivocal status regarding the localization sensitivity and the ability of the Wisconsin Card Sorting Test to identify specific neurocognitive processes become apparent from several studies, the results from the present study suggest that transient ischaemic attacks in the left hemisphere are associated with Perseverative Error responses. Therefore it appears that the Perseverative Error score is a sensitive measure of executive dysfunction and the findings suggest that difficulties in conceptual flexibility may be predicted by stenosis in the left cerebral artery.

The findings obtained thus far suggest that stenosis forms a salient predictor of selected neuropsychological test score variances in the left and right transient ischaemic attack groups. Since these two experimental groups were compared with a control group without historical evidence of cerebrovascular disease, it was`hypothesized that demographic variables may predict neuropsychological test scores in the controls. This hypothesis was tested and the results and discussion are presented next.

8.5 Hypothesis Four

Age, education and per capita income did not form significant predictors of neuropsychological test score variance in a control group of medical patients.

Hypothesis 4 was tested by conducting a stepwise regression analysis on the neuropsychological test scores of the control group entering age, education and per capita as predictor variables. The results reflected in Table 33 below indicate that education formed a significant predictor of score variance and these effects were obtained on certain neuropsychological tests. Hypothesis 4 was therefore rejected.

Table 33

Summary Table of Education as Predictor of Neuropsychological Test Scores in the Control Group (n = 40)

Neuropsychological Test	% Variance Predicted	F
Digits Forward	30.68	16.82***
Digits Backward	17.83	8.25**
Digits Total	37.51	22.81**
PASAT: 2.4 seconds	29.28	15.73**
PASAT: 2.0 seconds	22.35	10.94**
PASAT: 1.6 seconds	19.43	9.17**
PASAT: 1.2 seconds	14.81	6.61**

***$p \leq 0.001$

**$p \leq 0.01$

The results in Table 33 indicate that education significantly predicted the score variance of the Digit Span and PASAT tests in the control group. Of the Digit Span Tests, the strongest correlation was obtained with Digits Total ($r = 0.61$, $p \leq 0.05$) and Digits Forward ($r = 0.55$, $p \leq 0.05$), with Digits Backward showing a lower correlation value of 0.42 ($p \leq 0.05$).

Since Digits Total is derived from the cumulative score of Digits Forward and Digits Backward, its usefulness as a reliable index of brain dysfunction has been questioned (Kaplan, Fein, Morris & Delis, 1991). Alternatively, Kaplan et al. (1991) suggest that treating Digits Forward and Digits Backward independently may elicit the similarities and differences in underlying cognitive processes, a process consistent with the theoretical viewpoint outlined in Chapter 3 of this study.

Previous studies tend to support the association of education with Digits Forward performance. Ardilla, Rosselli and Ostrosky-Solis (1992) reported that among the normal aged over 60 years, there was a decided education effect on Digits Forward performance with individuals at higher education levels performing significantly better than those in lower education levels.

In the present study, the finding of a stronger relationship between education and Digits Forward appears to support the findings of Ardilla, Rosselli (1992). Digits Forward has been described as a measure of freedom from distractibility (Kaufman et al. 1991) and focussed attention (Anderson, 1994) which suggests that, in the absence of any evidence of cerebrovascular or psychiatric disease, these measures of attention are strongly influenced by education.

The association of education and PASAT performance has been reported inconsistently in the literature. Stuss, Stethem and Poirier (1987) found that education significantly affected performance on the PASAT among adults. Britain, LaMarche, Reeder, Roth and Boll (1991) on the other hand found that in their studies while IQ affected PASAT performance, there were no significant education effects.

In the present study, the highest correlation between education and PASAT scores was obtained for stimulus presentation at 2.4 seconds ($r = 0.54$, $p \leq 0.05$). There is a gradual reduction in the strength of the relationship with reducing inter-stimulus intervals, with correlation values declining to 0.47, 0.44 and 0.38 for the 2.0-, 1.6- and 1.2-second stimulus presentations, respectively. These results suggest that with decreasing inter-stimulus intervals, the relationship between education and performance on the PASAT decreases suggesting that factors other than education may influence test performances.

The findings from the regression analyses performed on the control group indicate that education formed a significant influence on neuropsychological tests measuring attention. The findings regarding the significant association of education with Digit Span and PASAT test performances is unexpected since earlier ANOVA results suggested that the control group was similar to the left transient ischaemic attack group in education, but significantly higher than the right transient ischaemic attack group on this variable. These results suggest that there is a varied influence of demographic variables on neuropsychological test performances and these influences have implications for the neuropsychological sequelae of transient ischaemic attacks. It becomes apparent from the regression analyses conducted thus far that the elucidation of the neuropsychological sequelae of transient ischaemic attacks should be undertaken by independent analyses of left and right transient ischaemic attack groups.

To conclude the discussion on the prediction of neuropsychological test scores in transient ischaemic attack and control samples, a summary of the findings obtained will be presented next.

8.6 Summary of Findings Obtained from Regression Analyses

A review of the regression analyses in the preceding sections suggests that stenosis emerged as a salient predictor of selected neuropsychological test score variances in the combined, as well as in the left and right transient ischaemic attack groups. These findings, in turn, suggest that circumscribed areas of neurocognitive difficulties may be associated with stenosis in the left and right transient ischaemic attack groups.

With respect to the combined transient ischaemic attack group, score variances on the Digit Span (Forwards, Backwards and Total), the PASAT (all levels), Trails A and Trails B were significantly predicted by stenosis. At this initial level of analysis, the findings suggested that the performance on these tests were closely associated with both left and right hemisphere functioning.

However, subsequent independent regression analyses conducted on the left and right transient ischaemic attack groups yielded a more refined picture of these findings. Stenosis in the left carotid artery appeared to predict the score variances obtained in the combined transient ischaemic attack group regression model with the values changing significantly on some tests.

While there was a close similarity in the predicted variances of the Digit Span tests, differences were obtained for the PASAT when the left, right and combined transient ischaemic attack groups were compared. At all levels of stimulus presentation, the predicted values for the PASAT increased significantly in the left transient ischaemic attack group suggesting that stenosis in the left carotid artery was a better predictor of performances on this test. A similar trend was found for Trails A and Trails B whereby the predicted score variance more than doubled for the left transient ischaemic attack group when compared to the combined sample. In addition, the Wisconsin Card Sorting Test Perseverative Error score was significantly predicted by stenosis in the left transient ischaemic attack group. Using the findings from factor analytic studies, these results suggest that the areas of neurocognitive functioning predicted by stenosis in the left hemisphere relate to attention (focussed, sustained and divided) and cognitive flexibility.

A slightly different picture emerged from the regression analyses performed on scores in the right transient ischaemic attack group. The predicted variances for the Digit Span tests were similar to those obtained for the combined group suggesting that focussed, sustained and divided attention are predicted to the same extent by stenosis in the right hemisphere. However, for the PASAT (2.4 second presentation), the score variance predicted was significant but low ($r = 0.3$, $p \leq 0.05$) (Table 32).

However, stenosis significantly predicted Trails B variance (39.16%) in the right transient ischaemic attack group suggesting that there was a strong correlation ($r = 0.65$, $p \leq 0.05$) between performance on this test and stenosis in the right carotid artery (Table 32). Thus, circumscribed areas of neurocognitive dysfunctioning relating to attention and cognitive flexibility appear to be influenced by stenosis, with some overlap in the effects across the two hemispheres.

The role of stenosis in predicting neuropsychological test scores will be examined from two viewpoints--the neuropathological process underlying stenosis and factor analytic studies. Studies have demonstrated that stenosis contributes significantly to neurological events accompanying cerebral transient ischaemic attacks (Hobson, 1995; Golledge, Cuming, Ellis, Beattie, Davies and Greenhalgh, 1996). In the study by Golledge et al. (1996), varying degrees of stenosis was associated with neurological symptoms. In general, the higher the degree of stenosis (that is, between 75 and 99%), the more severe the neurological signs and symptoms. Research in regional cerebral blood flow suggests that there is strong agreement between per cent hemispheric differences in blood flow and judgments of laterality of neuropsychological findings indexed by global measures (Brown, Ewing, Weiss, Robertson and Welch, 1983). These findings support the view that there are alterations in neuropsychological functioning associated with changes in cerebral blood flow and that these two measures may be significantly correlated.

One of the major causes of stenosis is atherosclerosis, considered to be a noninflammatory degenerative disease that results in narrowing or obstruction of the lumen of arteries (Cohen, 1995). The atherosclerotic process is not uniform across the cerebral vasculature with certain sites having a predilection for the deposition of atheromatous tissue (Absher and Toole, 1995). The narrowing of the arteries implies that there is a gradual decrease in the supply of oxygen and glucose to the areas supplied by these vessels which results in a compromise in neurological functioning.

Atherosclerosis itself has been proposed to represent a neuropathological process associated with a number of well-recognized systemic risk factors such as hyperlipidaemia, hypertension, cigarette smoking and diabetes mellitus (Zarins, 1991; Chervu, 1995). Smoking is reported to be related to a higher incidence of stenosis (Cuming, Worrell and Woolcock, 1993). Rapp, Ovarfordt and Krupski (1987) have shown that hypercholesterolaemia has a strong association with early stenosis, whereas hypertension, even when treated, is associated with both early and late stenosis.

In the present study, data regarding the presence or absence of hypertension, cigarette smoking and diabetes mellitus were obtained at the nominal data level (that is, whether the disease was present or absent) for the transient ischaemic attack group and, although entered into the regression equation as dummy-coded variables, these factors did not enter the prediction model. The quantification and frequency of cigarette smoking, as well as the refined measurement of both hypertension and cholesterol level, were not elicited in this study. The shortcomings in quantifying these important risk variables may have contributed to the findings that they failed to reach significance in predicting neuropsychological test performance.

The literature reviewed in Chapter 5 did not reveal any studies that employed regression analyses to identify which demographic, medical or psychological factors influenced neuropsychological test scores in transient ischaemic attack and control samples. Thus far, the present study found that stenosis significantly influenced scores on certain neuropsychological test in transient ischaemic attack patients, the effects showing similarities and differences in left and right hemisphere samples.

While demographic variables did not significantly predict test score variance in the left, right or combined transient ischaemic attack groups in the present study, other studies have suggested the role of demographic variables in neuropsychological test performance in similar samples. In the study by Bornstein (1983), differential relationships of age and education to neuropsychological test scores in a mixed group of transient ischaemic attack and stroke patients were reported. This author found significant relationships between age and WAIS Performance IQ and the Picture Completion subtest, as well as right Tactual Performance, left Grooved Pegboard and right Static Steadiness test performances. Although not clear from Bornstein's (1983) report, education appeared to correlate significantly with all WAIS subtests, with the exception of Block Design and Object Assembly, as well as the Visual Reproduction and Associate Learning subtests of the Wechsler Memory Scale ((WMS-R).

The nature of the relationships between demographic variables and neuropsychological test performance appears to be undergoing modification judging from the results of recent studies. Reitan and Wolfson (1996) reported that age correlated significantly with all the WAIS Verbal subtests for a brain damaged sample, but such significant correlations were not obtained for a control sample. No significant correlations were obtained for the WAIS Performance subtests. Education, on the other hand, was reported to correlate significantly with WAIS Verbal and Performance subtest scores in the control sample, while such significant correlations were found only with WAIS Verbal subtest scores in the brain damaged subjects. These findings suggest that age and education may not form important predictors of neuropsychological test scores in certain types of neurological samples with demonstrable diseases, particularly for those tests traditionally considered to be nonverbal in nature.

Thus the findings of this study provide support for the cognitive neuropsychological approach to the study of the neuropsychological sequelae of transient ischaemic attacks. In the control group, certain neuropsychological test scores were predicted by education suggesting that cognitive processes in this sample were differentially influenced by this demographic variable. The findings that stenosis differentially predicted neuropsychological test score variances in the left and right transient ischaemic attack patients and education emerged as a significant predictor in the controls suggest that these groups may themselves differ in performance on certain neuropsychological tests. The next chapter will thus present the results obtained from a statistical comparison of the left and right transient ischaemic attack and control groups on neuropsychological test performance. Also, a discussion of these results in the context of the appropriate hypotheses presented in Chapter 1 will follow.

CHAPTER NINE

Discussion of Hypotheses Relating to Differences Among Study Groups

9.1. Introduction

The results and discussion presented in Chapter 8 suggested two major findings. Firstly, there were significant differences in the demographic profiles of the left and right transient ischaemic attack and control groups. Second, regression analyses indicated that stenosis formed a significant predictor on certain neuropsychological test score variance in the left and right transient ischaemic attack groups while education formed the major predictor in the control group.

Similarities and differences in the predicted variances in the left and right hemisphere groups were obtained which, in keeping with the cognitive approach to neuropsychological analysis proposed in this study, suggest that stenosis had a differential influence in these groups. Thus, the next series of analyses is related to investigating whether there were significant differences in neuropsychological test scores among the left and right transient ischaemic attack and control groups. The pertinent results of the MANOVA reflected in Table 27 (Chapter 7) are summarized in Table 34 below.

Table 34

MANOVA Summary Findings Comparing Left and Right Transient Ischaemic Attack and Control Groups on Neuropsychological Test Performance

Neuropsychological Test	F
Digits Forward	29.50***
Digits Backward	79.91***
Digits Total	55.98***
PASAT: 2.4 seconds	27.06***
PASAT: 2.0 seconds	27.39***
PASAT: 1.6 seconds	26.23***
PASAT: 1.2 seconds	37.82***
Trails A	23.33***
Trails B	63.79***
Rey Auditory Verbal Learning Test: Trial 1	10.58***
Block Design	22.20***
Verbal Fluency	16.24***

***$p \leq 0.001$

The data in Table 34 indicate that there were significant differences between the left and right transient ischaemic attack and the control groups on several tests. These tests include the Digit Span

(Forward, Backward, Total), PASAT (all levels), Trails A, Trails B, the Rey Auditory Verbal Learning Test (Trial 1), Block Designs and Verbal Fluency. It is interesting to note that although the Rey Auditory Verbal Learning Test (Trial 1), Block Designs and Verbal Fluency did not enter the regression models conducted on the left and right transient ischaemic attack and control groups, significant differences on these tests among the study groups were found. These findings suggest that the left and right transient ischaemic attack and control groups were different in circumscribed areas of neurocognitive functioning, some of which were not predicted by stenosis. The differences between the three study groups form the focus of the three hypotheses which are presented next.

9.2 Hypothesis Five

There were no significant differences in neuropsychological test scores between the left and right transient ischaemic attack groups

In order to test Hypothesis 5, post-hoc Tukey tests were conducted on the MANOVA results presented in Table 34 to establish on which tests the left and right transient ischaemic groups differed significantly. These results are reflected in Table 35 below.

Table 35

Summary of Tukey Test Findings Comparing Left (n = 40) and Right (n = 40) Transient Ischaemic Attack Groups

Neuropsychological Test	Mean Difference
Digits Forward	9.950 - 11.425*
Digits Total	15.225 - 16.875*
PASAT: 2.4 seconds	31.500 - 35.700*
PASAT: 2.0 seconds	27.550 - 31.800*
PASAT: 1.6 seconds	20.700 - 25.725*
PASAT: 1.2 seconds	13.900 - 19.050*
Trails B	123.20 - 112.200*

*$p \leq 0.05$

Table 35 (continued)

Neuropsychological Test	Mean Difference
Rey Auditory Verbal Learning: Trial 1	6.475 - 5.625*
Block Design	30.750 - 28.250*
Verbal Fluency	31.150 - 26.425*

*$p \leq 0.05$

It becomes apparent that the left and right transient ischaemic attack groups differed significantly on Digits Forward, Digits Total, all levels of the PASAT, Trails B, the Rey Auditory Verbal Learning test, Block Designs and Verbal Fluency. Of these tests, the left transient ischaemic attack group performed significantly worse than the right transient ischaemic attack group on Digits Forward, Digits Total, the PASAT (all levels) and Trails B ($p \leq 0.05$). The left transient ischaemic attack group performed significantly better than the right transient ischaemic attack group on the Rey Auditory Verbal Learning Test (Trial 1), Block Designs and the Verbal Fluency test ($p \leq 0.05$).

Differences in neuropsychological test performances between left and right transient ischaemic attack groups have been previously reported in the literature. Hemmingsen, Mejsholm, Boysen and Engell (1982) showed that their left hemisphere group showed significant improvements on Word Pairs, Trails B and the Story Recall tests. On the other hand, the right hemisphere group showed improvements on the Visual Gestalt, Block Design and Digit Span tests, the latter not differentiated according to Digits Forwards, Digits Backward and Digits Total.

In the study by Greiffenstein, Brinkman, Jacobs and Braun (1988), the right hemisphere transient ischaemic attack group showed significant post-operative test score gains on the WAIS Performance IQ ($t = -3.88$, $df = 7$, $p \leq 0.05$), Trails A, Trails B, Finger Tapping (left and right hands), and the Digit Symbol tests. No post-operative increases were found for the left hemisphere group.

Mononen, Lepojarvi and Kallanranta (1990) reported the changes in pre-to post-operative scores on selected tests in patients with left and right hemisphere transient ischaemic attacks. They found that preoperatively, the left transient ischaemic attack group had lower mean scores on the Digit Span, the Stroop Colour Word Test (although the Word, Colour or Colour-Word scores were unspecified). The left transient ischaemic attack group showed significant post-operative performances on the Stroop Colour Word Test (again unspecified as the exact index score) and an unspecified serial verbal learning test.

Mononen et al. (1990) also found that the right transient ischaemic attack group performed significantly better post-operatively on Word Fluency, an unspecified serial learning test, Visual Memory and Recognition of Concrete Pictures, and an unspecified Stroop Colour Word Test scores. These neuropsychological test findings have two important implications--that stenosis in the carotid artery has different implications for neuropsychological functioning in the left and right hemispheres and, the neuropsychological test scores may be interpreted in terms of circumscribed neurocognitive domains of behaviour.

In the present study, the findings that the left transient ischaemic attack group performed significantly poorer than the right transient ischaemic attack group on certain tests appears to support and extend the findings of Hemmingsen et al. (1982) and Greiffenstein et al. (1988). For the Digit Span test, only Digits Forward and Digits Total were found to be significantly lower in value in the left transient ischaemic attack group. While the poorer performance on Digits Total has been previously reported in the literature (Hemmingsen et al., 1982; Greffeinstein et al., 1988), the Digits Forward results have not been previously reported in research on transient ischaemic attack subjects. These findings with regard to Digits Forwards represent fine-grain changes in attention function consistent with the modular theories of cognitive neuropsychology.

Kaufman et al. (1992) suggested that Digits Forward measures the efficiency of attention, a factor called freedom from distractibility which is found within a cognitive model of attention, while Anderson (1994) reported that Digits Forward is a measure of focussed attention. Thus it appears that when compared to the right transient ischaemic attack group, the left transient ischaemic attack group were significantly worse on these measures of attention.

Support for the poorer performance on attention tests appears to be forthcoming in the results obtained on the PASAT. The left transient ischaemic attack group performed significantly poorer on all levels of the PASAT and also showed a decline in the accuracy of performance as the inter-stimulus interval decreased. Although a similar negative gradient in the pattern of performance on the PASAT was found in the right transient ischaemic attack group, the significant differences between the left and right transient ischaemic attack groups were maintained on all trials. These findings are presented in Figure 9.

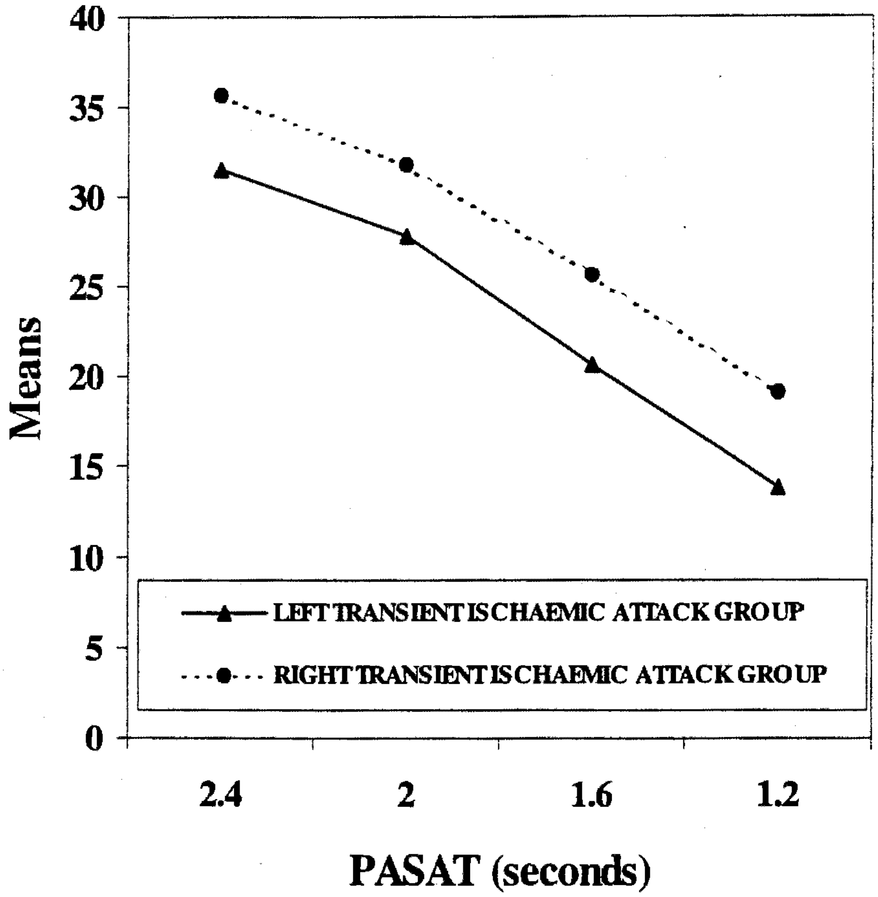


Figure 9. Patterns of performances in the left and right transient ischaemic attack groups on the PASAT

From the review of the literature (Chapter 5), it appears that the present study was the first to employ the PASAT as a measure of neuropsychological functioning in transient ischaemic attacks. This neuropsychological test has been traditionally used as a measure of information processing in mild-head injured patients (Lezak, 1995). According to Gronwall (1977), the PASAT is a sensitive measure of mild concussion in which information processing capacity is impaired. Spreen and

Strauss (1991) reported that the PASAT is a measure of sustained attention, while Van Zomeren and Brouwer (1987) found that divided attention loaded strongly in factor analytic studies of this test.

These findings suggest that in comparison to the right transient ischaemic attack group, sustained and divided attention in the left transient ischaemic attack group starts at a lower baseline (Mean for 2.4 second presentation = 31.5) and decreases in performance are noted with an increase in the speed of stimulus presentation (Mean for 1.2 second presentation = 13.90). It appears that a similar gradient of change is found for the right transient ischaemic attack group (Mean for 2.4 second presentation = 35.50; Mean for 1.2 second presentation = 19.05) but the gradient is found at a higher level when compared to that for the left transient ischaemic attack group. Thus it appears that while stenosis significantly impaired performance on sustained and divided attention tasks, these effects were more pronounced in the left transient ischaemic attack group.

The left transient ischaemic attack group showed significantly poorer scores on Trails B when compared to the right transient ischaemic attack subjects. Previous research on transient ischaemic attack patients suggest equivocal findings regarding the laterality effect on Trails B performance. Hemmingsen, Mejsholm, Vorstrup, Lester, Engell and Boysen (1986) found significant post-operative improvement on Trails B in both the left and right transient ischaemic attack groups. Greiffenstein et al. (1988) on the other hand found that when Trails B was used as a component of a speed/concentration composite score, the right transient ischaemic attack group showed significant post-operative gains compared to the left hemisphere.

In the present study, the left transient ischaemic attack group's poorer performance on Trails B may be considered impaired when compared to the right transient ischaemic attack group. Using factor analysis as a basis for test score interpretation, both Trails A and Trails B load on number recognition (and letter recognition for Trails B), visual scanning, visual-spatial functioning, and visuomotor co-ordination (Reitan and Wolfson, 1993). However, Trails B is considered to be a more complex task (Lezak, 1995), and factor analysis of this test also yields a cognitive flexibility component (Reitan and Wolfson, 1993). Since Trails A test scores were not significantly different in the left and right transient ischaemic attack groups, these findings may be extrapolated to suggest that poorer Trails B performance may be due to impaired cognitive flexibility in the left transient ischaemic attack group.

A further analysis of the data in Table 35 indicates that the left transient ischaemic attack group performed significantly better than the right transient ischaemic attack group on three neuropsychological tests. On the Rey Auditory Verbal Learning test (Trial 1), the left transient ischaemic attack group recalled a significantly higher mean number of words (Mean = 6.475, $p \leq 0.05$) than the right transient ischaemic attack group (Mean = 5.625, $p \leq 0.05$). Differences in performances on verbal recall tests among lateralized transient ischaemic attack samples have been reported in the literature on transient ischaemic attacks, with the direction of these differences tending to favour a left hemisphere group bias in post-operative studies.

In a study using a similar verbal task, Hemmingsen et al. (1982) found that the left transient ischaemic attack group showed post-operative increases on Word Pairs (a verbal associative learning task). Similar score increases on this test were not obtained in the right transient ischaemic attack group. One of the confounding variables that could have accounted for these results in the Hemmingsen et al. (1982) study was the high number of females on the study, which may have biased the findings on verbal tests (Matthews, 1992). Also, no information on the educational background of the subjects was available in that study and education has been reported to influence scores on Word Pairs (Lezak, 1995).

In the study by Hemmingsen, Mejsholm, Vorstrup, Lester, Engell and Boysen (1986), the post-operative performance of the left transient ischaemic attack group was significantly better on Word Pairs (Associative Learning), with no such effects documented for the right transient ischaemic attack group. Once again, no details on the educational level of the left and right transient ischaemic attack groups was available in the study.

In another study by Casey, Ferguson, Kimura and Hachinski (1989), left and right transient ischaemic attack subjects who had undergone unilateral endarterectomy were compared to a control sample of transient ischaemic attack patients who had not undergone surgery. There were no significant differences between the groups in age, years of education and follow-up interval. Despite its limited utility for diagnosis, global IQ scores were used by Casey et al. (1989) for analysis. The authors found that all groups showed a significant improvement in Verbal IQ ($F(1,33) = 6.07$, $p \leq 0.05$) suggesting that improvements verbal tests were not predicted by laterality, that is, there were no greater significant gains in left compared with right transient ischaemic patients. These findings suggest that in the presence of the equivalent levels of education, there may be no significant differences in the performances of left and right transient ischaemic attack groups on verbal recall tests.

In the present study, the significantly better left transient ischaemic attack group performance on Trial 1 of the Rey Verbal Learning Test may be explained by an analysis of the demographic results discussed in Hypothesis One. It has already been established that although the two groups did not differ significantly on age (Tables 3), the left transient ischaemic attack group had a significantly higher number of years of education (Mean = 11.725) when compared to the right transient ischaemic attack group (Mean = 10.80, $p \leq 0.05$). In their review of the normative data on the Rey Auditory Verbal Learning Test, both Anderson (1994) and Lezak (1995) report that age and education form significant effects for performance on this test and suggest that norms stratified on these variables are needed.

The other demographic variable that discriminated between the left and right transient ischaemic attack groups was per capita income (used in this study as a measure of SES). No evidence of a systematic investigation of the effect of SES on the neuropsychological test performances of transient ischaemic attack patients were found in the literature review (Chapter 5). In a related study, Gamache, Black, Smith, Giodani, Berent, Sackellares and Boll (1984) used multiple regression analyses to consider the effects of various demographic variables on the neuropsychological test performances in a sample of seizure patients. While the effects of education on various individual tests of Halstead-Reitan Neuropsychological Battery were well documented, SES effects were not found. However, a significant Pearson correlation ($r = 0.40$, $p \leq 0.05$) was obtained between educational level and SES. These findings suggest that while studies investigating the independent influence of SES (measured in various ways) on neuropsychological test performance in transient ischaemic attack groups are lacking, the potential effect of this variable cannot be ignored.

In the present study, the higher educational level of the left transient ischaemic attack group appears to be a reasonable explanation for the significantly better performance of this group on the Rey Auditory Verbal Learning test (trial 1). It appears therefore that even in the presence of significantly reduced blood flow, left transient ischaemic attack subjects with significantly higher educational and SES levels may recover their verbal learning skills when compared to the right transient ischaemic group of lower educational and SES levels. While this result is clearly consonant with the general findings regarding lateralised effects among normal groups, the role of education and SES in transient ischaemic attack patients need further study.

On Block Design, the performance of the left transient ischaemic attack group was significantly poorer when compared to that of the right transient ischaemic attack group (Means = 30.750 and 28.250, respectively, $p \leq 0.05$). These findings appear to contribute to the mixed findings obtained in studies on the lateralised effects of transient ischaemic attacks on Block Design (Chapter 5). Hemmingsen et al. (1982) reported that at eight months, post-operatively, all the patients in their sample showed a significant improvement on Block Design scores. However, when the left and right hemisphere groups were separated, the Block Design scores of the right transient ischaemic attack group was significantly better than the minor stroke comparison group.

Greiffenstein et al. (1988) reported no significant post-operative improvement Block Design scores either in the left or right transient ischaemic attack group. Similar nonsignificant findings were obtained by Casey, Ferguson, Kimura and Hachinski (1989) who essentially found no significant pre-to-post-operative improvements on Block Design or on any of the tests they administered.

The findings of improved performance on Block Design in left transient ischaemic attack patients appears to be consistent with the general findings obtained from lateralised studies on neurological studies. In general, right rather than left hemisphere patients perform more poorly on Block Design in variety of neurological samples (Lezak, 1995). Factor analytic studies on the Wechsler Intelligence Scales invariably demonstrate high loadings for Block Design on the Perceptual Organization factor (Zillmer, Waechtler, Harris and Kahn, 1992). These findings suggest that the right transient ischaemic patients performed more poorly on tests of visuoperceptual and visuoconstructive abilities.

The findings obtained in the present study suggest that, when compared to the right transient ischaemic attack group, the left transient ischaemic attack group did not show impairment on visuoperceptual and visuoconstructive abilities. These findings appear to support the general theoretical principle that the right hemisphere may facilitate these abilities and thus were impaired in the presence of reduced blood flow (Kolb and Whishaw, 1996). However, the findings of demographic differences between these two groups may offer a fuller explanation for the findings obtained.

The results in Chapter 7 indicated that the left hemisphere group had a significantly higher educational and SES (income) level than the right transient ischaemic attack group. Some studies have reported that education may have an effect Block Design performance but that these effects vary with different age groups. Kaufman, McLean and Reynolds (1988) found the Block Design performances were affected by education in 16- to 19-year old group although this effect was low. There appears to be a progressively increased effect of education with higher age so that Kaufman, McLean and Reynolds (1991) reported that in their study, education accounts for 15% to 24% of the variance among 35- to 74-year-old group. These findings suggest that in the presence of higher education among the left transient ischaemic attack patients, it is possible that education may have played a mediating role in producing significantly higher Block Design scores in this group. Similar results for the effects of SES on Block Designs have not been systematically reported (Anderson, 1994).

Another possible explanation for the higher scores of the left transient ischaemic attack group may lie in the scoring method employed in this study. The scores on the Block Design subtest are quantified in numeric values, based on faster construction of the designs within given time limits (Lezak, 1995). This is really a test of information processing (Anderson, 1994) and this scoring process may mask other kinds of cognitive difficulties of the patient. With this in mind, Kaplan, Fein, Morris and Delis (1991) developed an alternative administration process that was based on more extensive qualitative scoring that reviews strategies adopted and the types of errors committed by subjects in pattern construction. Kaplan et al. (1991) maintain that their scoring strategy is more likely to predict laterality of lesions reliably, a procedure that was not adopted in this study.

Using this approach, Kaplan et al. (1991) have shown that, on the Block Designs, left and right hemisphere patients produce varying kinds of difficulties which reflect the different information-processing strategies adopted by the respective hemispheres. Thus, it is also possible that employing a purely actuarial system may have spuriously resulted in left-right differences in the transient ischaemic attack groups. Clearly, this issue needs further investigation.

The findings that the Verbal Fluency scores of the left transient ischaemic attack group were significantly better than those of the right transient ischaemic attack group appear to be inconsistent with the lateralised findings in transient ischaemic attack groups. In the study by Hemmingsen et al. (1982), there were no significant improvement on the Word Fluency test in the left or right hemisphere subjects when compared with a minor stroke group, at eight weeks, post-operatively. It may be that the higher educational level of the transient ischaemic attack group mediated their better performance on this test. Also, these findings suggest that poorer Word Fluency scores were associated with both the left and right hemisphere groups.

In the study by Mononen, Lepojarvi and Kallanranta (1990), the combined transient ischaemic attack group performed significantly better than patients with generalized cerebrovascular disorders at two weeks and two months, post-operatively. However, when the groups were separated on the basis of laterality of ischaemic attack, the right hemisphere group performed significantly better than the generalized cerebrovascular group on Word Fluency and such findings were not obtained for the left hemisphere group. The effects of practice and the questions of bilateral transient ischaemic attacks formed important confounding variables in the Mononen et al. (1990) study.

In the study by Benke, Neussl and Aichner (1991), the Word Fluency score was obtained from the generation of names of animals, items beginning with a letter (unspecified in the study) or items in a supermarket. The authors found that the sample of generalized transient ischaemic attack patients performed significantly poorer than a sample of non-neurological volunteer patients and relatives ($p \leq 0.05$). Again, this study made no attempt to look for lateralized effects on Verbal Fluency.

In the present study, the higher Verbal Fluency score in the left transient ischaemic attack group is not unexpected given the equivocal findings for this test obtained from studies on the effect of laterality. Miceli, Caltagirone, Gainotti, Masullo and Silveri (1981) reported that frontal lesions, irrespective of the side of the lesion, were associated with lower Word Fluency scores, with left frontal lesions tending to produce lower scores than right lesions. Regard (1981) found that in his study of lateralised lesions, left hemisphere lesions in a group of general neurological patients was associated with greater impairment on the Word Fluency test, although no scores are reported.

In a study of normal volunteers, Parks, Lowenstein, Dodrill, Barker, Yoshii, Chang, Emran, Apicella, Sheramata and Duara (1988) conducted positron emission tomography (PET) scans on subjects while the Word Fluency test was completed. They found that Word Fluency activates bilaterally the temporal and frontal lobes, the latter associated more with unspecified prefrontal areas.

The findings obtained in the present study may be explained by the significantly higher education and SES results obtained in the left transient ischaemic attack group. An examination of the norms published by Spreen and Strauss (1991) reveals that in older and less well-educated, subjects (50-54 years with 12 years or less education), mean scores are reported as 41.52 (S.D. = 12.33). However, in the 55-59 year age group with a similar education, mean scores slowly decline to a value of 37.57 (S.D. = 10.90). On the other hand, for those subjects with education levels greater than 13 years, the mean score Verbal Fluency score for the 50-54 year group is 41.16 (S.D. = 11.42) and for the 55-59 year age group, the value is reported as 45.96 (S.D.= 11.22). These findings suggest that within the same age cohort, education appears to play a mediating role in Verbal Fluency scores.

Yeudall, Fromm, Reddon, and Stefanyk (1986) found that Verbal Fluency correlated significantly with education ($r = 0.32$, $p \leq 0.05$). Since education was the only demographic variable showing a positive association with Verbal Fluency scores, these findings suggest that the effect of education may be a consistent finding.

Therefore, in the present study, one possible explanation for the obtained findings is that the higher education level of the left transient ischaemic attack group was a mediating factor in the higher Verbal Fluency scores. It is therefore assumed from the higher educational level of the left hemisphere group that this group may either have had a higher premorbid level of Word Fluency, which may have facilitated a return to their higher level of performance.

9.3 Summary of findings obtained from left and right transient ischaemic attack group comparisons

On comparing the left and right transient ischaemic attack groups, clear differences in their performances on various neuropsychological tests become apparent. These differences suggest that, in keeping with the cognitive neuropsychology model, there may be varying consequences for neuropsychological functioning in these study groups. Thus it appears that compared to the right transient ischaemic attack group, the left group was more impaired on sustained and focussed attention and cognitive flexibility. On the other hand, the right transient group was more impaired on verbal learning, verbal fluency and visuoperceptual and visuoconstructive skills. These differences were found in study groups with similar ages but with more educated and higher SES left transient ischaemic attack when compared to the right group.

9.4 Hypothesis Six

There were no significant differences in neuropsychological test scores between the left transient ischaemic attack and control groups

Hypothesis 6 was tested by computing the post-hoc Tukey test on the MANOVA results obtained in Table 34. The results are reflected in Table 36 below.

Table 36

Summary of Tukey Test Findings Comparing Left Transient Ischaemic Attack and Control Groups

Neuropsychological Test	Mean Differences
Digits Forward	9.95 - 11.925*
Digits Backwards	5.275 - 7.675*
Digits Total	15.275 - 19.600*
PASAT: 2.4 seconds	31.500 - 37.200*
PASAT: 2.0 seconds	27.550 - 34.075*
PASAT: 1.6 seconds	20.700 - 26.450*
PASAT: 1.2 seconds	13.900 - 21.000*

*$p \leq 0.05$

Table 36 (Continued)

Neuropsychological Test	Mean Differences
Trails A	39.350 - 33.575*
Trails B	123.200 - 82.950*
Rey Auditory Verbal Learning: Trial 1	6.475 - 5.975*
Block Design	30.750 - 26.925*
Verbal Fluency	31.150 - 28.350*

*$\underline{p} \leq 0.05$

The results in Table 36 suggest that two major findings were obtained when the left transient ischaemic attack group was compared with controls. Firstly, the left transient ischaemic attack group performed significantly poorer than the controls on Digit Span (Forwards, Backwards and Total), the PASAT (all levels), Trails A and Trails B. Second, an unexpected surprising finding was that the left transient ischaemic attack group performed significantly better than the controls on the Rey Auditory Verbal Learning test (trial 1), Block Design and the Verbal Fluency test. On the basis of these results, Hypothesis 6 is refuted.

The left transient ischaemic attack group performed significantly poorer than controls on Digits Forward (Means = 9.95 and 11.925, respectively), Digits Backwards (Means = 5.275 and 7.675, respectively) and Digits Total (Means = 15.275 and 19.600, respectively). These results suggest that the left transient ischaemic attack group performed significantly poorer on measures of focussed attention, immediate verbal memory and divided attention (Kaplan et al., 1991; Anderson, 1994).

Inconsistent findings with regard to Digit Span have been reported in those studies reviewed in Chapter 5. All of the studies reviewed reported results for Digits Total with no differentiation of Digits Forward and Digits Backward. The results of some of the studies reviewed are consonant with those obtained in the present investigation. Hemmingsen et al. (1982) and Hemmingsen et al. (1986) reported that the left hemisphere group did not report significant improvement in Digit Span Total scores eight months, post-operatively, when compared to a minor stroke group. However, it is possible that while differences on Digit Span Total were not obtained on both their studies, Hemmingsen et al. (1982; 1986) did not conduct independent analyses on Digits Forward and Digits Backwards thereby limiting the extent of their findings.

Mononen et al. (1990) reported findings similar to those obtained by Hemmingsen et al. (1982; 1986). Mononen et al. (1990 found that the pre-operative Digit Span Total scores in the left transient ischaemic attack group was significantly lower than the right transient ischaemic attack group. Post-operatively, no significant gains in Digits Total were found in the left transient ischaemic attack group.

The findings obtained in the present study appear to extend those of previous investigations. The findings that the left transient ischaemic attack group performed significantly worse than the controls suggest that this experimental group was impaired on Digit Span. In addition, it appears that focussed attention and immediate memory (Digits Forward) as well as divided attention (Digits Backward) are impaired in the left transient ischaemic attack group.

Similar findings were obtained for the PASAT in the present study. The left transient ischaemic attack group performed significantly poorer at all levels of this test when compared to the controls. These findings suggest that in addition to immediate memory and focussed attention, sustained attention was also significantly impaired in this group. These findings support and extend those obtained in studies employing the Digit Span.

Apart from the effect of stenosis on the poorer performance of the left transient ischaemic attack group on Digit Span and the PASAT, the summary of demographic findings in the study sample as reflected in Table 8 (Chapter 7) may offer additional explanation for these findings. These results indicate that the left transient ischaemic attack group was significantly older but similar to the controls in education. However, while higher education was argued to facilitate the better performance of the left transient ischaemic attack group when compared to the right hemisphere group, it appears that these education effects are not found when these comparisons are made with a control group.

The left transient ischaemic attack group performed significantly poorer than the controls on Trails A and consistent with the findings obtained when the left and right transient ischaemic attack groups were compared, the left transient ischaemic attack group performed significantly worse than the controls on Trails B. These findings suggest that when the three study groups are compared, the left transient ischaemic attack group was significantly impaired on number recognition (and letter recognition for Trails B), visual scanning, visual-spatial functioning, visuomotor co-ordination and cognitive flexibility (Reitan and Wolfson, 1993).

Within the context of the demographic findings, it appears therefore that higher education and SES do not offer any protection against impairment in attention and cognitive flexibility in the left hemisphere group. It may be that these functions reflect information-processing skills which appear to be at risk and thus were compromised in the left transient ischaemic attack group.

A surprising finding was that the left transient ischaemic attack group performed significantly better than the controls on the Rey Auditory Verbal Learning (Trial 1), the Verbal Fluency and the Block Design tests. It was expected that the left transient ischaemic attack group would perform more poorly than the controls on these test since they had suffered a significant neurological event. The literature review in Chapter 5 suggests that the findings obtained for the Rey Auditory Verbal Learning test have not been previously reported. However, suggestions of improved performances on verbal learning tests have been forthcoming in the literature. Hemmingsen et al. (1982) reported that the left hemisphere group showed significant improvement on Word Pairs (a verbal learning task) at eight months, post-operatively. No such improvements were noted in the right hemisphere group. In a follow-up study, Hemmingsen et al. (1986) confirmed that the left transient ischaemic attack group performed significantly better three to five months, post-operatively, while such findings were not obtained for the right hemisphere group.

The findings of Hemmingsen et al. (1982; 1986) suggest that when transient ischaemic attack groups are matched with controls, the former groups still show an increase in verbal learning skills suggesting that such abilities either remain intact or improve after surgical intervention. Therefore, in the present study, one possible explanations for the better performance of the left transient ischaemic attack group on the Rey Auditory Verbal Learning test is that this group may be due to the better premorbid verbal learning abilities of this group when compared to the controls. While the educational levels of the left transient ischaemic attack and control groups did not differ significantly, the former group was higher in SES. It is possible that higher SES and education in the left transient ischaemic attack group was associated with specific vocation types in the left transient ischaemic attack group which, in turn, may have facilitated their verbal learning skills. However, since occupation was not recorded in this study, the explanation of SES, education and vocation needs further study. Despite the tentative nature of this explanation, it appears that education and SES facilitated some protection against the loss of verbal learning skills even in the presence of significant stenosis in the left hemisphere.

It appears that similar arguments may be advanced for the findings for Verbal Fluency. In terms of previous findings on the Verbal Fluency test, it was expected that left transient ischaemic attack subjects would perform more poorly than controls. In the Hemmingsen et al. (1982) study, no significant improvements in Verbal Fluency scores were obtained in the left hemisphere group at eight months, post-operatively. These authors did not report the pre-operative scores for the left hemisphere group independently but found that the entire transient ischaemic attack group had mean scores on the Verbal Fluency test that were significantly lower than appropriate norms. When compared to the right transient ischaemic attack group matched for age and education, no significant differences in Verbal Fluency scores were found.

In the study by Mononen, Lepojarvi and Kallanranta (1990), the score on the Word Fluency test was obtained by the sum of the number of S and A words generated in sixty seconds. The transient ischaemic attack group showed significant gains in Word Fluency scores at two months, post-operatively. When the group was separated into left and right transient ischaemic attack patients who were reportedly comparable for age and education, the right transient ischaemic attack group showed significant improvement at two months, post-operatively, on the Word Fluency test.

It appears that demographic factors may provide some explanation for the significantly better scores of the left transient ischaemic attack group obtained in this study. This group had a higher SES than the control group (although they were similar in education). As indicated previously by a review of the norms provided by Spreen and Strauss (1991), it appears that age effects are not significant for similarly educated individuals until the >75 year age group. These findings suggest the it may be SES and related occupational factors (which were not elicited in this study) that contributed to the findings. The findings of Hemmingsen et al. (1982) suggest that after surgical intervention, improvement in performance on the Word Fluency test may be recorded. Thus, it may that in the present study, the use of medical therapy may have resulted in the preservation or recovery of verbal fluency skills in the left transient ischaemic attack group.

Next, the findings obtained by comparing the right transient ischaemic attack group with the controls are discussed.

9.5 Hypothesis Seven

There were no significant differences in neuropsychological test scores between the right transient ischaemic attack and control groups

Hypothesis 7 was tested by computing the post-hoc Tukey test on the MANOVA results obtained in Table 34. The results are reflected in Table 37 below.

Table 37

Summary Table of Tukey Test Findings Comparing Right Transient Attack (n = 40) and Control Groups (n = 40) on Neuropsychological Test Performance

Neuropsychological Test	Mean Difference
Digits Backwards	5.450 - 7.675*
Digits Total	16.875 - 19.600*
PASAT: 2.0 seconds	31.8 - 34.075*
Trails A	37.450 - 33.575*
Trails B	112.20 - 82.95*

*$p \leq 0.05$

The results in Table 37 suggest that the right transient ischaemic attack group performed significantly worse than the controls on Digits Backwards, Digits Total, PASAT (2.0 seconds), Tails A and Trails B. Therefore, Hypothesis 7 is rejected.

The findings that the right transient ischaemic attack performed significantly worse on Digits Backward (Mean = 5.450) than the controls (Mean = 7.675) is an extension of the findings reviewed in Chapter 5. In the Hemmingsen et al. (1982) study, while the right hemisphere group showed post-operative increases in Digit Span Total scores, no comparisons were made with an appropriate control group. In addition, no attempt was made to separate the analyses for Digits Forward, Digits Backwards and Digits Total.

Similarly, the finding of significantly poorer performance on the PASAT (2.4 seconds) suggests that the right transient ischaemic attack group showed impairment in information-processing and sustained attention abilities when compared to controls. As been reported in the previous discussion, Gronwall (1977) reported that the 2.0 second presentation of the PASAT is a more reliable indicator of poor information processing abilities in mild head injury and may reflect diffuse brain damage.

In the present study, the finding that Digit Span Backwards and the PASAT (2.0 seconds) were signficantly worse when compared with the controls suggest that divided attention and sustained attention were impaired in this experimental group. Similar findings were obtained in the study by Rueckert and Grafman (1996) who investigated sustained attention in ten patients with MRI and/or CT evidence of frontal lesions. Three patients showed evidence of bilateral damage. On the Continuous Performance Test, the right hemisphere patients showed longer reaction times and missed more targets when they were compared with both left hemisphere patients and a control group. In the Rueckert et al. (1996) study, there were no significant differences in age and education among the three study groups.

However, the finding that the right transient ischaemic attack group had a lower educational level and were older than the controls may mediate some of the findings obtained in this study. It is possible that these variables in the right transient ischaemic attack group may have mediated the significantly poorer performance of this group on this test. While systematic studies of the effect of education on Digits Backwards are lacking, Botwinick and Storandt (1974) have reported that the cut-off scores for within normal limits, borderline defective, and defective, are dependent on the educational background of the patient.

The right transient ischaemic attack group also performed significantly poorer than the controls on Trails A and Trails B, suggesting impairment is number and letter recognition, visual scanning and cognitive flexibility (Reitan and Wolfson, 1993).in this group with lower education and higher age. According to Stuss, Stethem and Poirer (1987), normative studies show an increase in time taken to complete both Trails A and Trails B with each succeeding decade. Based on these findings that there age decade associated changes in Trails A and Trails B performance, Spreen and Strauss (1991) report the norms for these tests according to decades (p. 326).

Education effects for Trails B have been reported in the literature. Heaton, Grant and Matthews (1986) found that to complete Trails B, normal adults 40 to 60 years old with less than 12 years of education needed a mean time of 102.2 seconds; individuals with 12 to 15 years of education, 69.7 seconds and those with 16 and more years of education, 57.9 seconds. Bornstein (1983) found that the correlation coefficient between education and Trails A and trails B was 0.19 and 0.33, when the effect of age was partialled out.

In the present study, apart from stenosis, the right transient ischaemic attack group was significantly older (though in the same age decade as the controls) and had a lower educational level and was lower SES. However, the stepwise regression analyses revealed that neither age, education nor SES formed significant predictors of the variances of Trails A and Trails B (Tables 15 and 16).

Thus it appears that the poorer scores of the right transient ischaemic attack group when compared to the controls may have been due to the stenosis in this hemisphere.

Thus it appears that there are similarities in the neuropsychological sequelae of transient ischaemic attacks in left and right hemisphere samples which may be delineated according to a neurocognitive model. These similarities and differences appear to be found within the context of differing demographic profiles of these samples which argue against the treatment of left and right transient ischaemic attack groups as a homogeneous group.

Next, a chapter integrating and summarizing the findings obtained from the regression analyses and statistical tests of difference will be presented.

CHAPTER TEN

Overall Integration and Summary of Findings

10.1 Introduction

The hypotheses generated in Chapter 1 were systematically analyzed using two major statistical tests--multiple stepwise regression and MANOVAs. When MANOVA results were significant, post-hoc Tukey tests were conducted to determine the location of these differences between groups and the neuropsychological tests on which these findings were obtained. These results were discussed independently in Chapters 8 and 9. This chapter aims to provide a summary of the findings obtained in this study.

10.2 Overall Integration of Regression Analyses and Tests of Group Differences

10.2.1 Stenosis.

From the regression analyses, the salient statistical finding that stenosis contributed significantly to neuropsychological test performance in transient ischaemic attack patients appears to parallel the neuropathological findings in the literature (Rutherford, 1995). In fact, the finding that significant stenosis undermines neurological and neuropsychological functioning has been the criterion underlying recommendations for carotid endarterectomy surgery in transient ischaemic attack patients.

Recent neuropsychological studies tend to indicate that neurological variables may be more contributory to neuropsychological sequelae as indexed by sensitive neurophysiological markers (for example, Taghavy and Hamer, 1995). Previous studies have reported that transient ischaemic attacks may be accompanied by impaired neuropsychological test performances, but it has been undetermined whether these lowered scores were due to neurological (vascular disease), demographic (age, education), medical risk (hypertension) or psychological variables. Thus, there appears to still be a need for further exploration of the variables influencing neuropsychological outcome in transient ischaemic attacks, particularly with a view to elucidating the contribution of pertinent variables to neuropsychological test performances.

In the present study, significant differences in demographic variables were obtained between the transient ischaemic attack and control groups. As a combined group, the transient ischaemic attack group was significantly older, of a higher SES but similar in education when compared to the controls. Though these differences were significant, these demographic variables did not predict neuropsychological test score variance in the transient ischaemic attack group.

In the present study, the stepwise regression analyses identified stenosis as a critical variable contributing to the scores on certain neuropsychological tests in the transient ischaemic attack group. When the left and right transient ischaemic attack groups were analyzed independently, stenosis once again emerged as a predictor of score variance on selected neuropsychological tests in each group. This finding was obtained in the left transient ischaemic attack group even though the mean age of this group was significantly higher than both the right transient ischaemic attack and control groups, respectively. Thus unexpectedly, age did not form a significant predictor of the neuropsychological test scores of the left transient ischaemic attack group in the presence of identifiable stenosis. Similarly, higher age and lower education and SES did not form significant predictor variables of score variance in the right transient ischaemic attack group.

10.2.2 Age and Education.

While the investigation of demographic variables did not yield significant results with regard to predicting neuropsychological test scores in the transient ischaemic attack group, there have been suggestions of differential relationships between age and education, respectively, and neuropsychological test performance in the literature. In the study by Bornstein (1983) on a combined group of transient ischaemic attack and stroke patients, significant relationships between age and WAIS Performance IQ and the Picture Completion subtest, as well as right Tactual Performance, left Grooved Pegboard and right Static Steadiness test performances were reported. Although not clear from the author's report, education appeared to correlate significantly with all WAIS subtests, with the exception of Block Design and Object Assembly, and the Visual Reproduction and Associate Learning subtests on the Wechsler Memory Scale ((WMS-R).

Reitan and Wolfson (1996) reported that age correlated significantly with all the WAIS Verbal subtests for a mixed brain damaged sample but such significant correlations were not obtained for the WAIS Performance subtests nor the control sample. Education was reported to correlate significantly with WAIS Verbal and Performance subtest scores in the control sample, while such significant correlations were found only with WAIS Verbal subtest scores in the brain damaged subjects. These findings suggest that age and education differentially influences neuropsychological test scores in brain-damaged samples, and these differential relationships may vary according to cerebral pathology.

10.2.3 Left and Right Transient Ischaemic Attack and Control Groups.

When the combined transient ischaemic attack group was compared with the controls, significant differences were obtained on Digit Span (Forward, Backward and Total scores), PASAT (all levels) and Trails A and B--these results being partially consistent with the findings obtained on the stepwise regression analyses. These results suggest that when compared to the control group, the transient ischaemic attack group of patients performed significantly worse on measures of attention, visuospatial scanning and cognitive flexibility. These results suggest that the domains of attention, visuospatial scanning and cognitive flexibility may be areas of neurocognitive functioning that are susceptible to significant carotid stenosis in transient ischaemic attack patients.

However, when laterality was entered as a variable in the MANOVA, (since laterality was reported to be an inconsistent predictor of scores in certain neuropsychological tests), differential findings were obtained (Tables 22 and 23). The left transient ischaemic attack group performed significantly worse than the right transient ischaemic attack on Digits Forward, Digits Total, PASAT (all levels of presentation) and Trails B. The right transient ischaemic attack group on the other hand performed significantly poorer than the controls on Digits Backward, Digits Total, PASAT (2.0 second presentation), Trails A and Trails B. The left and right transient ischaemic attack groups were not differentiated by scores on Digits Backward.

These overall findings suggest that the transient ischaemic attack group may be more significantly impaired than the control group on measures of attention (Digit Span and PASAT tests) and complex visuospatial functioning (Trails B). In terms of the findings of the regression analyses (Tables 8 to 20), it appears that stenosis may be the more likely explanation for the significantly poorer test performances in the transient ischaemic attack group. Thus it appears that stenosis may be an influencing factor in determining performances on those tests loading heavily on attention and complex visual-spatial functioning.

These findings appear to be in support of those reported by other investigators. For example, Bradvik, Sonesson and Holtas (1989) reported that speed of processing, spatial ability and spatial organization were the main impaired areas of functioning in their sample of transient ischaemic attack patients.

Further support for the possible significantly poorer test performances of transient ischaemic attack patients on attention-based tasks appears to be provided by Taghavy and Hamer (1995). These authors reported electrophysiological evidence for the involvement of attentional processes in the poorer neuropsychological test performances in their subjects. Pattern reversal visual evoked potential values indexed by N250 latencies were found to be significantly prolonged (and therefore poorer) in transient ischaemic attack patients when compared to controls. These prolonged N250 patterns were linearly correlated with test scores on non-specific cognitive tests.

The neuropsychological test findings obtained in the transient ischaemic attack group suggest certain patterns in this sample. While the transient ischaemic attack group performed significantly poorer than the controls on attention tasks in general, certain lateralized findings become apparent from the results in Table 35. The left transient ischaemic attack group performed significantly poorer than the right transient ischaemic attack on all measures of attention (with the exception of Digits Backward) suggesting that the left hemisphere may be involved in these tasks. Even basic tasks requiring minimal attentional effort and control which may be accomplished through automatic language processing, such as the Digits Forward (Cohen, 1993) appeared to be significantly impaired in left transient ischaemic attack subjects.

10.2.4 Digits Backward.

Digits Backward requires more than focussed attention and freedom from distractibility. In addition to short-term recall, Digit Backward requires a cognitive operation using the short-term memory in the role of working memory whereby the sequential order of the symbols is reversed. The role of other mental operations necessary in successfully performing Digits Backward has been reported by several authors.

Craik and Lockhart (1972) noted that, in order to perform Digits Backward successfully, a person is required to hold the symbols in memory for a longer duration and to perform an operation on them. According to Lezak (1995), the Digits Backward task involves mental double tracking in which both the short-term memory and the reversing operations must proceed simultaneously. Bender (1979) suggested that the ability to reverse digits is probably characteristic of normal cognitive function and language processes related to the brain's normal function of temporal ordering. Factor analysis (Larabee and Kane, 1986) reveals that both verbal and visual processes contribute to the reversed digit span performance. Weinberg, Diller, Gerstman and Schulman (1972) hypothesized from their studies that the reversing operation depends on internal visual scanning. Support for the hypothesis of Weinberg et al. (1972) was provided by Rapoport, Webster and Dutra (1994) who found that among right cerebrovascular accident patients, visual imagery played a primary role in performance on Digits Backward.

In the present study, both transient ischaemic attack groups had significantly poorer mean scores on Digits Backward when compared to the control group but did not themselves differ on this measure. These results suggest that both the left and right hemispheres participate in performing Digits Backward--the left hemisphere to encode the digits verbally and the right hemisphere to perform visual scanning of the encoded symbols and then to reverse their order. Indirect support for this proposal derives from the report of Burgess, Flint and Adshead (1992) who noted that their factor analytic studies on the WAIS-R yielded a perceptual organization factor with its highest loadings on Digits Backward.

Other sources of evidence for the involvement of frontal-based neurocognitive mechanisms in performing the Digits Backward task were the studies by Risberg and Ingvar (1973). They investigated the regional cerebral blood flow patterns during the performance of this task among normal subjects. These authors reported that the greatest increase in regional cerebral blood flow during the performance of Digits Backward occurred over the frontal-prefrontal areas with significant hemispheric differences. On the basis of their findings, Risberg and Ingvar (1973) concluded that the frontal lobes (in particular the prefrontal lobes) were important in the regulation of overall attentional tone.

Recent reports tend to emphasize that Digits Backward is more sensitive to brain damage, particularly to damage which is more diffuse in nature (Lezak, 1995). The results of the present study further suggest that the diffuse nature of brain damage to which Digits Backward is sensitive may in fact be demonstrative of the participation of both hemispheres in performing this task. Thus the poorer performance of the left transient ischaemic attack group on both Digits Forward and Digits Backward reflects the two-stage (verbal-visual) deficit in this group. Therefore, if the verbal process is not functioning adequately, as is suggested to be the case in the left transient group, then the visual scanning process is also likely to be compromised. Thus, the findings of significantly poorer performance on the Digits Forward and Digits Backward in left transient ischaemic attack patients is to be expected within the context of this argument.

10.2.5 PASAT.

The results on the PASAT test may be discussed in a manner that is consistent with the findings for Digits Forward and Digits Backward. Factor analytic studies on the PASAT have yielded several factors loading on test scores among normal subjects. In the study by Deary, Langan, Hepburn and Frier (1991), varimax rotation analyses revealed high loadings on the freedom from distraction factor. Other primary areas of assessment of the PASAT include sustained attention and immediate verbal memory (Spreen and Strauss, 1991) and divided attention (Van Zomeren and Brouwer, 1987). In the present study, the left transient ischaemic attack group performed significantly worse than both the control and the right transient ischaemic attack groups, while the latter had significantly worse scores than the controls only on the 2.0 second rate of presentation. On the 2.4, 1.6 and 1.2 second rate of presentation, no significant differences were obtained in the performances of the right transient ischaemic attack and control groups.

Generally, the poorer results on the PASAT have been interpreted as a deficit in information processing, implying the use of the information processing model of cognition as an underlying theoretical explanatory framework for PASAT test interpretation (Lezak, 1995; Spreen and Strauss, 1991; Stuss, Stethem and Poirer, 1987). The specific information processing model employed, however, has not been specified but is assumed to follow the prototypical model of Broadbent (1958) who proposed that the nervous system acts as a single communication channel so that it is meaningful for this stage of information processing to have limited capacity. Consequently this channel selects information from all sensory events having some feature in common.

Incoming information (such as digits) may be held in a temporary store (immediate memory, or short-term memory) at a stage prior to the limited capacity channel. The maximum time of storage is considered to be on the order of seconds. In the left transient ischaemic attack group, the findings on the Digit Span Forward subtest suggest that there may be a compromise in this function when compared to the right transient ischaemic and control groups. Thus, the poorer performance of the left transient ischaemic attack group on the PASAT across all levels of the test appears to stem from this early stage of information processing. The sustained performance demanded on this test is dependent on the intactness of this early stage of information processing.

The right transient ischaemic attack group on the other hand performed similarly to the controls on three levels of the test. This finding suggests that the early stage of immediate verbal memory may be intact and since manipulation of the digits requires working memory, the right transient ischaemic attack group is able to perform this skill adequately. It appears therefore that sustained attention in the auditory modality is intact for this group of subjects. Therefore, these findings seem to suggest that while the PASAT is sensitive to transient ischaemic attacks, this sensitivity may be limited to attacks involving the left hemisphere. Clearly more studies of different groups of patients with lateralized damage are required to clarify these findings.

10.2.6 Trails A and Trails B.

Both Trails A and Trails B have been classified as tests of complex attention (Lezak, 1995). The results indicate that both the left and right transient ischaemic groups performed significantly worse than the controls but did not themselves differ on Trails A suggesting that both hemispheres may be equally involved in performing this task. Factor analytic studies by Mirsky, Fantie and Tatman (1995) indicate that visual-perceptual scanning and skilled manual responses loaded strongly on this test. Incorporating these two factors into one, Mirsky et al. (1995) derived a focus-execute factor. In previous transient ischaemic attack studies (Delaney, Wallace and Egelko, 1980), the poorer performance of the transient ischaemic attack group on Trails A was reported and explained as due to poor sequential symbol processing. It appears that in the present study, poor sequential symbol processing, which also has an attention component (Anderson, 1994), may be compromised in transient ischaemic attack patients irrespective of the laterality of the neurological event.

However, on Trails B, a different type of result is obtained. While both transient ischaemic attack groups each performed significantly poorer than the controls, the right transient ischaemic attack group performed significantly better than the left. Factor analysis (Lezak, 1995; Anderson, 1994) suggest that a more complex cognitive function of alternate focussing is involved in the performance of Trails B. This alternate focussing skill involves the inhibition of a spontaneous response based on a previous response parameter (digit), while responding to an alternate stimulus (letter). This alternate focussing strategy appears to be more severely compromised in the left transient ischaemic attack subjects relative to both the controls and the right transient ischaemic group.

One possible explanation for this graded finding is that Trails B is a reflection of the composite attentional abilities required to complete the Digit Span test, and the poorer mean score of the left transient ischaemic attack on Trails B is a reflection of their poorer performances on Digits Forward, Digits Backward and the PASAT. The slightly improved mean score of the right transient ischaemic group relative to the left group may be considered to correspond to the similar performance of this group on Digits Forward when compared to controls (Table 22).

Support for these proposals may be found in the correlation values between the Digit Span tests and Trails A and Trails B. In the left transient ischaemic attack group, significant negative correlations were obtained between scores on Digits Forward and Trails B ($r = -0.460$, $p \leq 0.05$), between Digits Backward and Trails B ($r = -0.632$, $p \leq 0.0001$) and Digits Backward and Trails A ($r = -0.474$, $p \leq 0.05$). In the right transient ischaemic attack group, significant negative correlations were obtained between Digits Forward and Trails B ($r = -0.527$, $p \leq 0.01$) and Digits Backward and Trails B ($r = -0.420$, $p \leq 0.05$). No significant correlations were obtained between Trails A and Digits Forward or Backward, respectively.

The poor performance of the left transient ischaemic attack group on Trails A has been reported to be a gross indicator of unspecified brain damage (Reitan and Wolfson, 1993) but is considered not to be useful for lateralizing brain lesions (Corrigan and Hinkeldey, 1987), which appears to be consistent with the findings in this study. The results of the present study thus appear to support this suggestion since no significant differences were obtained between the left and right transient ischaemic attack groups on Trails A.

The findings derived from statistical analyses of Hypotheses 1 and 2 suggest that stenosis formed a critical predictor variable of neuropsychological test scores in the left and right transient ischaemic attack groups. The neuropsychological test scores predicted by stenosis were found to be significantly poorer in the transient ischaemic attack than those in the control group. The neuropsychological tests reflecting poorer performances in the transient ischaemic attack groups relate to domain of functions relating to attention as the underlying construct. Since attention forms the basic function underpinning other behaviours (Mirsky, Fantie and Tatman, 1995), it is not unusual to expect changes in other domains of functioning as well.

These findings may be explained in various ways. The salient variable influencing neuropsychological test performance in the transient ischaemic attack groups was found to be stenosis. It is possible that in these patients, stenosis differentially affected neuropsychological functioning depending on the nature of the ability. Attention is generally conceptualized as a hierarchy of functions (Mirsky et al., 1995) in which basic elements involving uneffortful attention (as measured by Digit Span) are incorporated into more sophisticated forms (Digits Backward and PASAT). Thus the complex of abilities comprising the psychological function of attention may become impaired since basic elements are affected. Cohen (1995) supports this argument by noting that general changes in the neurological structures primarily alters attention, and that such alterations may have their roots in vascular changes. Stenosis thus appears to influence those test performances measuring the different aspects of attention processing as suggested by the findings of this study.

Trails A and B also have an attention component since successful performance requires constant and changing attention to relevant stimuli (Anderson, 1994). Therefore it may be argued that the significantly poorer performances of the transient ischaemic attack patients may reflect the attention component of this task. Alternatively, significantly poorer performances on Trails A and Trails B may support the findings of Reitan and Wolfson (1993) who reported that these tests are sensitive to all forms of brain damage. The relationship of stenosis (the main contributor to significantly poorer test scores) to atherosclerosis may be found in the sequence of neurovascular events that have been proposed to take place in stenosis.

10.2.7 Medical and Demographic Variables.

According to Zarins (1991), stenosis produces ischaemia in that neurons are deprived of their main energy substrates (oxygen and glucose) of cellular functioning. Additionally, a decrease in blood flow is accompanied by a reduction in the capacity of neurons to excrete by-products of cellular metabolism. The cellular response is reportedly one of compensation in which neurons adjust their functioning and rate of firing, and there may be compensatory mechanisms in the general vasculature described as collateral vascular supply. The functional integrity of these neurons therefore appears to depend on the successful self-adjustment of these neurons through revascularization in the forms of anastomosis or collateral vascular supply, as well as medical intervention in the form of chemical therapy promoting blood flow (such as anticoagulants) or surgical intervention (carotid endarterectomy).

The successful adjustment made by neuronal tissue perhaps reflects the character of transient ischaemic attacks as those neurological conditions in which lasting neurological sequelae are not found (Norris, 1991). However, while neurological functioning depends significantly on the integrity of organic substrates, neuropsychological functions are additionally determined by other non-organic factors. Age, education and SES are accepted as major demographic mediators of neuropsychological functions (Lezak, 1995). The findings of Reitan and Wolfson (1996), as well as those of the present study, have suggested that age and education may have a differential role in neuropsychological function in the presence of brain damage. It may be that the differential sensitivity of age and education to varying domains of neuropsychological functions reflects the nature of the functions tested.

The findings of this research suggest that those functions that are time-based and that have a strong attention factor for successful performance may be more susceptible to transient disruptions of vascular supply to the brain.

Previous research (Meier and Strauman, 1991) noted that younger stroke patients (below 60 years of age) have a more favourable recovery course and a much higher likelihood of returning to at least a semiautonomous level of functioning. Benton (1981) proposed that the recovery patterns in brain injury are difficult to document because the aging processes considered normal may vary in different individuals. Facilitative factors may protect against age-related declines in visuospatial, visuoconstructional, and memory functioning with age (Bornstein and Suga, 1988). Statistically, it appears that individuals with high initial ability levels tend to survive longer and to achieve higher performance levels as they age since their baseline levels were higher. These subjects with comparatively higher baseline levels of performance may reflect a masking of subtle yet significant neuropsychological changes in the presence of brain damage. Alternatively, higher baseline levels of functioning may provide a basis for appropriate behavioural compensation in these patients.

In the present study, the combined transient ischaemic attack group had a higher mean age (although they fell in the same age decade as the controls) but a similar number of years of education as the controls. Yet the presence of a higher mean education level did not appear to offer any protection against neuropsychological changes to the varied functions of attention.

These findings are even more important in view of the lack of CT evidence of infarcts, suggesting that stenosis not warranting surgical intervention and which may not result in gross structural alterations to neuronal tissue, may nevertheless result in changes to the functional capacity of those neurons.

Another finding that deserves mention is that the number and duration of the transient ischaemic attacks did not form predictor variables of neuropsychological test scores. This finding is unexpected since it is assumed that these variables relating to the temporal presentation of the neurological symptoms are assumed to reflect the severity of the underlying neuropathology (Cohen, 1995). However, it must be remembered that in the present research, the variables describing the duration and number of transient ischaemic attacks and symptoms were obtained on the basis of self-report by the patients themselves, and thus were largely dependent on the memory and accuracy of these data.

Next a concluding chapter proposing recommendations for further study of the neuropsychological sequelae of transient ischaemic attacks is presented.

CHAPTER ELEVEN

Recommendations for further study

11.1 Introduction

The present study investigated the neuropsychological sequelae of transient ischaemic attacks in the carotid arterial circulation. In Chapters 8 and 9, specific hypotheses were tested, and new findings thus derived. Thereafter, within the context of several methodological shortcomings, an integration and summary of the findings obtained as well as concluding comments with regard to the neuropsychological sequelae of carotid transient ischaemic attacks were presented in Chapter 10.

Based on the findings obtained, recommendations for further study of the neuropsychological sequelae of transient ischaemic attacks is presented in this chapter.

11.2 Research Approach

The literature on the underlying neuropathology of cerebrovascular diseases and, in particular, transient ischaemic attacks, suggests that there are several mediating demographic, medical, sociocultural and psychiatric variables underlying these neurological disorders. Each of these variables may independently influence performance on neuropsychological tests. The studies reviewed tend to compare transient ischaemic attack patients either with those showing other types of cerebrovascular diseases, or with subjects having no documented medical or psychiatric illnesses. Thus, transient ischaemic attack (experimental) and comparison groups are matched *a priori* on pertinent demographic variables, namely, age, sex and education.

However, given the heterogeneity of cerebrovascular diseases, it is difficult to obtain experimental and control samples matched on pertinent demographic and disease factors as it may take several years to obtain statistically valid sample sizes. Moreover, given the dynamic changes in the process of the disease and that, with time, some transient ischaemic attack patients may fall in the reversible ischaemic neurologic deficit or stroke categories, obtaining balanced group designs in this manner is not always feasible.

Thus, while group comparison studies are useful to investigate neuropsychological sequelae of transient ischaemic attacks, the findings of the present study suggest that matching subjects on certain demographic variables (for example, age) may mask subtle demographic differences between groups. As an alternative, using the principles of multiple regression analyses aimed at identifying those variables significantly influencing neuropsychological test scores appears to be a more statistically appropriate approach.

The natural history of transient ischaemic attacks suggests that the disease evolves within the context of several demographic and health-related variables which independently influence neuropsychological test scores. Thus, multiple regression analyses may provide statistical determinations of the effect of transient ischaemic attacks on neuropsychological test scores in the context of demographic and disease variables. The present study used multiple regression analyses as a basis for identifying significant predictor variables of neuropsychological test scores.

Thus, on the basis of these research principles and the findings obtained in this study, several recommendations for an appropriate research approach to investigate the neuropsychological sequelae of transient ischaemic attacks in several diverse samples are proposed.

11.2.1 Selecting Appropriate Study Samples

The literature review conducted in Chapter 5 suggests that the general approach in investigations on the neuropsychological sequelae of transient ischaemic attacks has been the use of group comparison studies. This research approach tends to view transient ischaemic attack subjects as the experimental group, and the transient ischaemic attack(s) itself as the independent variable. The neuropsychological test performances of the experimental group are then compared to other comparison groups.

The group design employed in these comparison studies fall in two broad types. In some instances the comparison groups constituted stroke patients who were selected on the basis of similar age, sex and education, and who had neurological impairments with associated cerebral infarcts, confirmed through radiological investigation. In other studies, transient ischaemic attack patients were compared with a group of control subjects who were similar in age, sex and education but with no historical evidence of neurological or major psychiatric disease.

One major difficulty associated with this methodological process of subject selection is the lengthy period involved in selecting samples of experimental and comparison groups who are matched on pertinent variables. An appropriate alternative to this approach are epidemiologically-based studies that will include all patients who have been diagnosed with transient ischaemic attacks in a database of subjects with this cerebrovascular disease. This research approach will ensure that the diversity of a disease that is inherently heterogeneous in its demographic and neuropathological profiles will be included in subsequent analyses.

Epidemiological studies have the advantage of including all patients who meet the criteria for a transient ischaemic attack. The geographical location of an epidemiological study should be carefully described and defined. All medical facilities, private and governmental, that will be assayed in the study, should be included in the pool of institutions. All patients diagnosed at Neurological and Neurosurgical Units, as well as those who were diagnosed by their family doctors and have chosen to attend private medical institutions, should be included in the database of transient ischaemic attack patients. In this way, the sample of transient ischaemic attack patients studied would be more representative of the population under investigation.

Furthermore, including patients from governmental and private medical institutions will provide a broader database to explore the findings suggesting a relationship between the laterality of transient ischaemic attacks and per capita income, education and other SES indicators.

While the proposed research process is comprehensive in its breadth, there are several precautionary measures with regard to data gathering that need to be considered. The use of multiple data gathering sites in epidemiological research suggests that personnel with varying levels of qualifications and experience will be involved in this process. To overcome this source of data confounding, it may be simple to develop a standard research protocol that is extensively piloted before the final study is implemented. Establishing inter-rater reliability indices for the research workers may further serve to reduce errors resulting from experimenter sources as suggested by Michel (1986).

In addition, the use of research staff solely in the role of data gathering in transient ischaemic attack patients at cerebrovascular clinics may be an expensive and unjustifiable exercise. With respect to brain visualisation data, the problem appears to be twofold. Firstly, the problem of standardisation in brain visualisation techniques as well as the criteria used by the radiological staff may pose a serious problem since there appear to be differences in the technological systems utilised by various centres (Moore, 1993). Second, the use of such techniques requires highly skilled personnel and in the present climate of economic frugality, the deployment of staff to conduct examinations and tests only on transient ischaemic attack patients may be unjustifiable. Despite these difficulties, it may still be useful to document as many cases of transient ischaemic attack patients as is possible, also noting the differences and similarities adopted by the various research centres in the diagnosis and management of these disorders.

11.2.2 Data Capture.

Several findings obtained in this study suggest that further analyses are required to investigate the role of certain variables that predicted neuropsychological test scores. These predictor variables fall in two categories.

11.2.2.1 Demographic Variables.

The findings that education and SES (per capita income) influenced the emergence of left or right transient ischaemic attacks is worthy of further study. The findings that higher education and higher per capita income were associated with left transient ischaemic attacks have not been previously reported in the literature. As indicated in Chapter 8, education and per capita income form part of the complex of interacting variables constituting SES which was inadequately measured in this study by quantifying per capita income. Therefore, it may be worthwhile to systematically investigate the role of the variables associated with SES (education, informal training, occupation level, income, family size, housing) in the aetiology of left and right transient ischaemic attacks.

In addition, on the basis of preliminary discussions with vascular surgeons at the Vascular Surgery Unit, it became apparent that Indian male subjects constituted the majority of patients and thus these subjects comprised the sample in this study. Whether or not this anecdotal information is correct will be determined by the large-scale epidemiological study that has been proposed. Given the changing demographic profiles in the province of Kwazulu Natal, and the greater involvement of women and other socially and politically disadvantaged groups in the education and employment sectors, it may be useful to broaden future studies to include all sex and race groups.

In addition to the expected sex differences in the epidemiological profiles of cerebrovascular disease, several studies have reported that there are also racial differences in the incidence and pathogenesis of these diseases (Inzitari, Hachinski, Taylor and Barnett, 1990). More recent studies suggest that cerebrovascular diseases appear to follow racial trends with Black Americans mirroring their White counterparts in the mortality rates after stroke (Pickle, Mungiole and Gillum, 1997). These studies were largely conducted in the U.S.A. and while their applicability to South Africa may be important, more local studies of this nature need to be undertaken. South Africa has a widely heterogeneous population which provides a unique opportunity to develop an appropriate database of transient ischaemic attack patients across race, sex, SES and occupational groups. Systematic studies should be undertaken to verify and extend the findings obtained thus far from epidemiological studies particularly with respect to their applicability to neuropsychological outcome.

The database will also provide an opportunity for the systematic long-term monitoring of those transient ischaemic attack patients who develop recurrent episodes of this disease or display full blown strokes.

11.2.2.2 Medical Data. Stenosis formed a significant predictor of neuropsychological scores on certain tests. The present study initially aimed at quantifying the degree of carotid artery stenosis according to currently used categories--mild stenosis (<50%), moderate (50 - 75%) and severe (75 - 99%). However, given the limited technology available at the institutions where the study was conducted, it was not possible to obtain this level of data. In future studies, the classification of individual cases of transient ischaemic attacks as mild, moderate or severe stenosis will refine the operationalization of this variable. Systematic measurement of the intra-arterial lumen of standard sites in the cerebral vasculature will provide an objective measure of the degree of stenosis. The system described by Norris, Bornstein and Chambers (1991) which classifies stenosis into mild (less than 50%), moderate (50-75%) and severe (greater than 75%) categories may be used to provide discrete categories for further analyses. In this way, regression analyses performed on large samples will allow for a more systematic investigation of the predictive power of stenosis with regard to neuropsychological test scores.

As an alternative to the measurement of intra-arterial diameter using expensive magnetic resonance imaging equipment, the clinical diagnosis of carotid bruits by employing experienced and similarly trained medical personnel using standard noninvasive methods may provide a useful preliminary step in identifying those candidates who are more likely to benefit from intra-luminal measurement. The clinical method may provide a quick, gross index of stenosis in large samples thus incurring minimal cost.

Several other medical variables warrant more systematic and detailed documentation. The role of diabetes, hypertension and cardiac disease has been confirmed in the aetiology of atherosclerosis and thromboembolism which primarily underlie transient ischaemic attacks. While these diseases have been documented in the present study, this has only been done at a nominal level, that is, the presence or absence of the disease was recorded. As stated previously, it is possible that the failure to record these variables in more systematic fashion, for example, the duration and familial history of the disease, levels of blood sugar and insulin at the time of assessment, as well as the medical treatment of diabetes, may account for these variables not achieving predictor variable status in neuropsychological test performances. Therefore, systematic documentation of several pertinent medical variables will serve to further elucidate the role of these factors in the neuropathology of transient ischaemic attacks as well as their influence on neuropsychological test scores.

CT scans were the routine neuroimaging techniques used at the hospitals when this study was conducted. It is now widely accepted that CT scans are limited in their resolution power and thus offer images restricted to the gross structural integrity of the brain. The current imaging technology of choice is magnetic resonance imaging (MRI) which offers greater resolution power and therefore gives a greater likelihood of the identification of brain infarcts. More specifically, the documentation of magnetic resonance imaging (MRI) T1 and T2 signals provides a comparative measure of pathological and normal tissue, respectively, and may offer more refined structural indices which may be correlated with neuropsychological scores.

In addition, the identification of small (lacunar) brain infarcts deep in white brain matter is another variable that should be documented since this neuropathological feature is considered an important index of the severity and generalizability of the transient ischaemic attack. Thus, the use of MRI and its various diagnostic features in the study of transient ischaemic attacks should be undertaken in future studies.

The elucidation of those human brain regions that process different cognitive functions appears to be a fruitful research model which is in keeping with the modularisation approach to neuropsychology. The localization of functional systems is currently being measured using radiographic techniques such as positron emission tomography (PET) that provide images of brain metabolism or blood flow while subjects perform certain cognitive tasks (Leary, Andreasen, Hurtig, Hichwa, Watkins, Ponto, Rogers and Kirchner, 1996). PET studies have been found to be useful in localizing studies, for example, Leary et al. (1996) reported that using oxygen-15-labelled water, the classical view of language localization based upon lesion analysis has received partial support. They reported that apart from the involvement of the left posterior temporal lobe (Wernicke's area) in auditory speech perception, homologous regions in the right temporal lobe have also been found to be active during speech perception. Their findings suggest that the right hemisphere plays a greater role in language processing that had been previously suggested by lesion studies.

Thus, using measures of structural lesions (MRI's) in conjunction with those yielding data on the functional, metabolic status of the brain (PET) and correlating these measures with specific neuropsychological test scores should be undertaken in future studies.

The hallmark of transient ischaemic attacks is that there is recovery of neurological functioning without residual signs and symptoms. Part of the underlying mechanism thought to account for this recovery is the presence of several compensatory mechanisms in the cerebrovasculature, the chief of which is the circle of Willis. The findings of this study suggesting that only circumscribed areas of neuropsychological functioning were negatively affected in transient ischaemic attacks indicate that similar cerebrovascular compensatory mechanisms may explain these results. The use of magnetic resonance angiography (MRA) for flow quantification may thus serve to elucidate the role of these compensatory mechanisms in the normal performances of patients on certain neuropsychological tests.

Thus, the use of refined neuroimaging techniques both elucidating structure (as in the case of MRI) and functional activity (as in the case of PET) may be useful for identifying the specific involvement of various cognitive and associated neural structures in transient ischaemic attacks. In addition, the visualization of the entire cerebrovascular system through MRI and MRA is important to document the patency of the circle of Willis and other compensatory vessels. These data may thus offer a more comprehensive account of the dynamic changes in both the cerebrovascular and neurocognitive systems, the latter based on inferential analyses of neuropsychological test scores.

11.3 Recommendations for Neuropsychological Assessment

11.3.1 Using the Modular Cognitive Neuropsychological Approach.

The present study was based on assumptions derived from a cognitive neuropsychological approach based on a modular view of the human mind. The view of cognition as modular, at least in some loose sense of the term, has been the accepted framework in neuropsychological research (Deluca, Johnson, Ellis, & Natelson, 1997). The findings obtained in this study suggesting that there are circumscribed areas of neuropsychological impairment in the transient ischaemic attack groups tends to support this modular view. Moreover, there appears to be qualified support for Fodor's (1983) proposal that the human mind is composed of relatively seamless, all-purpose central processes along with a number of distinct, highly specialized, structurally idiosyncratic input modules.

The modular view of cognition becomes even more plausible in the context of the theoretical views on the organization of function in the human brain. The theories of Luria (1980) appear to be partially consistent with those of cognitive neuropsychology since both schools of thought suggest that psychological systems have an organization that encompasses both elemental and gestalt features. These proposals suggest that psychological processes may be deconstructed into individual processes which are presumably organized in cognitive processes correlating with distributed networks of neural structures. Mesulam (1985) was able to propose a neural network for directed attention on the basis of data emanating from various research techniques, viz., neurological, neuropsychological, radiological and clinical. More recently, Rueckertt and Grafman (1996) proposed revisions to the distribution of various language functions in the brain by proposing an approach that represents a convergence of the cognitive properties of attention and language and the proposals of Fodor (1983).

Transient ischaemic attacks offer a unique opportunity to study highly localizable lesions since the pathology of this disease results in demarcated areas of loss of blood supply. Thus, using the high resolution powers of MRI, the vascular visualization techniques of MRA, as well as the metabolic status of regions of the brain using PET, and correlating these with carefully selected neuropsychological tests, will expand and develop the modular structure that underlies cognitive neuropsychology.

11.3.2 Neuropsychological Measures

Stenosis significantly predicted performance in selected neuropsychological tests in the transient ischaemic attack groups. The findings that the left transient ischaemic attack group performed significantly poorer than the right group on Digits Forward, the PASAT (all levels), Trails B, trial 1 of the Rey Auditory Verbal Learning test, Block Design and Verbal Fluency should be further investigated. In particular, the graded findings obtained on the PASAT suggesting that the left transient ischaemic attack group performed worse than the right group at all levels of this test should be further studied in neurological samples of patients with lateralized lesions.

Mesulam (1985) provided a model that proposes the distribution of neural networks underlying spatial attention in the right hemisphere based on data that were largely nonverbal in nature. It may be possible that performance of the PASAT may result in the selective stimulation of distributed neural areas in the left hemisphere since the left transient ischaemic attack patients performed significantly worse than the right transient ischaemic attack and control groups.

The findings that higher education may mediate recovery from brain damage has been previously reported by Reitan and Wolfson (1996) and appears to receive tentative support in this study. Thus, the role of higher education in mediating performance on trial 1 of the Rey Auditory Verbal Learning Test, Block Design and Verbal Fluency in patients with neurological disease should be systematically studied in other patient groups. It is possible that these findings may provide opportunities for intervention and management of neuropsychological disorders in these patients.

Furthermore, using the epidemiological research approach outlined earlier in this chapter will provide a systematic approach to the investigation of the influence of several demographic variables on neuropsychological test performances. This process may serve two related functions.

Firstly, the psychometric investigation of tests showing significant differences between the transient ischaemic attack and control groups may provide further information on the validity and reliability of these measures.

Second, by embarking on an epidemiologically-based study, the urgent need to develop an appropriate database for the rigorous standardisation of several neuropsychological tests in South Africa will be catalyzed (Nell, 1994). The development of a database of carefully documented cases of cerebrovascular diseases will thus provide an opportunity to conduct regression analyses in order to identify those variables that contribute significantly to the variance of scores on selected neuropsychological tests.

Cerebrovascular disease patients could then be compared on these tests with samples of hospitalised patients without evidence of neurological diseases, but who are similar on those demographic variables considered significant contributors to neuropsychological test scores. On the basis of a combined database which includes normal subjects (control group) and transient ischaemic attack patients (experimental group), statistical tests of discriminant function analysis may be performed to establish group membership using the experimental and controls groups as the study groups. The data thus derived from the control group will provide the basis for normative data for these selected tests. The use of these statistical methods will therefore provide a statistical basis of deriving normative data for various groups identified on those variables (such as education etc.) showing statistically significant influence on test scores. In this way, the judicious use of statistics may assist to circumvent the arguments of race and politics that are pervasive in discussions on appropriate norms.

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APPENDIX A

BIOGRAPHICAL QUESTIONNAIRE

Biographical Data Sheet

A. Basic Biographical Data

1. Name____________________________________

2. Age____________________________________ (Years)

3. Educational Level____________________________(Years)

4, Monthly Income____________________________(South African Rands)

5. Family Size____________________________________

6. Total Family Income__________________________(South African Rands)

7. Per capita Income____________________________(Rands Per Person)

B. Health Data

8. Are you a smoker? Yes No

9. Do you drink alcohol? Yes No

10. Do you have any of the following illnesses? a. Hypertension

b. Diabetes

c, Heart Conditions

d. Overweight

11. If yes to any of 10, what treatment have you been placed on?

12. Have you been treated for a psychological or psychiatric problem?

13. If yes to 12, what was the diagnosis?

14. What kind of treatment did you undergo for the problem indicated in 12 and 13?

a. drug therapy b. psychotherapy c. both drug and psychotherapy

15. Do you have any physical disabilities? Yes No

16. If yes, please specify.

C. <u>Transient Ischaemic Attack Data (For Experimental Subjects Only)</u>

17. In which year (s) did you first have TIAs? First__________________

Subsequent_____________

18. Where were you at the time?________________________________

19. Who was present at the time of the symptoms?___________________

20. How long do you think the symptoms lasted?

a. less than thirty minutes

b. 30 to 60 minutes

c. more than one hour

21. What did you do when the symptoms had gone away?

22. Are you on drug treatment at this time?

23. What drugs are you taking?

Thank you for your kind participation in this study. Please feel free to ask whatever questions you may find necessary. If you choose to discontinue with this study at any stage, please feel free to inform me and this will be done immediately. Your decision to discontinue with this study will in no way whatsoever compromise the quality of health care you receive now or in the future.

APPENDIX B

SUBJECT NEUROPSYCHOLOGICAL DATA

Subject Neuropsychological Data

23. Digit Span Forward: ____________________

24. Digit Span Backward: ____________________

25. Digit Span Total : ____________________

26.PASAT: 2.4 seconds ____________________

26.PASAT: 2.4 seconds ____________________

27.PASAT: 2.0 seconds ____________________

28.PASAT: 1.6 seconds ____________________

29.PASAT: 1.2 seconds ____________________

30. Trails A: ____________________

31. Trails B: ____________________

33. Rey Auditory Verbal Learning Test: Trial 1: __________

34. Rey Auditory Verbal Learning Test: Trial 2: __________

35. Rey Auditory Verbal Learning Test: Trial 3: __________

36. Rey Auditory Verbal Learning Test: Trial 4: __________

37. Rey Auditory Verbal Learning Test: Trial 5: __________

38. Rey Auditory Verbal Learning Test: Trial 6: __________

39. Rey Auditory Verbal Learning Test: Trial 7: __________

40. Block Design: ____________________

41. Verbal Fluency: ____________________