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LA THÈSE A ÉTÉ
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NEUROPSYCHOLOGICAL ASSESSMENT OF CHANGES FOLLOWING CAROTID ENDARTERECTOMY

A THESIS SUBMITTED TO THE SCHOOL OF GRADUATE STUDIES AND RESEARCH IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

by

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ABSTRACT

A study was performed to examine the question of whether the removal of obstructive carotid lesions (carotid endarterectomy) has restorative or solely prophylactic effects. Fifty-five operated subjects grouped on the basis of the side of endarterectomy were compared with patients undergoing surgical procedures not involving the brain and cerebral vasculature and a second group of controls with vascular symptoms but no surgical intervention. It was found that patients undergoing right carotid endarterectomy improved on more measures than any other group. When the data were analyzed according to the severity of symptoms, it was found that patients presenting with stroke improved on more measures than those presenting with TIA. Further it was found that right operated stroke patients improved on a greater number of measures than left operated stroke patients, but there was no difference between right and left operated TIA patients. There were no demographic or medical differences for these findings. The left operated stroke patients were somewhat more impaired on a few measures than were the right operated stroke patients. In addition it was found that the left stroke patients were operated upon significantly later in their hospital course than left operated TIA patients. This pattern was not found among the right operated patients. These findings were discussed in terms of several possible explanations. These possibilities included a basic hemispheric difference in regard to the effects of cerebrovascular disease, the possibility that the left operated group exceeded some critical level of impairment, or that the time of surgery is crucial if partial restorative effects are to be achieved.

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CHAPTER I

INTRODUCTION

The problem of cerebrovascular disease has been known to the medical sciences since the time of Hippocrates and recently has become the subject of increased clinical and experimental study. This increased interest is reflected in the many international conferences which have been convened (e.g. the Annual Princeton Conferences on Cerebrovascular Disease) and the new journals specifically devoted to research in this area (e.g. Stroke). Contemporary investigations have made major advances in understanding many issues related to cerebrovascular disease. Some of these issues will be reviewed in the following sections. The epidemiology of stroke is presented in terms of the prevalence in the general population. Etiological factors are then considered including the various mechanisms of stroke, and factors which influence the pathogenesis of cerebrovascular disease. A number of factors have been identified which may limit the extent of the neurological deficits following stroke and these factors are discussed followed by a classification of ischemic strokes. This classification system is based on the relative persistence of neurologic residua. The outcome of medical and surgical treatments are examined in regard to the relative risks and long term success (survival rates). Several studies which have attempted to demonstrate psychological improvements following surgical treatment are critically reviewed and the present investigation is proposed in view of the weaknesses of these previous studies.

The methodology section describes the subjects and the sequence in which the data were obtained. The neuropsychological, medical and surgical measures are also described. This is followed by a presentation of the results of the statistical analyses and a discussion of these results.

Review of the Literature

Epidemiology

Cerebrovascular disease (C.V.D.), or stroke is a major cause of death (mortality) and disability (morbidity) in individuals beyond the age of 65. In most developed countries C.V.D. follows coronary heart disease and cancer as the third ranking cause of death (Wylie, 1972). It has been estimated that there are 500,000 new strokes each year in the United States, and that 200,000 deaths per year (or 11% of the total mortality) are attributable to cerebrovascular disease. In an additional 11%, stroke is an indirect or contributory cause of death (Wolf, Dawber, Thomas, Colton and Kannel, 1977).

The President's Commission (1964) estimated that there were 2,000,000 people alive in the United States in 1964 with a history of some form of cerebrovascular disease. Based on census data, Harris, Cox and Smith (1971) reported that there were 130,000 patients in Great Britain with significant impairment due to stroke, and that new cases were added at the rate of 2/1,000 population per year.

Although the prevalence of cerebrovascular disease increases with age, approximately 20% of cases occur in persons under the age of 65

(Kannel and Wolf, 1975). There are approximately 20/1,000 population in the 45 to 54 age group, 60/1,000 between the ages of 65 to 74 and 95/1,000 at the ages of 75 to 84 (N.I.H. 1971).

Investigators in several countries have examined the mortality rates related to cerebrovascular disease. Segi, Kurihara and Tsukahara (1966) compared age adjusted death rates in 30 countries and found the highest rates in Japan. The 1960-61 rates per million population were 2,267 males and 1,594 females in Japan, 811 males and 713 females in Caucasians in the United States, 1,300 males and 1,211 females for non-whites in the U.S., and 764 males and 757 females in Canada. Wylie (1972) reports that the death rate from stroke in England and Wales over the years 1949 to 1967 averaged 1,600/million population.

Several studies have examined the incidence of new cases of cerebrovascular disease. Eisenberg, Morrison, Sullivan and Foote (1964) reported an annual incidence rate of 2.3/1,000 population in Middlesex County, Connecticut. A similar survey in three counties in Missouri reported incidence rates of 2.5/1,000 in whites and 4.1/1,000 in non-whites, although the non-white population was quite small (Goldner, Payne, Watson, and Parrish, 1967).

Acheson and Fairbairn (1970) report an incidence rate of 1.2/1,000 population in the geographic area surrounding Oxford, England. Wylie (1972) reviewed data from hospitals discharges in England and Wales and calculated an overall incidence rate of 1.7/1,000 population.

There also have been reports of the incidence of stroke in several areas in Canada. LaRiche, Bond and Stiver (1965) reviewed information from a nonprofit medical care plan in Ontario. Although only 2.3% of the

population was 65 years of age or older, these authors found an incidence of 2.2/1,000.

The Vital Statistics Division of the government of British Columbia reported data based on claim forms submitted to the health insurance program for government employees and their dependents. The annual incidence of cases treated for cerebrovascular disease over the years 1961-67 averaged 2.2/1,000 population (Division of Vital Statistics). A review of hospital discharges in Saskatchewan over the years 1959-63 yielded an average annual incidence of 2.4/1,000 population (Saskatchewan Department of Public Health).

The Ottawa and surrounding region has a population of approximately 1,000,000. Based on reported incidence rates in the United States (Goldner, et al., 1967; Eisenberg, et al, 1964) and in Canada (LaRiche, et al, 1965; Saskatchewan Department of Public Health; Division of Vital Statistics, British Columbia), approximately 2,000 new stroke victims can be expected each year in the Ottawa region.

Etiology

A stroke, or "cerebrovascular accident" (C.V.A.), is a sudden onset of neurological deficit due to a vascular cause. There are two primary mechanisms by which vascular disease affects neural tissue. Cerebral ischemia is produced by a lack of adequate blood supply to a part of the brain, usually caused by obstruction of one of the cerebral vessels, while hemorrhagic strokes are caused by a rupture of a blood vessel and subsequent bleeding into a brain parenchyma or surrounding space (e.g., subarachnoid hemorrhage). The two conditions may exist simultaneously,

with one being the consequence of the other. Ischemic strokes are the most common, accounting for 59% of all strokes in a major prospective epidemiological study (Wolf, et al., 1977).

The normal function of the human brain depends on the oxidative metabolism of glucose for the production of energy and maintenance of cellular activity. Although it comprises only 2% of the body mass, the brain receives 15% of the cardiac output and consumes 20-25% of the arterial oxygen content (Robertson and Dinsdale, 1972). The cerebral oxygen reserve is extremely limited and normal metabolism can be maintained for only 8 to 10 seconds after the oxygen supply fails (Meyer, Guiraud and Bauer, 1975). Because of this lack of storage capacity, the brain requires extensive rapid replenishment of oxygen. Under normal conditions, adequate supplies of oxygenated blood are provided via the cerebrovascular system. Disruption of the vascular supply results in impaired cerebral function which may be reversible, but may become irreversible if the oxygen deprivation persists for longer that 6 to 8 minutes (Meyer, et al., 1975).

In ischemic cerebrovascular accidents, interruption of local cerebral blood supply leads to a loss of neural function and subsequent destruction of neural tissue (necrosis). This process of an irreversible anoxic injury to a region of brain tissue followed by necrosis is referred to as infarction.

Gilroy and Meyer (1975) state that virtually all ischemic strokes are the consequence of cerebrovascular arteriosclerosis and Fisher (1975) argues that in developed countries, atherosclerosis is the basic process in greater than 90% of cases of infarction due to cerebral thrombosis.

On the other hand, Robertson and Dinsdale (1972) conclude that 60% of ischemic cerebrovascular disease is due to atherosclerosis and its complications, while 30% is due to emboli arising primarily from the heart. At any rate, there is general agreement that arteriosclerosis is a major factor in cerebrovascular disease.

Arteriosclerosis is a chronic degenerative process which involves blood vessels throughout the body and is the most frequent disease of the cerebral vessels (Moossy, 1959, 1966). Pathological changes may begin early in life, but generally are related to older age with an increase in severity after the age of 50 (Fisher, 1975; Moossy, 1959). The principal pathological alteration is the formation of atheromatous plaques in the vessel wall. These plaques are composed of collagenous bundles which enclose a mass of fatty debris and microscopically are seen to contain cholesterol clefts. Macroscopically the lesion may have a smooth or irregular surface.

Two principal theories have been advanced to explain the development of the atherosclerosic changes. The lipid theory assumes that the initial lesion occurs from deposition of lipids (including cholesterol) in the vessel wall via the bloodstream. The alternative theory suggest the formation of a thrombus on the vessel wall as the precipitating event in the formation of the atherosclerotic plaque. The thrombus which is rich in lipids is incorporated into the vessel wall by growth of the endothelial lining of the vessel. Subsequently, the thrombus undergoes degeneration leading to a lipid deposit within the vessel wall. The two theories of atherogenesis converge at this point. There is a gradual accumulation of lipid material and a loss of elastic tissue which leads

to the further development of the atherosclerotic plaques.

The importance of lipids as a major factor in cerebral atherosclerosis was indicated in a study by Mathew, Davis, Meyer and Chandar (1975). These authors found elevated lipid levels in 32% of a series of cases with ischemic stroke. Of those cases with elevated serum lipid values, two thirds had elevated triglyceride levels, and these patients had an increased incidence of occlusive extracranial disease compared to patients without abnormal lipid values or those with other types of lipid disorders. In addition, Randrup and Pakkenberg (1967) and Duncan, Lees, Ojemann and David (1977) reported abnormal lipid levels in patients with radiographically demonstrated atherosclerotic lesions in the carotid arteries.

Plaques have a tendency to form at certain points in the vascular system. An early study by Chiari (1905, cited in Meyer, et al., 1975) reported that the internal carotid artery was second only to the abdominal aorta as the most common site of atheromatous plaques. It is generally held that points of bifurcation or tortuosity of vessels are sites of predilection for plaque formation (Fisher, 1975; Robertson, and Dinsdale, 1972; Meyer, et al., 1975; Feigin and Budzilovich, 1975). In the internal carotid artery the origin is the most frequently affected site.

This is the point where the common carotid artery bifurcates to form the internal and external carotid arteries. The terminal portion of the internal carotid artery is referred to as the carotid siphon. Due to the fact that the carotid siphon follows a highly curved course, it also tends to be a frequent site for the development of atheromatous lesions

(Mitchell and Schwartz, 1965). In fact, the carotid siphon is the second most common site of occlusion in the internal carotid system (Meyer, et al., 1975). In addition to the internal carotid arteries, several other major cerebral vessels are frequent sites of atheromatous lesions including the junction of the vertebral and basilar arteries, the stem of the middle cerebral artery, the anterior cerebral artery as it bends around the corpus callosum and the posterior cerebral artery as it passes the cerebral peduncle (Fisher, 1975). Atherosclerotic changes have also been demonstrated in small cerebral vessels with diameters as small as 200-300 . In the presence of hypertension, degenerative vascular changes (lipohyalinosis) may involve arteries 70-200 in diameter (which normally are not subject to atherosclerotic changes) (Fisher, 1975).

Cerebral atherosclerosis tends to be multifocal in that involvement of one major vessel is associated with disease in at least one of the other major cerebral vessels. In a series of 75 unselected cases at autopsy, Lhermitte, Gauthier and Derouesne (1966, cited in Meyer, et al., 1975) found that of cases with at least a 75% stenosis of one internal carotid artery, in only 10% was the contralateral internal carotid free from atherosclerotic disease. Bauer, Meyer, Fields, Remington, MacDonald and Callen (1969) report that 55-60% of cases with occlusive cerebrovascular disease had arteriographic evidence of bilateral arterial disease. In an earlier study (Bauer, Sheehan, Wechsler and Meyer, 1962), 72% of the patients had multiple vessel involvement, and Fields, Bruetman and Weibel (1965) report that in clinical situations it is an exceptional case to find only one artery involved by arteriosclerotic stenosis or thrombotic occlusion.

Occlusive cerebrovascular disease can result in neurological symptoms by a number of pathological processes of which the formation of an artheromatous plaque is only an initial stage. As the plaque increases in size, due to the continued incorporation of successive thrombi and deposition of lipid material, the lumen of the vessel becomes progressively narrowed by a thickening of the vessel wall (a process referred to as mural thrombosis). In isolated internal carotid artery disease, the stenotic process must be considerable before creating a significant hemodynamic hazard. Mann, Herrick, Essex and Baldes (1938) concluded that a stenotic lesion of 70% of the lumen was necessary to compromise the blood flow, while Brice, Dowsett and Low (1964) reported that a stenotic lesion of 85% would significantly impair blood flow. Gilroy and Meyer (1975) described flow meter studies performed on man during carotid artery surgery and reported that significant flow reductions beyond a point of stenosis did not occur until the lumen was reduced by 70 - 90%. In the presence of multifocal disease, a stenosis of 50% may be sufficient to impair blood flow (Roberts, Hardesty, Halling, Reivich and Toole, 1964). As the plaque begins to encroach upon the lumen it may serve as the foundation for the collection of platelets, fibrin and white blood cells on the surface of the plaque. These cellular components organize to form thrombi in response to damage of the vascular endothelium. These surface thrombi may attract additional material from the blood stream leading to a progressive thrombosis and ultimate occlusion of the vessel (Feigin and Budzilovich, 1975). In the early stage of thrombus formation before organization is complete, the thrombus is somewhat loosely organized and free in the bloodstream. Platelet aggregates from the thrombus may break

away and be carried in the blood stream to impair flow in a vessel further on in the vascular system, e.g., small intracranial vessels. The occlusion of a distal vessel by material brought to that point from some proximal location is referred to as embolism and has been demonstrated to occur in cerebral arteries (Swank and Hain, 1952). In addition to platelet emboli from a surface thrombus, the plaque may become ulcerated and constitute a source of emboli.

Turbulence of blood flow occurs at points of bifurcation, tortuosity and at points of change in vessel diameter. This turbulence increases stress and destruction of the endothelial lining of the vessel. For this reason, turbulence is believed to play a major role in the development of sclerotic lesions and is reflected in the predilection of atheroma for points of branching and tortuosity (Meyer, et al., 1975; Robertson and Dinsdale, 1972). Turbulence is also reported to be a prominent factor in the ulceration of stenotic plaques (Barnett, 1977). Turbulent flow at the point of a stenotic lesion may cause the breakdown of the endothelial lining of the plaque (Gilroy and Meyer, 1975). The ulcerated surface may then be a source of platelet aggregates or lipid crystals which can break off and produce embolic events in the distal cerebral vasculature. In addition the ulcerated surface may attract the formation of a new thrombus with similar embolic potential. Most small emboli do not lead to alterations of cerebral blood flow and are probably broken up as they flow through the cerebral circulation (McDowell, 1975). These emboli from ulcerated plaques are usually quite small and generally obstruct vessels less than 100 . The majority of emboli sufficiently large to

cause infarction of cerebral tissue tend to originate in the heart (Robertson and Dinsdale, 1972; McDowell, 1975).

In summary, neurological dysfunction may occur within seconds following disruption of the cerebrovascular supply of glucose and oxygen. The disruption may be caused by a lack of blood in part of the brain (ischemia) or by bleeding into the cerebral tissue (hemorrhage). Ischemic strokes are the most common and are caused by occlusion of a cerebral vessel usually due to the formation of arteriosclerotic plaques. These plaques tend to form at certain points in the vascular system, usually where there is stress on the endothelial lining of the vessel wall. The two main theories of atherogenesis postulate platelet aggregation or lipid accumulation as the initial stage of plaque formation. Plaques may lead to neurological symptoms by the process of thrombosis or embolism.

Factors Influencing the Expression of Deficits

In spite of the fact that a number of mechanisms may produce symptoms of cerebral ischemia, the presence of these pathological changes does not necessarily produce symptoms. Whisnant, Martin and Sayre (1961) reported a series of unselected cases at autopsy. In patients with no history of cerebrovascular disease, 30% had a stenosis of 50% or greater in at least one of the cervical arteries. In a similar study of unselected autopsy cases (Schwartz and Mitchell, 1961), it was found that 90% of males and 85% of females had stenosis at some point along one of the four major vessels. Furthermore, 43% of the males and 35% of the females had severe narrowing. Only 29% of these cases had demonstrated signs of occlusive

cerebrovascular disease during life. Whisnant (1971) described a case which emphasizes the point that disease of major cerebral vessels may not produce symptoms. The case was a 63 year old male who had died of a myocardial infarction. At autopsy he was found to have occlusion of the internal carotid artery, external carotid artery and the carotid sinus on the right as well as a severe stenosis of the innominate artery (which gives rise to the common carotid artery). On the left side there was occlusion of the external carotid and common carotid arteries and a severe stenosis of the subclavian artery. In terms of cerebrovascular symptoms, this patient was completely asymptomatic throughout life. This case illustrates the flexibility and dynamics of the cerebral circulatory system.

A number of factors are important in mediating the expression of neurological symptoms subsequent to cerebral ischemia. These factors include the extent of collateral blood supply, the rate of progression of the disease process, the degree of involvement of other cerebral vessels and the presence of other disease processes which may complicate the primary disease entity.

The potential for collateral flow within the brain is based on the major conducting vessels that supply blood to the brain. The brain is supplied with oxygenated blood by two principal arterial systems which orginate with four major cerebral vessels. The anterior circulation of the brain is provided by two internal carotid arteries while the posterior circulation is supplied by two vertebral arteries.

In the carotid system, the right common carotid artery arises from the brachiocephalic trunk while the left common carotid artery arises

from the aortic arch. The common carotid arteries ascend in the neck and bifurcate at the level of the upper border of the thyroid cartiledge to form internal and external branch. The internal carotid artery passes upward to penetrate the skull and dura. The terminal portion of the internal carotid artery divides to form the middle cerbral and anterior cerebral arteries. The middle cerebral is the larger of the two branches and supplies most of the lateral surface of the cerebral hemisphere. Penetrating branches enter the brain to supply the basal ganglia and internal capsule above the level of the globus pallidus.

The anterior cerebral artery is the smaller of the terminal branches of the internal carotid artery. This artery supplies the anterior 4/5 of the medial surface of the cerebral hemispheres, as far back as the parieto-occipital fissure. Branches of the anterior cerebral artery also supply the corpus callosum, cingulate gyrus, and the orbital surface of the frontal lobe.

Each internal carotid artery supplies approximately 1/3 of the total cerebral blood supply. The remaining 1/3 is supplied by the second major arterial system, the vertebrobasilar system.

This system is comprised of a right and left vertebral artery which supply the cervical region of the spinal cord. The vertebral arteries penetrate the dura at the level of the medulla and join at the level of the ponto-medullary junction to form the basilar artery. Together these vessels are known as the vertebrobasilar system which supplies the brain stem, cerebellum, and major portions of the diencephalon. The terminal branches of the basilar artery are the right and left posterior cerebral arteries. Each of these vessels passes medially and supplies the medial

and interior surface of the temporal lobe and the occipital lobe. Penetrating branches supply various brainstem structures including nuclei of cranial nerves III and IV, the periaqueductual gray, medial longitudinal fasciculus, and the inferior and superior colliculi.

The three major intracerebral vessels (anterior, middle and posterior cerebral arteries) are interconnected via a group of anastomotic vessels. The anterior cerebral arteries are connected by an anterior communicating artery. Each internal carotid artery gives rise to a posterior communicating artery which passes posteriorly to contact the posterior cerebral artery which is the terminal branch of the posterior circulation. Taken together, these cerebral arteries and their anastomotic connective vessels are referred to as the Circle of Willis. This structure is named in honor of the 17th century physician, Thomas Willis, who was the first to explain the clinical significance of this circle in patients with cerebrovascular occlusion (Adams, 1974).

The Circle of Willis constitutes the primary source of intracranial anastomosis and provides a potential mechanism for collateral supply. Under normal conditions there is no significant flow either between the hemispheres or between the anterior and posterior circulation (Kramer, 1912) because of the near equal perfusion pressure of the blood entering the two sides of the brain. Vacsular disease may alter the conductivity of the vessels and reduce the pressure or volume of blood on the affected side (as occurs with stenotic lesions). In this case the interconnections between the major vessels may provide a means of circumventing the effects of vascular obstruction. The interhemispheric interconnection between the two internal carotid arteries is more efficient than the

intrahemispheric interaction between the anterior and posterior circulation (Meyer, et al., 1975).

A second major source of intracranial anastomeses are the connections between the distal endarteries of the major cerebral arteries. The terminal branches of these vessels converge at the border zones (or so-called watershed areas) between major arterial distributions and provide a second mechanism by which the effects of vascular disease may be limited. These distal vessels are of very small caliber and rarely are of sufficient size to compensate for the occlusion of a major cerebral vessel (Robertson and Dinsdale, 1972). They may, however, be successful in limiting the magnitude of an infarct by providing supply to a distal territory. These borderzone anastomoses occur between the middle cerebral artery distribution and the anterior and posterior cerebral arteries.

In addition, a third major source of collateral supply is potentially available via extracranial to intracranial anastomosis. The primary source of these interconnections is between the opthalmic artery and branches of the external carotid arteries (Fields, Edwards and Crawford, 1961). The opthalmic artery is the first major intracrancial branch of the internal carotid artery, and it connects with branches of the external carotid artery which supplies the orbit. In cases of occlusion of the internal carotid artery, blood can flow in a retrograde manner and preserve flow in the diseased artery.

There are numerous factors which impinge on the efficiency of the collateral circulation. Anatomic variations are frequent among the components of the Circles of Willis. Fields, et al. (1965) reported that

in most series of cases, 50% had anomalies. The most frequent of these findings was a carotid origin of the posterior carotid artery. This artery normally originates from the posterior circulation, and cases in which this anomaly occurs have a tenuous connection between anterior and posterior circulations (Fields, 1972). Another frequent abnormality is hypoplagia or agenesis of the segment of anterior cerebral artery artery running between the carotid origin and the anterior communicating artery. In this case both anterior cerebral arteries are supplied through the internal carotid system on the side opposite the hypoplagic segment (Sedzimir, 1959). These abnormalities may occur singly or in combination but in any case they represent a reduction in the potential collateral circulation. Support of this can be gained from the observation of increased incidence of cerebral infarction in patients with an incomplete Circle of Willis (Alpers, 1959).

In addition to congenital anomalies, collateral flow at the base of the brain may be compromised by occlusive disease either of the major cervical vessels or of the cerebral vessels themselves. Thrombi may spread from the carotid artery in the neck or stenotic lesions may form at points of branching in the cerebral vessels. Both lesions will limit the anastomotic potential, particularly in those cases whose collateral supply is already threatened by congenital anomalies.

The terminal endarteries may also be affected by atheromatous processes and this may result in local occlusion or may limit the ability of these vessels to dilate in response to obstruction in the proximal portions of the arterial trunk. This will result in reduced collateral capacity through the borderzone areas. As is often the case, both large

and small vessels may be involved and when this occurs, there is an increased tendency for clinical symptoms to appear (Hsieh, 1967).

The mechanism of disease is also an important contributory factor in determining the extent to which anastomotic vessels can circumvent an occlusive event. Collateral flow is normally not operative and does not immdiately become effective upon occlusion of a vessel. Embolic events which develop abruptly may provide insufficient time for the collateral circulation to prevent infarction. On the other hand, anastomotic flow is much more likely to occur in cases with a slowly progressive occlusion. For example, the gradual development of a stenotic artheromatous plaque may permit the distal segments of the vasculature to adapt to alterations in the flow requirements. If the distal vessels are not also diseased, they may provide an effective collateral channel to maintain the viability of the tissue in the distribution of the occluded vessel. The efficiency of the collateral channels in slowly progressive atherosclerotic disease is attested to by the frequency of asymptomatic carotid artery occlusions (Fisher, 1975; Robertson and Dinsdale, 1972). Further, it is not uncommon to find small non-fatal infarcts in brains of patients who died from other causes (Fisher, 1961). Robertson and Dinsdale (1972) report that up to 25% of elderly patients are found to have small infarcts at autopsy, many in association with little or no clinical deficit.

It is clear that a major consideration in regard to the expression of a vascular occlusion will be the importance of the vessel itself that is involved. Occlusion of a major cerebral vessel or its tributaries is much more likely to produce clinical symptoms than would be involvement

of a small distal arterial branch. Furthermore, involvement of distal branches tends to lead to more circumscribed symptomatology.

In summary, a number of factors may influence the nature and severity of the neurological deficit subsequent to a cerebrovascular accident. The relative importance of the involved vessel affects the nature and extent of the deficit. The amount of potential collateral circulation is related primarily to the condition of the Circle of Willis. Additional sources of collateral flow are the extracranial to intracranial anastomoses, and the connections between the distal endarteries of the major arterial systems. The rate of progression of the occlusive disease process is important since a rapid development (embolism) may provide insufficient time for the collateral flow to limit infarction.

Classification of Ischemic Stroke

Cerebrovascular accidents in the carotid artery distribution are commonly classified on the basis of the duration and permanence of the neurological symptoms produced. Regardless of the specific underlying etiological mechanism, many patients present with a sudden onset of symptoms which clear completely usually within 24 hours. This type of vascular episode is referred to as a transient ischemic attack (TIA). The criteria of classification varies among authors but the most commonly accepted definition of TIA is "a temporary and focal episode of neurologic dysfunction of presumed vascular origin usually lasting 2-15 minutes but occasionally as long as 24 hours" (Sandok, et al., 1978). Some attacks may last only a few seconds, and Fisher (1976) argued that 70% of TIAs last less than 10 minutes. The characteristic features of

TIA are the focal nature of the symptoms, usually within a recognized distribution of a cerebral vessel, the brief duration of the symptoms, the lack of any residual neurologic deficit, and the tendency for the attacks to recur (Meyer, et al., 1975). Perhaps the greatest clinical significance of TIA is in their prognostic significance and in the possibility that an attack may lead to treatment and prevention of permanent neurologic deficit. In some patients, TIA may serve as a warning of impending catastrophic stroke, while some patients continue to experience TIA without subsequent infarction and others have a TIA as an isolated incident (Heyman, 1974). The urgency of initiating treatment following the onset of TIA is underscored by the report of Whisnant, Matsumoto and Elveback (1973) who reported that 51% of patients with TIA who proceed to infarction will do so within 12 months of the first TIA. Furthermore, Marshall (1964) reported that of patients who experience TIA prior to a completed stroke as many as 75% have only one or two TIAs prior to their infarct.

Among cases with TIA who receive no treatment for their symptoms, the reported incidence of cerebral infarction varies considerably. Marshall (1964) presented a series of chronic TIA patients with only a 2% incidence of infarction. Toole (1977) attributed this low incidence to the fact that the patients at greatest risk had already been selected out of the series by virtue of infarction. On the other hand, Acheson and Hutchinson (1971) reported an infarction incidence rate of 62.3% in a group of untreated TIA patients. The unusually high incidence rate is to a large extent due to the definition used for TIA. These authors used a maximum of one hour as the definition of TIA. From a somewhat different

approach Hurwitz, Groch, Wright and McDowell (1959) reported that 39% of cases with completed stroke had experienced prior transient episodes and Fields and Remington (1969) reported that 74% of patients with occlusion of the carotid artery had previous TIAs.

The general consensus is that approximately one third of untreated TIA patients will proceed to suffer a cerebral infarction within 5 years of the first attack, approximately one third will continue to have TIAs without infarction, and the remaining patients experience a spontaneous cessation of vascular episodes (Gilroy and Meyer, 1975). Of those cases who do progress to infarct, 21% will do so within the first month and 51% within 12 months following the initial TIA (Whisnant, et al., 1973). Six months following the initial onset of TIA the stroke occurrence rate is approximately five times the expected rate for a similar aged normal population (Matsumoto, et al., 1973). Zeigler and Hassanein (1973) reported that if a patient has not gone on to suffer a completed stroke within two years, the frequency of TIAs are likely to diminish.

Some patients experience neurological symptoms of vascular etiology which persist longer than 24 hours, and hence do not meet with the generally accepted definition of a transient ischemic attack. Although there may have been some degree of cerebral infarction, these patients achieve a complete or nearly complete resolution of their symptoms. Meyer, et al. (1975) and Millikan (1975) refer to this category of vascular disease as Reversible Ischemic Neurological Deficit (RIND). Meyer, et al. (1975) suggested that these patients follow a clinical course similar to patients with TIAs. Loeb, Priano, and Albano (1978) grouped patients with TIAs and others experiencing Stroke with Full

Recovery under the general classification of Reversible Ischemic Attack. Stroke with full recovery was defined as "sudden episodes of focal cerebrovascular deficit persisting beyond 24 hours with complete regression over an average period of four weeks."

In many cases of cerebrovascular disease there is some degree of persistent neurological deficit. The deficit may develop in a gradual stepwise fashion. In patients suffering what has been termed Stroke in Evolution, there are episodes of vascular neurological deficit, followed by a partial remission of symptoms. There continue to be episodes of deficit and partial remission over the course of several hours or days until the patient is left with a serious and permanent neurological deficit.

The course of a slowly progressive neurological deficit may also be spread over several months or years. The course of deterioration is steady but usually marked with identifiable episodes of deterioration. This syndrome has been referred to as Multi-Infarct Dementia or Arteriosclerotic Dementia (Gilroy and Meyer, 1975), and requires diagnostic differentiation from other conditions which may present with similar histories and symptoms (e.g., Alzheimer's Disease).

In general, the most severe of the cerebrovascular accidents is the completed stroke and may be defined as a neurological deficit which has persisted for considerable time (months) (Meyer, et al., 1975). The specific symptoms that result from a completed stroke varies from the relatively limited deficits associated with focal infarcts, to the extensive deficits that follow massive hemispheric infarction. Obviously, the actual symptoms produced depend to a great extent on the

area of the brain involved. Other factors also influence the expression of deficits including the rate of progression of the underlying disease process, the relative efficiency of the collateral supply, the general health of the cerebral vasculature, and the presence of systemic conditions which may limit the capacity to respond to alterations of the vascular supply such as hypertension, polycythemia and impaired cardiac output.

To summarize, ischemic stroke can be classified in terms of the course of development and persistence of the neurological deficit. Symptoms may be temporary (TIA) or permanent (completed stroke). Transient ischemic attacks are of great clinical significance because approximately 50% of patients with this type of disease who suffer a completed stroke will do so within 12 months of the initial episode. With the early recognition of the condition, treatment can be instituted which may prevent the occurrence of a more serious cerebrovascular accident. Cerebrovascular disease may also produce neurological deficits over a gradual course of days (stroke in evolution) or years (multi-infarct dementia).

Treatment of Ischemic Cerebrovascular Disease

To a considerable extent, however, the difference between TIA and completed stroke is quantitative rather than qualitative. Underlying causes and precipitatory events are similar in many cases and frequently the methods of treatment are largely identical. When a patient presents to hospital with a history of abrupt onset of neurologic symptoms (with presumed vascular etiology) there is no way of differentiating patients

whose deficits will be transient from those whose deficits will be persistent. The goal in either case is to limit the extent of permanent deficit and improve the quality of survival. To a large extent, this is accomplished by efforts to reduce the risk of subsequent vascular symptoms. Both medical and surgical measures have been advocated toward this end.

Medical Treatment of Cerebrovascular Disease

The medical approach with the longest history involves the use of anticoagulant drugs, such as heparin and the coumarin derivatives. Several investigators have attempted to explore the utility of anticoagulant therapy in the treatment of cerebrovascular disease with equivocal results. Carter (1961) studied patients with stroke in evolution and found a difference in outcome as measured by judgment of improvement. The difference was significant only when the combined groups of patients judged as improved or recovered were compared with combined groups of patients judged to have had no improvement and those who had died. There was no effect of anticoagulant therapy in patients whose stroke had progressed to completion prior to initiation of treatment.

Reports of anticoagulant therapy in patients with embolic stroke have concluded that early treatment led to more frequent improvement and fewer deaths among treated patients. Carter (1957) reported that 69% of the treated group demonstrated improvement or full recovery and Wells (1959) reported 56% of treated patients as improved. The untreated groups demonstrated 32% and 40% improvement respectively.

Whisnant (1977) summarized four studies of anticoagulant therapy in

acute thrombotic cerebral infarction and concluded "that among patients treated and those not treated with immediate and long term anticoagulants, there was no difference in the immediate recovery from stroke, the recurrence rate of cerebral infarction, and the number of patients with cerebral hemorrhage was increased among the treated groups."

Several reports have appeared in the recent literature concerning the use of anticoagulants in patients with transient cerebral ischemia. The Veteran's Administration study of atherosclerosis (1961) reported that there was one cerebral infarct among 22 patients treated with anticoagulants, while none of 15 untreated patients suffered subsequent cerebral infarction. Treated patients were followed on an average of 9.3 months, while untreated controls were followed on an average of 12.8 months. Not surprisingly, the study concluded that anticoagulant therapy was an ineffective mode of treatment.

Baker, Schwartz and Rose (1966) reported a 13% infarction rate among untreated control patients compared to a 7% cerebral infarction rate for anticoagulated patients. Frank (1967) pooled that data from Baker, et al. with three other studies of anticoagulant therapy (Baker, Broward, Fang, Groch, Heyman, Karp, McDewett, Scheinberg, Schwartz and Toole, 1962; Pearce, Gubbay and Walton, 1965; Siekert, Whisnant and Millikan, 1963). When the retrospective data of Siekert, et al. were eliminated, the pooled result of the three controlled studies yielded a 5.6% stroke rate in treated patients, and a 15.7% rate in the untreated patients. This difference was statistically significant but when the data from the Veterans Administration Cooperative study were added, the difference was no longer significant (5.4% versus 12.9%) (Brust, 1977).

Whisnant (1977) reviewed data from the population study of Rochester, Minnesota over the period 1955-69 and concluded that there was no difference in long term survival between patients treated with anticoagulants and those without such treatment. As Whisnant pointed out, "the aim of anticoagulation in patients with TIA is to prevent stroke." Whisnant, Matsumoto and Elveback (1973) reported the relative probability of stroke occurrence after the onset of the initial TIA. In the first year of observation, both treated and untreated patients had a much greater incidence of stroke compared to the general population under study. There was, however, a significantly lower probability of stroke occurrence among the anticoagulated patients at 1, 3 and 5 years of follow-up. When the first year of follow-up was examined, the authors found that the difference between the groups was established in the first one to two months of observation after the initial TIA. Baker, et al. (1962) concluded that anticoagulation was of some benefit in the short term therapy (4-6 months) of patients with TIA.

These studies suggest some benefit in the use of anticoagulants, particularly in patients with stroke in evolution and within the first few months following the initial TIA. However, patients treated with anticoagulants are at increased risk for cerebral hemorrhage. Hill, Marshall and Shaw (1962) reported a risk of converting a completed ischemic stroke into a hemorrhagic stroke and recommended that anticoagulation not be used in the treatment of patients with a stable completed stroke.

Whisnant (1977) reported that after the initial TIA, 7% of patients treated with anticoagulants versus 3% of untreated patients suffered

cerebral hemorrhage. Of the total of 14 patients suffering hemorrhage following the onset of TIA, 10 were treated with anticoagulants, although only one hemorrhage occurred within the first year.

Whisnant, Cartiledge and Elveback (1978) reported that in TIA patients 55-74 years old, the risk of intracranial hemorrhage was 8 times greater in patients treated with anticoagulants. Most of the patients experiencing hemorrhage had been treated with anticoagulants for one year or more. Although anticoagulant therapy seemed to have some benefit in treatment of cerebrovascular disease, the treatment was not without risk, particularly in patients maintained for extended periods of time.

Recent investigators have also attempted to evaluate the utility of treatment with antiplatelet drugs. Interest in this approach has been prompted by reports implicating platelet emboli in the production of TIA (Fisher, 1959; Russell, 1961) and in the pathogenesis of arteriosclerosis (Ross and Glomset, 1976). One widely used drug that has antiplatelet properties is aspirin. Dyken, Kolar and Jones (1973) found no difference in the ultimate cerebral infarction or death rate between aspirin treated and untreated groups. On a regimen of 300 mg B.I.D., only 13% of the treated group continued to experience TIA while 82% of the untreated group continued. When the dosage was doubled to 600 mg B.I.D., the remaining two patients ceased having TIA. Acheson, Danta, and Hutchinson (1969) found no evidence of a reduction of TIA frequency, stroke or death in a trial of the drug dipyridamole (Persantine).

Evans (1968) investigated the short term relief of subjects suffering from attacks of amaurosis fugax (transient monocular blindness). Thirteen patients treated with sulfinpyrazone (Anturan) on a schedule of 200

mg QID experienced at least 50% reduction of episodes while none receiving placebo experienced such improvement.

Fields, Lemak, Frankowski and Hardy (1977) reported the results of a large cooperative study on the utility of aspirin in the treatment of transient ischemic attacks. When death, cerebral or retinal infarction, and recurrence of TIA were used as comparison points at six month follow-up, there was a differential effect in favor of the aspirin treated group. When the comparison was restricted to the comparison of occurrence, death and infarction, there was no significant difference between the treated and placebo groups.

A large scale cooperative study of antiplatelet agents has also been conducted in Canada involving 585 patients with TIA or stroke with mild residual deficit. When endpoint comparisons were made of death and cerebral infarction, the results favored the aspirin treated group. Although the overall difference failed to reach significance, 36 of 289 aspirin treated patients and 49 of 296 non-aspirin treated subjects suffered a stroke. For unexplained reasons, the beneficial effects of aspirin treatment were observed only for males.

These studies seem to indicate some degree of effectiveness of treatment with antiplatelet agents, almost exclusively though, in reducing the number of subsequent TIAs. A recent study by Ross (1979) reported failure of anticoagulants and antiplatelet drugs in controlling TIA. Thirty patients with unilateral internal carotid artery occlusion continued to have symptoms under medical treatment. Two thirds of the patients presented with TIA and the author reported poor outcome in all 30 patients.

In summary, anticoagulants and platelet aggregation inhibitors have been the substances primarily employed in the medical treatment of cerebrovascular disease. Anticoagulants may be effective in prevention of stroke within the first few months following the onset of TIA. However, long term anticoagulant therapy is associated with an increased risk of cerebral hemorrhage. Recent investigations have suggested that antiplatelet agents may be effective in reducing the number of subsequent TIAs in patients with TIA as the presenting symptom. There is no consistent evidence that either anticoagulants or antiplatelet agents have significantly improved the long term survival of patients receiving these medications.

Surgical Treatment of Cerebrovascular Disease

The alternative to medical treatment of cerebrovascular disease is a surgical procedure called carotid endarterectomy. The procedure was first successfully performed and reported by Eastcott, Pickering and Rob (1954) and is being performed with increasing frequency in patients with accessible lesions and those without contraindications to surgery.

Not all patients with cerebrovascular disease are candidates for this procedure and the selection criteria vary considerably among surgeons and hospitals. In general, patients with amaurosis fugax, transient ischemic attacks, small completed infarcts with minor residual deficits, strokes in evolution and generalized cerebral ischemia may be candidates for endarterectomy (Sundt, House, Sharbrough and Messick, 1977). Patients with generalized cerebral ischemia are those with either severe bilateral

carotid stenosis, or a unilateral occlusion accompanied by a severe contralateral stenosis.

The criteria of what constitutes an operable lesion varies considerably but is based on the angiographic demonstration of a stenotic lesion at or near the bifurcation of the carotid artery. Lesions occur at other points in the carotid artery system, but intracranial stenoses (e.g., in the carotid siphon) are not amenable to carotid endarterectomy. The degree of stenosis is the second major criterion of selection for carotid endarterectomy. Gilroy and Meyer (1975) suggest that patients should have an accessible lesion of 30% or greater or have an ulcerated plaque. (As mentioned previously, plaques may become ulcerated and provide a source of emboli. This accounts for the tendency of surgeons to regard a non-stenotic ulcerated plaque as warranting corrective surgery.) If the ulcerative lesion is small, the patient may be managed with anticoagulants while if the ulceration is deep, surgical remediation tends to be the indicated approach (Sundt, et al., 1977).

Sandok, Furlan and Whisnant (1978) report that a carotid stenosis of 50% or greater is felt to be indicative of surgery, while Zeigler and Hassanein (1973) reported that stenoses of 70% or greater were associated with an increased risk of stroke than stenoses of a lesser degree. It has been reported, however, that unilateral carotid stenosis of less that 85-90% does not appreciably reduce blood flow (Brice, et al., 1964). However, in cases with bilateral involvement, stenosis of 75% or less may significantly reduce flow (Meyer, et al., 1965). If one carotid artery is completely occluded, a contralateral stenosis of only 50% may impair flow (Roberts, et al., 1964).

The presence of other factors may preclude endarterectomy, even in patients with surgically accessible and sufficiently severe lesions. Patients with disease of small intracranial vessels and no cervical involvement, and patients with associated medical conditions such as recent myocardial infarction may be unsuitable for endarterectomy. In addition, a small percentage of patients refuse surgery and elect medical treatment for their symptoms.

The operative procedure entails exposing the carotid artery in the neck, at the level where the common carotid artery divides to form the internal and external carotid arteries. As previously mentioned, this is the most common site in the carotid system for formation of atherosclerotic plaques. Once the carotid artery has been exposed, an incision is begun from 1-2 cm below the bifurcation in the common carotid artery and extended distally 2-3 cm into the internal carotid artery, beyond the border of the atheromatous plaque. The common carotid, as well as the internal and external carotid arteries are clamped during the period of incision. Some surgeons utilize an indwelling shunt to preserve blood flow during the procedure and the shunt is installed when the initial incision is made. Total clamping time (or cannulation) for this aspect of endarterectomy typically ranges from 45 to 90 seconds. When the shunt is in place, the plaque is dissected from the wall of the artery. The plaque usually separates easily from the arterial wall and the dissection is carried upward into the internal carotid artery. When the plaque has been removed the carotid arteries are again clamped, the incision is sutured and the shunt is removed prior to the last few sutures. Clamping

(decannulation) normally ranges from 1-2 minutes and the total operative time is usually approximately one hour.

As was the case with anticoagulant and antiplatelet therapies, there is no clear consensus on the effectiveness of endarterectomy in reducing the occurrence of subsequent completed stroke. Most evaluative studies have compared the relative efficacy of surgical and medical treatment in the reduction of stroke.

Thompson, Austin and Patman (1970) followed 293 patients who had undergone endarterectomy for TIA. Of the patients that survived surgery, 93.7% were judged as having improved neurologic status. Toole, Janeway, Choi, Cordell, Davis, Johnston and Miller (1975) found that in their patients who survived surgery, there was no difference between medically and surgically treated groups. DeWeese, Rob, Satran, Marsh, Joynt, Simmons and Nichols (1973) reported that in patients undergoing endarterectomy for TIA, there was long term relief of symptoms in 84%.

Most investigators appear to agree with the results of Bauer, Meyer, Fields, Remington, MacDonald and Callen (1969) who reported the finding of the Joint Study on Extracranial Arterial Occlusion on the long term results of surgical treatment. These authors found that in patients with unilateral or bilateral carotid stenosis, transient or mild neurological deficits, and without accompanying lesions, the operated patients had a greater survival rate at 42 months than the non-surgical patients (81% versus 64%). In patients with a unilateral occlusion and contralateral stenosis (so called "generalized cerebral ischemia"), patients with mild or transient neurological deficits showed no differential response to medical or surgical treatment. However, in the group with more severe

neurologic residua, there was a significant difference in favor of the medically treated group in terms of survival rate at 42 months (89% versus 24%). Patients with this angiographic pattern of stenosis were grouped according to the results of a neurological examination and the patients with the least severe symptoms (TIA or relatively mild deficits) were compared in regard to treatment outcome. The untreated group had a 36% survival rate, while the surgical group had a 49% survival rate. Sundt, et al. (1977) argued that the low survival rate in the non-surgical group suggested the danger of excluding these patients from candidacy for endarterectomy. As the authors themselves pointed out, the high overall mortality rate in these patients may have been due to the temporal proximity between an acute stroke and surgery. In general, the results of this study favored surgical treatment only in cases with carotid stenosis and a mild transient neurological deficit.

Fields, Maslenikov, Meyer, Hass, Remington and MacDonald (1970) reported a follow-up of the prognosis of the patients of the Joint study (Bauer, et al., 1969). These authors reported that when the course after hospitalization was compared, surgical treatment was more effective in preventing subsequent stroke. This approach excluded the operative and immediate post-operative morbidity and mortality statistics. When these data were included, there was no difference between medical and surgical groups. The best results were obtained in patients with typical hemispheric transient episodes with an angiographically demonstrable lesion in the internal carotid artery on the side appropriate for the symptoms.

A recent study by Barwinsky and Newman (1979) reported the results of 131 endarterectomy patients followed for up to 9 years. These authors concluded that in regard to prevention of stroke in the relevant internal carotid artery the operative results were as good as with any medical treatment.

Regardless of the effectiveness of endarterectomy in either prevention of subsequent stroke or improvement of long term survival, there is a risk of morbidity or mortality related to this procedure. In addition there is risk associated with angiography which is mandatory in patients being considered for endarterectomy. For example, Hass, Fields, North, Crickheff, Chase and Bauer (1968) reported a 0.7% mortality rate and a 0.5% severe morbidity rate associated with angiography. There was also a further 5.5% incidence of minor complications.

Faught, Trader and Hanna (1979) reported that cerebral complications occurred in 12.2% of their series of 147 patients and that the deficits were permanent in 5.2%. Of 21 risk factors investigated, the number of previous TIAs and the presence of an arterial stenosis of greater than 90% were associated with an increased risk of complications.

Numerous studies have also reported risks associated with carotid endarterectomy. Thompson, Austin and Patman (1970) reported a 1.4% operative mortality rate and a morbidity rate of 3%. Toole, et al. (1975) followed 160 patients with TIA of whom 82 were treated surgically. In the immediate post operative period there was a 22% morbidity and a 6% mortality, but in those who survived operation, there was no difference between medically and surgically treated patients in survival rate at four years.

Blaisdell, Clauss, Galbraith, Imparato and Wylie (1969) reported an overall surgical mortality of 4.5% in 2,400 operations performed between 1961 and 1968 in 24 cooperating centres. There was considerable variability in the mortality rates among the hospitals in the study ranging from less than 2% in seven hospitals to as high as 36% in one center. The hospitals with the most cases, and hence the most experience in performing the operations, had the lowest mortality rates.

Further evidence that complication rates are related to a certain extent to the skill of the surgeon is provided by a recent report of Fleming, Schutz, Hogan and Hogan (1979). These authors reported that in a series of 365 endarterectomies, the operative mortality had decreased steadily on a yearly basis. In the last 150 cases, there have been no deaths and 1.3% of these cases suffered persistent morbidity with transient morbidity in an additional 3.3%.

Sundt, Sandok and Whisnant (1975) have argued that the risk of complication varies with the clinical picture presented in a given patient. In their series patients with no associated medical problems and a typical angiographic pattern had a risk of approximately 1%. Risk was slightly increased (2%) in patients without medical complications but whose angiographic examination revealed contralateral carotid artery occlusion, or an unusually long or high stenotic lesion. A 7% risk of complication was present in patients with medical problems such as hypertension, angina, myocardial infarction or pulmonary disease. The highest risk (10%) was found in neurologically unstable patients with frequent TIAs or those with an accumulating neurological deficit.

In summary, the surgical removal of a stenotic plaque has been proposed as a means of reducing the risk of subsequent stroke. This procedure, carotid endarterectomy, is performed on patients who have a surgically accessible lesion of sufficient severity with no medical contraindications. There is a risk of morbidity and mortality associated with the operative procedure which is related to the experience of the surgeon. There is no clear consensus on the relative merits of endarterectomy, but it is held by many investigators that surgical intervention is at least equally as effective as medical treatment in stroke prophylaxis.

Psychological Studies of Carotid Endarterectomy

In spite of the risks associated with carotid endarterectomy in some patients, the prevailing neurological and neurosurgical opinion holds that in certain cases it may be an effective prophylactic method to reduce the incidence of subsequent stroke (Millikan, 1960; Murphy and Maccubbin, 1966; Bauer, et al., 1969; Sundt, et al., 1977). Although the medical community gives little credence to a restorative function subsequent to endarterectomy, there have been reports of patients who claim to "feel smarter" following this procedure (Goldstein, Kleinknecht, and Gallo, 1970). In view of the fact that these subjective reports are in conflict with conventional medical and surgical opinion, several investigations have been conducted to elucidate the prophylactic versus restorative roles of endarterectomy.

Murphy and Maccubin (1966) attempted to assess change in neurological function by rating patients as normal, mild, or severe in terms of

neurological signs before and after endarterectomy. There were few changes when pre- and post-operative ratings were compared. At a later follow-up rating, there were very few instances of recurrence of the initial symptoms. The authors interpreted these findings as being supportive of a solely prophylactic effect of endarterectomy. Drake, Baker, Blumenkrantz and Dahlgren (1968) examined groups of Veteran's Administration (V.A.) hospital patients with unilateral stenosis, bilateral stenosis, inaccessible stenotic lesions, elderly patients without cerebrovascular disease, and a small group of non V.A. patients with bilateral carotid disease. The patients were assessed on the Neurological Index of Mental Impairment (NIMI) prior to surgery and then after 6 and 12 months follow-up. The NIMI assesses patients on levels of intellectual and social functioning and was purported by the authors to correlate highly with tests of intellectual loss. A higher percentage of patients with bilateral and unilateral disease were rated as being more impaired initially and there was no difference at follow-up between the patients who underwent surgery and those who did not.

Williams and McGee (1964) presented the first study which employed objective psychological tests to determine the effects of carotid artery surgery. The authors used the Wechsler Bellevue Intelligence Scale, the Wechsler Memory Scale, the Trail Making Test and the Rorschach on six patients tested both before and one month after surgery. No statistical analysis of the data was presented although very minimal psychological improvement was felt to occur. Considerable reduction of neurological symptoms was noted in these patients. The results of this study have

been cited as evidence for a prophylactic role of endarterectomy (King, Gideon, Haynes, Dempsy and Jenkins, 1977).

Several recent authors have followed the lead of Williams and McGee in the use of psychometric measures to establish the psychological changes subsequent to endarterectomy. Duke, Bloor, Nugent, and Majzoub (1968) administered the Trail Making Test, the Finger Tapping Test and the Wechsler Adult Intelligence Scale to 47 subjects (38 males and 9 females) with a mean age of 57.81 years. The subjects were divided into a small vessel disease group, a large vessel disease nonoperated group, and a large vessel disease operated group of which only the latter group underwent surgical intervention. The large vessel operated group had significantly greater pathology based on ratings of arteriograms than the large vessel nonoperated group (the presenting symptoms of the three groups were not described). The small vessel group had a significantly shorter mean retest interval than either of the large vessel groups. There were no differences between the first and second testing in any of the groups on the Trail Making Test or the Finger Tapping Test which the authors attributed to the "gross nature of these measures." The small vessel group showed improvement in all three IQ scores, while the large vessel unoperated group failed to show improvement on these measures. The operated group made gains on PIQ and FSIQ. Among the operated group, patients with left-sided operations showed improvements in PIQ and FSIQ, while patients with right-sided operations showed gains in all three IQ scores. The authors suggested that the lack of improvement in VIQ scores among the operated group was related to a reduced sensitivity of Verbal as compared to Performance subtests to practice effects. The results

were interpreted as suggesting the prevention of further deterioration rather than the restoration of premorbid skills. This study failed to clearly report the criteria for inclusion into the operated group, nor did it report whether the unoperated group was treated in some other way (e.g., anticoagulant therapy).

Goldstein, et al. (1970) studied the neuropsychological changes associated with carotid endarterectomy. The Halstead-Reitan Neuropsychological Test Battery was administered to six men ranging in age from 57 to 72 who had been referred to a neurosurgical service following complaints of transient ischemic episodes. The subjects were tested three to four days prior to and approximately three months following the operation. There were significant improvements on many of the tests, but the authors acknowledged the difficulty of determining the extent that the results reflected practice effects. Prior exposure was thought to have had minimal impact on the improvement in some tests (Finger Tapping and Seashore Rhythm Test). On the Category Test, it was felt that the initial performance was so poor that practice effects could not account for the entire post-surgical improvement. In spite of the small sample, the authors contended that the extensive neuropsychological assessment and statistical design considerations supported the conclusion of an improvement in the general condition of the brain following carotid endarterectomy.

Horne and Royle (1974) attempted to determine cognitive changes after endarterectomy by administering a limited battery of tests. The Wechsler Memory Scale, the Benton Visual Retention Test, and six subtests from the Wechsler Adult Intelligence Scale were administered to 16 patients in the

week preceding the operation. The tests were readministered at various postoperative intervals. In order to minimize practice effects, alternate forms of the Wechsler Memory Scale and Benton Visual Retention Test were administered on second testing. The only significant postoperative changes were the improvements in the Object Assembly subtest and the prorated Performance IQ of the WAIS. Cases rated as mild (on the basis of angiographic evidence) showed no greater improvement than those rated as severe, although the mild cases had consistently better scores. These results led the authors to propose the need for more exacting experimental designs in future investigations.

In a study by Perry, Drinkwater and Taylor (1975) the Halstead-Reitan Neuropsychological Test Battery was administered preoperatively and again three months postoperatively to a group of 20 men with a mean age of 54.8 years. Among the subjects the nature, frequency and duration of symptoms varied widely. There was a significant overall improvement as well as improvement on the Category Test and the time component of the Tactual Performance Test. Although a significant increase in carotid artery blood flow was obtained, there was no significant correlation between increased blood flow and change in the Impairment Index. The possible effects of prior exposure to the tests were not addressed. Since tests relatively insensitive to practice (Finger Tapping, Speech Sounds, Seashore Rhythm) failed to show improvement, while those sensitive to the effects of repeated testings (Category and Tactual Performance Test) did show significant gains, these data suggested that practice effects may have been an important consideration.

Haynes, Gideon, King and Dempsey (1976) studied intellectual and personality changes associated with endarterectomy. Sixteen subjects with a carotid stenosis of 50% or greater were administered a short form of the Minnesota Multiphasic Personality Inventory (Kincannon, 1968), six subtests from the Wechsler Adult Intelligence Scale, and when time permitted, the Trail Making Test. The tests were administered just prior to, and six weeks following surgery. Significant gains were observed in the prorated PIQ, decreases in time required to complete the Trail Making Test, and decreases in indicators of personality disturbance. Although this study included a control group and reported some details of the surgical procedure, the retest interval was extremely brief which because of the measures used, made practice effects a considerable problem. In addition, the authors failed to address the fact that the control groups' performance was worse on most measures on second testing.

In a similar study by King, Gideon, Haynes, Dempsey and Jenkins (1977) the methodology of Haynes et al. (1976) was employed with 11 subjects. These authors found the essentially same results and interpreted their findings in the same manner as Haynes, et al. (1976).

Shatz, Schwartz, Robbins, Whitman and Lenaghan (1979) reported a follow-up of eleven patients undergoing endarterectomy and followed for an average of eighteen months. Patients were assessed on the WAIS, Finger Tapping Test and abbreviated version of the MMPI. Large gains are reported on Verbal IQ, Performance IQ and Full Scale IQ as well as non-dominant finger tapping. The improvement of 13 points on all three IQ measures was greater than would have been expected on the basis of practice effects and was without precedence in relation to other studies

of endarterectomy. There were numerous methodological flaws including lack of a control group and the failure to report the severity of symptomatology in these patients. In addition, 8 of 11 subjects were female in contrast to most other series of patients which tend to be primarily male. The small number of subjects and the lack of information regarding symptom severity seriously compromises the usefulness of these data.

Kelly, Garron and Javid (1979) compared a group of carotid endarterectomy patients with a smaller group of patients undergoing surgery for peripheral vascular disease. Both groups were reported as improved on some measures while the endarterectomy group alone showed mean improvement on tests of memory and fluency. The results of this study are difficult to compare with other studies due to the fact that measures of performance were used that have not been reported in previous studies.

Matarazzo, Matarazzo, Gallo and Weins (1979) have reanalyzed test-retest data on the Halstead-Reitan Neuropsychological Test Battery gathered in three previously published studies. The samples used in the most recent investigation included 20 young police officers, 16 patients with diffuse cerebrovascular disease, 35 chronic schizophrenics from a longitudinal study and 17 endarterectomy patients. The endarterectomy patients and police officers were the only patients tested by the authors. The groups differed widely on terms of age and duration of test-retest interval. These authors examined the data by comparing the test-retest results among the four groups and individually for the endarterectomy patients. Matarazzo, et al. concluded that there was no

evidence for improvement of cognitive function among endarterectomy patients that could not be explained on the basis of practice effects. The methods of accumulating subjects as well as the differences between subject groups in this study has serious limitations and conclusions based on these findings are not warranted.

In general, there is no clear agreement among these studies using psychological assessment techniques as to whether endarterectomy is restorative or only prophylactic. Studies arguing for prophylaxis and other reports arguing for restorative effects suffer from numerous methodological and procedural shortcomings which undoubtedly has contributed to the persistent failure to arrive at a clear answer to the question of whether significant psychological improvement occurs subsequent to endarterectomy.

The present investigation is proposed to provide clarification of this issue by resolving some of the methodological flaws that have limited previous studies. Specifically, earlier studies have been limited by the lack of control groups, the use of small or highly selected samples, the employment of abbreviated psychological measures, and the failure to account for practice effects. In addition, the majority of these studies completely ignore such potentially relevant variables as the side of operation, the duration of symptoms, time of clamping during operation, and the estimated degree of carotid stenosis. These studies are summarized in Table 1.

The goal of the current study is to determine whether carotid endarterectomy leads to improvement in psychological function as measured by an extensive battery of neuropsychological tests. The measures

Table 1

Summary of Previous Investigations on Psychological Changes Following Endarterectomy

Author and Year	Operated N	Controls	Side of Operation	Surgical Variables Described	Medical Variables Described	Objective vs Subjective	Prophylactic or Restorative
Williams & McGee (1964)	6	none	not reported	none reported	not reported	objective	prophylactic
Murphy & Maccubbin	165	none	not reported	none reported	not reported	subjective	prophylactic
Drake et al. (1968)	37 unilateral disease 53 bilateral disease	inaccessible stenosis-37 elderly patients-37	not reported	none reported	not reported	objective	prophylactic improvement only in non-VA operated patients
[illegible]e et al. (1968)	16	31 with unoperated vasc. dis.	not reported	none reported	index of cereb. vas. dis.	objective	prophylactic (operation permits benefits from practice)
Goldstein et al. (1968)	6	none	L=5 R=1	total clamp time	angiography & symptoms	objective	restorative (improves general condition of brain)
Horne & Royle (1974)	16	none	not reported	clamp time	not reported	objective	restorative (no deterioration, some slight improvement)

(continued)

Table 1 (continued)

Author and Year	Operated N	Controls	Side of Operation	Surgical Variables Described	Medical Variables Described	Objective vs Subjective	Prophylactic or Restorative
Perry et al. (1975)	20	none	not reported		symptoms & carotid blood flow	objective	restorative (improved cerebral function)
Haynes et al. (1976)	16	N=9 operated and no evidence of cereb. vasc. disease	not reported	operating & total clamp times	not reported	objective (abbrv.)	improved cognitive functioning-
Shatz et al. (1979)	11	none	L=7 R=4	none reported	not reported	objective	improved intelligence & left motor
Kelly et al. (1979)	35	17 peripheral vascular surgery	not reported	none reported	symptoms	objective	improvement in memory & fluency
Matarazzo et al. (1979)	17	20 police officers 35 schizophrenics 16 cereb. vasc. dis.	not reported	none reported	not reported	objective	prophylactic

employed attempt to sample a broad range of psychological functions including intelligence, memory, attention, abstract reasoning and sensory and motor skills. (The specific measures will be described in a later section.)

This battery of tests has been shown to be sensitive to the effects of cerebral damage (Klove, 1974; Reitan, 1964; Stuss and Trites, 1978). Specifically, these measures have been employed to study the behavioral deficits found in association with cerebrovascular disease. Reitan (1970) found that three groups of patients with cerebrovascular disease could be differentiated from normal controls. The vascular disease groups consisted of patients with right or left focal vascular lesions and a group with diffuse or bilateral disease. The normal control group performed better than all three vascular groups on every measure included in the study. The patients in the diffuse disease group had minimal or no positive findings on a standard neurological exam. The fact that this group was clearly differentiated from normal controls emphasizes the sensitivity of this neuropsychological test battery to the behavioral deficits observed in patients with cerebrovascular disease.

Meier and Resch (1965) employed a somewhat different group of measures in a study of 65 patients with acute onset of cerebrovascular symptoms. These authors examined the inferential concordance between a standard neurological examination and data from psychological testing and electroencephalography. Psychometric data was found to yield higher concordance with the neurological examination in regard to judgments of laterality and degree of damage. Both the EEG and psychological test data were more likely to suggest bilateral damage than was the data from

the neurological examination. It was suggested that psychometric or EEG data may be more sensitive to bilateral cerebral dysfunction although the authors acknowledged that measurement error or the method of inference may have contributed to the tendency to infer bilaterality.

Reitan and Fitzhugh (1971) studied the performance of patients with lateralized or generalized cerebrovascular disease. The greatest differences were obtained between the groups with lateralized lesions. Patients with right cerebral lesions performed better with the right hand on motor and psychomotor tasks and had a higher Verbal IQ than patients with left cerebral lesions. Patients with left cerebral lesions performed better with the left hand and had a higher Performance IQ than those with right cerebral lesions. The generalized disease group tended to occupy a position intermediate to the groups with lateralized lesions. In comparing the groups on tests of motor functions, most of the differences involved poor left hand performance by the right lesion group. Among tests of sensory function, the most pronounced deficits were observed in the tactile modality and most frequently reflected left sided perceptual deficits in the group with right cerebrovascular lesions. The authors concluded that consistent relationships existed between the laterality of cerebrovascular lesions and patterns of deficit on motor, sensory and intellectual measures. Further these authors suggested that in cerebrovascular disease, motor functions were more adversely affected.

These investigations have demonstrated the utility of this battery of tests in describing the deficits observed in cerebrovascular disease. Furthermore several of the previously cited studies of the effects of

carotid endarterectomy have used these measures in an attempt to demonstrate gains in psychological function (Goldstein et al., 1970; Perry et al., 1975). In view of the ability of these measures to reflect the integrity of cerebral function, this battery of tests will be used in the present investigation of the beneficial effects of carotid endarterectomy.

Hypotheses Under Investigation

Specifically certain questions will be examined:

1. Since several previous investigators have suggested that some psychological functions improve following endarterectomy the initial area of inquiry was to determine whether the patients undergoing endarterectomy demonstrate improvement on the neuropsychological test battery relative to control patients. To address this question of improved psychological function following endarterectomy, all subjects undergoing endarterectomy were separated into three groups on the basis of the side of operation and compared with a group of unoperated vascular control patients and a group of normal operated controls. The comparison of these groups was viewed as a test of the null hypothesis of no differences between groups in the improvement over the test-restest interval.

2. Previous investigations of the possible psychological benefits of endarterectomy have failed to consider the potential differential effects of the side of operation. The only study to comment on this issue (Shatz et al., 1979) suggested that the effects of unilateral operation are bihemispheric. To address the null hypothesis of no

differential effect of the side of operation, subjects undergoing endarterectomy were grouped on the basis of the side of operation and compared in regard to the improvement over the test-retest interval.

3. No previous investigation has examined the potential effect of the severity of initial neurological deficit on improvement subsequent to endarterectomy. Some authors have restricted the patient sample to a single type of ischemic vascular disease (Kelly et al., 1979) but there has been no attempt to compare groups with different degrees of deficit. This question was addressed by comparing a group of patients with transient ischemic attacks and subsequent endarterectomy with a group of endarterectomy subjects presenting with completed stroke. The null hypothesis was that the TIA group (with presumably no infarction) would be better able to demonstrate gains from carotid endarterectomy than a group with some infarction.

CHAPTER II

METHODS AND PROCEDURE

Subjects

Endarterectomy patients were consecutive cases referred from the neurosurgical service of the Ottawa Civic Hospital. These cases had undergone angiography which indicated the possibility of surgical intervention. A total of 55 subjects (38 males and 17 females) were divided into three groups based upon the side to be operated Right Carotid Endarterectomy (RCE), Left Carotid Endarterectomy (LCE) and Bilateral Carotid Endarterectomy (BCE).

Vascular control (VC) cases were individuals who had been evaluated as possible endarterectomy candidates, but whose lesions had been found to be unsuitable for surgical management because of complete occlusion, insufficient stenosis to warrant surgery or inaccessibility of the stenotic lesion. The operated normal controls (NC) were recruited from the neurosurgery and general surgery wards of the Ottawa Civic Hospital. Criteria for the selection of these patients were that they be candidates for some operative procedure of relatively short duration, that the procedure be performed under general anesthesia, and that the procedure not involve the brain or the cerebral vasculature. Among the operated controls, six patients underwent laminectomy, three had a Cloward procedure (fusion of vertebrae), three had procedures on the lower extremities and one patient had laparoscopy. The mean age, years of education, number of males and females and diagnostic classification for the endarterectomy and control groups are presented in Table 2.

Table 2

Group Composition in Regard to Age, Years of Education, Sex and Clinical Diagnosis

	LCE	RCE	BCE	NC	VC
$\bar{X}$ Age	63.65	63.32	57.83	43.45	50.78
# Males	13	17	8	6	10
# Females	7	6	4	7	4
$\bar{X}$ Education (Years)	9.95	11.27	8.25	12.77	10.38
TIA	12	8	5	-	7
Stroke	8	15	7	-	7

Procedure

1. Initial Medical Evaluation

On the day of admission to hospital all patients were given a complete physical examination (which included a neurological examination), and the patient's medical history as well as the family medical history was obtained and recorded on the patient's hospital chart. This history and examination were performed by physicians (residents) assigned to the service to which the patient was admitted. Blood samples were routinely drawn and blood levels of cholesterol, glucose, hemoglobin and hematocrit were obtained for most patients.

Patients suspected of carotid artery disease on the basis of their history, presenting symptoms, or the results of the neurological examination were referred to the neurosurgical service for angiographic investigation of the carotid arteries. Angiography typically occurred between days two and four of hospitalization. On the basis of angiography, some control patients were excluded as candidates for surgical treatment, usually because there was no demonstrable stenosis or the lesion was not amenable to surgery. Several of the vascular control patients were initially considered to be candidates for endarterectomy, but were ultimately managed without surgery. The remaining vascular controls underwent angiography for investigation of atypical vascular symptoms.

The operated control subjects also received a complete physical examination. Nine of these patients gave histories suggestive of peripheral neurologic disorders and underwent the appropriate diagnostic procedure (myelogram) for evaluation of these symptoms. In these

patients myelography was performed at the same approximate point in the hospitalization (between days two and four).

There were similarities between myelography and angiography in that both entailed the injection of contrast material to localize pathological conditions. Angiography involved injection of a radio-opaque material into the carotid artery while myelography entailed introduction of a radio opaque oil in the cerebrospinal fluid in the spinal canal. The major difference between these procedures was that as performed on the patients in the present study, angiography was conducted under general anesthesia, while myelography was conducted under local anesthesia. Following either procedure, patients were usually required to have 24 hours of bed rest. Two of the endarterectomy patients had undergone angiography during an earlier hospitalization and therefore did not receive angiography immediately prior to their surgery.

2. Neuropsychological Evaluation

Following the medical and neurological diagnostic procedures, patients were referred to the Neuropsychology Laboratory either for preoperative assessment or in a few cases, for further diagnostic investigation. For all cases, the assessment was performed approximately on day eight of hospitalization. Patients undergoing surgery were assessed within one to three days immediately prior to surgery.

The assessment consisted of a well standardized Neuropsychological Test Battery (Trites, 1977) which included measures of intelligence, memory, abstract reasoning, attention and an extensive examination of motor and sensory functions. The tests included in this battery are described below.

a) Tests of intelligence, memory and academic achievement

Levels of intelligence were assessed utilizing the Wechsler Adult Intelligence Scale (Wechsler, 1955). This widely employed measure consists of eleven subtests addressing a variety of verbal and nonverbal abilities as well as an overall measure (Full Scale IQ). The Wechsler Memory Scale (Wechsler, 1945) is comprised of seven subtests examining aspects of mental functioning such as general information and orientation, immediate recall of prose and nonverbal visual designs and verbal paired associate learning. Academic achievement levels in spelling, arithmetic and word recognition were assessed with the Wide Range Achievement Test (Jastak and Jastak, 1976).

b) Tests of Cognitive and Adaptive Abilities

This group of tests was introduced by Halstead (1947) and has undergone extensive refinement and elaboration by Reitan (1955, 1964). Included among these measures is the Halstead Category Test which is purported to be a measure of nonverbal abstraction and concept formation skills. In this test, a series of slides is presented and the subject's task is to discover an underlying principle that will permit a correct response to successive slides within a series. The test is divided into seven subtests which vary in difficulty. The Halstead Tactual Performance Test is regarded as a complex psychomotor problem solving task in which the subject is blindfolded and requested to place ten geometrically shaped blocks into corresponding spaces on an upright board. A measure of incidental learning is obtained by requesting the subject (without prior warning) to draw a picture of the board. The Finger Tapping Test provides a measure of motor speed by requiring the subject to tap a key

with the index finger as many times as possible within a ten second interval. (This measure is part of the Halstead-Reitan Neuropsychological Test Battery and therefore is included here rather than with other tests of motor function.)

A measure of sustained auditory attention and rhythmic pattern discrimination is provided by the Seashore Rhythm Test. In this measure paired rhythmic patterns are presented via a tape recorder, and the subject is required to judge whether the patterns are the same or different. The Halstead Speech Perception Test was also presented by a tape recorder and required the subject to indicate which of four nonsense words had been presented.

In addition to these tests included in the Halstead-Reitan Neuropsychology Test battery, several other measures of cognitive function were obtained. Included among these was the Trail Making Test (Reitan, 1958). This test has two parts, the second of which required the subject to sequentially alternate connecting series of numbers and letters. Visual attention skills were examined with the Knox Cube Test (Arthur, 1947). In this test the subject was required to imitate a pattern of movements. An aphasia screening examination was employed to detect a variety of aphasic and apractognostic deficits. This was accomplished by asking the subject to reproduce geometric forms, name items, demonstrate the use of items, write from dictation and several other tasks.

c) Sensory and motor functions

This battery of motor and sensory tests has been extensively developed by Klove and Reitan (1969). Grip strength was assessed by the

Smedley dynamometer. Dodrill (1979) has recently demonstrated the utility of this instrument as a neuropsychological measure. Fine manipulative skills were assessed by the Grooved Pegboard Test, in which small pegs were placed into holes in a board. The holes were in different orientations which required fine manipulation of the peg in order to match the orientation to the hole. Two measures from the Klove-Matthews Motor Steadiness Battery were also employed. The Maze Coordination test required the subject to move a stylus through an electrified maze. Contact with the edge caused scores to be recorded on a timer and a counter. A test of motor steadiness required the subject to hold a stylus in the middle of consecutive holes of decreasing diameter. Once again contact with the side of a hole caused scores to be recorded on a timer and counter.

Sensory measures included tests of unilateral and bilateral imperception in the tactile, auditory and visual modalities. Within each sensory modality, unilateral stimulation was followed by bilateral stimulation.

The ability to recognize which finger had been touched without the use of vision was measured by a test of finger agnosia in which the subject's fingers were touched with the eraser of a pencil while vision was obscured. With vision still obscured the subject was asked to identify numbers written on the fingertips and also to identify geometric shapes that had been placed in the hand. In this test of tactile form recognition the response was nonverbal in that the forms were placed in one hand and the other hand was used to indicate which form had been

presented. The validity and utility of this battery has been discussed previously.

Several patients did not receive the complete test battery for a variety of reasons. The most common reasons for incomplete testing were lack of adequate time or severe neurological impairment. On several instances, two or more patients were referred simultaneously for assessment with surgical procedures scheduled within a day or two of referral. Since the complete battery requires a full day to administer (and sometimes longer), it was impossible to obtain complete assessments in these cases.

Several of the patients with completed stroke (both those scheduled for endarterectomy and some vascular control patients) had neurological impairments such as severe aphasia or hemiplegia, which precluded complete assessment. In a very few instances, the patient was generally uncooperative during testing, or objected to specific tests.

When a complete evaluation could not be accomplished, an attempt was made to obtain a group of measures which was regarded as a minimal battery and was successfully obtained on all patients. Once this core evaluation was accomplished, measures were added as time or the patient's condition allowed.

3. Post Operative Course

Patients typically spent 24 hours in the recovery room, after which they were returned to their rooms on the neurosurgery service. Two patients suffered non-cerebral complications (compression of the trachea) which required their transfer to the intensive care unit prior to their return to the ward. Five patients (9%) experienced cerebral

complications which were felt to be related to the operative procedure but in all cases, these were extremely mild and transient. There was a 1.8% operative mortality rate which represents one patient who died from myocardial infarction 12 hours after his endarterectomy. These mortality and morbidity rates compare favorably with other reported series of cases.

When the patients had recovered from their operation, they were discharged from hospital and in most cases were given a prescription for 325 mg of aspirin 4 times per day for three months. The typical stay in hospital for unilateral endarterectomy patients was 21 days and for bilateral endarterectomy patients, the typical course lasted 31 days. Approximately one week was allowed for bilateral patients to recover from the initial procedure before being subjected to the second endarterectomy. The typical course for vascular control patients lasted 13 days and for the normal operated control patients, 16 days.

4. Post-operative Assessment

Approximately five months following their discharge, patients were contacted by letter and requested to return for a post-operative assessment. For each patient, an attempt was made to schedule for six months after the date of the initial assessment. In all cases the reassessment consisted of the measures which had been administered on first testing. Of the patients who were reassessed, only four were examined more than two weeks beyond the six month anniversary of the initial testing.

A total of 14 subjects (12 endarterectomy and 2 control) failed to return for reassessment. Table 3 shows that three patients died, four patients were unavailable due to geographical considerations, five

Table 3

Patients Not Receiving Reassessment

	Group	Age	Sex
Deceased	RCE	71	F
	LCE	71	F
	LCE	69	M
Geography	LCE	63	M
	BCE	61	M
	RCE	70	F
	NC	31	M
Declined	LCE	59	M
	LCE	49	M
	LCE	58	M
	LCE	60	F
	NC	31	F
Other	RCE	68	M
	RCE	71	M

patients declined to be reassessed, and two were unavailable for other reasons. Of the postoperative deaths not related to surgery, one patient died from a ruptured bowel approximately 3 weeks after discharge, while another patient died from a myocardial infarction 3 months after discharge.

At the time of reassessment, the patients were questioned regarding their general health during the test-retest interval. Areas of inquiry included whether there had been recurrence of their symptoms, occurrence of any new symptoms, and whether the patient felt there had been any side effects from their surgery. In particular, patients were asked if they noticed any "changes" in their cognitive processes, in an attempt to determine any subjective impressions in this matter.

Data Analysis

The data from the first and second neuropsychological assessment and an additional group of data obtained from the patient's medical chart comprised the final data file which was stored on computer disk. Statistical processing and data manipulation was accomplished by employing the Statistical Package for the Social Sciences (SPSS; Nie, Hull, Jenkins, Steinbrenner and Bent, 1975).

Design and Statistical Analysis

Although a total of 82 subjects were involved, there were approximately 160 variables which were included in the final data file, including the test results of first and second neuropsychological assessments, and the medical variables obtained from the hospital chart.

A variety of parametric procedures combined with univariate and multivariate analyses were employed to analyze the data.

The initial step of analysis involved factor analytic techniques to reduce the data to a more conveniently managed group of dependent variables. The results of the initial neuropsychological assessment were grouped into six sets of tests based simply on logical considerations. The results of the six separate factor analyses were employed to generate factor scores. These factor scores were then utilized as new dependent variables in multiple discriminant function analysis. This procedure provided a multivariate test of significance of the differences between groups at initial assessment based on what originally was a large number of variables. Univariate procedures were combined with this procedure to isolate the test scores which contributed to the overall multivariate differences.

It was also of interest to determine how the factors obtained at initial testing were changed at second testing. To accomplish this, the factor score coefficients obtained on first testing were applied to the test scores obtained on second testing. These factor scores obtained on second testing were then entered as dependent variables in multiple discriminant function analysis as an overall multivariate test of the difference between groups at second testing. Again univariate tests were employed to determine which test variables contributed to the multivariate differences. A further examination of the changes from first to second testing was accomplished by determining for each group the number of tests that showed significant improvement, and comparing the groups on

this basis. In order to limit the number of significance tests, only those measures included in the factor analyses were included.

The initial analysis was directed at the comparison of all five groups (three endarterectomy groups and two control groups). To test the hypothesis of no between group differences in terms of changes over the test-retest interval, the factor scores from the second testing were subtracted from the initial factor scores to yield change scores. Because of the statistical and methodological difficulties inherent in the use of change scores, the use of these scores was restricted.

There were several major analyses performed, and in each case the change scores were employed only in the initial aspects in an overall multivariate test of the group differences over the test-retest interval. Change scores were excluded from any subsequent analysis.

The initial question to be examined was whether the endarterectomy groups differed from the control groups in regard to the amount of change over the six month interval. This question was addressed by examining the data from the three endarterectomy groups and the two control groups. The factor change scores were employed in a multivariate test of the group differences over the six month interval. Following this, multivariate comparisons of the initial and second factor scores was performed. These multivariate analyses were elaborated by conducting univariate comparisons on the individual factor scores as well as on the original test variables. The null hypothesis predicted no difference between the groups of subjects.

The second area of inquiry entailed the examination of the differences between the individual groups of endarterectomy subjects,

specifically in relation to the question of differential response to surgery as a function of the side of operation. The method of analysis described above was again employed to test the null hypothesis of no differences between the individual groups.

A third area of inquiry was to determine if the severity of presenting neurological symptoms held any relationship to postoperative improvement. To address this question, three groups were formed consisting of endarterectomy subjects who had presented with transient ischemic attacks, endarterectomy subjects who had suffered a completed stroke, and the vascular control group. A transient ischemic attack was operationally defined as a vascular episode with no residual clinical deficit 24 hours following the onset of symptoms. A completed stroke was considered to be any neurological deficit (regardless of severity) which persisted longer than 24 hours. This use of 24 hours as a criterion for transient ischemic attack was consistent with the accepted classification of cerebrovascular disease (Sandok et al., 1978). Once again, the method of analysis as described above was employed to examine the differences between these groups. It was expected that since the subjects with TIA had presumably suffered no infarction, that group would be more likely to demonstrate gains than those patients who had suffered some degree of cerebral infarction.

CHAPTER III

RESULTS

Factor Analysis of Initial Neuropsychological Assessment

The measures from the initial neuropsychological assessment were grouped into the following six general classes of variables: a) general cognitive and intellectual tests; b) tests of adaptive abilities; c) sensory perceptual measures; d) motor tests; e) personality measures; and f) tests of sensory imperception. These groups of variables were entered into separate factor analyses which employed the method of principle factors with iterations and in each case a Varimax rotation was performed. The individual tests included in each of the factor analyses can be found in Tables 4 to 9. Also included are the abbreviations of the variable names to be used in subsequent tables.

The factor analysis of the general cognitive and intellectual tests yielded two factors with an eigenvalue of greater than one which accounted for 78.4% of the variance. The eigenvalues and percentage of variance accounted for related to these two factors are presented in Table 10 along with the varimax rotated factor matrix. Based on the factor loadings, the first factor was interpreted as a verbal abilities factor with the highest loadings on the spelling and reading components of the Wide Range Achievement Test and the Verbal IQ. The second factor was considerably weaker with an eigenvalue of slightly greater than one. It was interpreted as representing non-verbal abilities with the highest

Table 4

General Cognitive and Intellectual Tests

Grouped for Factor Analysis I
1. Wechsler Adult Intelligence Scale - Verbal I.Q. (VIQ)
2. Wechsler Adult Intelligence Scale - Performance I.Q. (PIQ)
3. Wide Range Achievement Test - Reading grade score (WRATR)
4. Wide Range Achievement Test - Spelling grade score (WRATS)
5. Wide Range Achievement Test - Arthimetic grade score (WRATA)
6. Wechsler Memory Scale - Memory Quotient (MQ)
7. Age at initial assessment (Age)

Table 5

Tests of Adaptive Abilities

Grouped for Factor Analysis II
1. Halstead Category Test - total errors (CATEGORY)
2. Halstead Tactual Performance Test - total time (TPT-T)
3. Halstead Tactual Performance Test - memory score (TPT-M)
4. Halstead Tactual Performance Test - localization score (TPT-L)
5. Halstead Speech Perception Test - total errors (SPEECH)
6. Seashore Rhythm Test - raw score (SEASHORE)
7. Trail Making Test - total time (TRAILS)
8. Knox Cube Test - raw score (KNOX)
9. Right-Left Discrimination Test - errors (RT-LT)

Table 6

Measures of Fine Sensory Perception

Grouped for Factor Analysis III
1. Finger Agnosia - Right hand errors (FINGAG-R)
2. Finger Agnosia - Left hand errors (FINGAG-L)
3. Fingertip Number Writing - Right hand errors (#WRITING-R)
4. Fingertip Number Writing - Left hand errors (#WRITING-L)
5. Roughness Discrimination - Right hand errors (ROUGHNESS-R)
6. Roughness Discrimination - Left hand errors (ROUGHNESS-L)
7. Tactile Form Recognition - Right hand errors (TACT FORM-R)
8. Tactile Form Recognition - Left hand errors (TACT FORM-L)

Table 7

Motor Tests

Grouped for Factor Analysis IV
1. Finger tapping test - right hand score (FINGTAPR)
2. Finger tapping test - left hand score (FINGTAPL)
3. Grip strength - right hand (GRIP-R)
4. Grip strength - left hand (GRIP-L)
5. Movement coordination - right hand (timer) (COORD-RT)
6. Movement coordination - right hand (counter) (COORD-RC)
7. Movement coordination - left hand (timer) (COORD-LT)
8. Movement coordination - left hand (counter) (COORD-LC)
9. Resting steadiness - right hand (timer) (STEAD-RT)
10. Resting steadiness - right hand (counter) (STEAD-RC)
11. Resting steadiness - left hand (timer) (STEAD-LT)
12. Resting steadiness - left hand (counter) (STEAD-LC)
13. Grooved Pegboard Test - right hand time (PEG-RT)
14. Grooved Pegboard Test - left hand time (PEG-LT)

Table S

Personality Scales from Minnesota Multiphasic Personality Inventory

Grouped for Factor Analysis V			
1.	MMPI-L	(lie)	(MMPIL)
2.	MMPI-F	(validity)	(MMPIF)
3.	MMPI-K	(correction)	(MMPIK)
4.	MMPI-Hs	(hypochondriasis)	(MMPIHs)
5.	MMPI-D	(depression)	(MMPID)
6.	MMPI-Hy	(hysteria)	(MMPIHy)
7.	MMPI-Pd	(psychopathic deviate)	(MMPIPd)
8.	MMPI-Mf	(masculinity-feminity)	(MMPIMf)
9.	MMPI-Pa	(paranoia)	(MMPIPa)
10.	MMPI-Pt	(psychasthenia)	(MMPIPt)
11.	MMPI-Sc	(schizophrenia)	(MMPISc)
12.	MMPI-Ma	(hypomania)	(MMPIMa)
13.	MMPI-Si	(social introversion)	(MMPISi)
14.	MMPI-Pn	(pseudo-neurological)	(MMPIPn)

Table 9

Tests of Sensory Imperception

Grouped for Factor Analysis VI
1. Ulilateral Tactile Stimulation - right face imperception (UtactRF)
2. Unilateral Tactile Stimulation - left hand imperception (UtactLH)
3. Unilateral Auditory Stimulation - right side imperception (UaudR)
4. Unilateral Auditory Stimulation - left side imperception (UaudL)
5. Bilateral Hand Stimulation - right hand imperception (BtactR)
6. Bilateral Hand Stimulation - left hand imperception (BtactL)
7. Bilateral Right Hand/left face stimulation - right hand imperception (BtactRH)
8. Bilateral Right Hand/left face stimulation - left hand imperception (BtactLF)
9. Bilateral Left Hand/right face stimulation - left hand imperception (BtactLH)
10. Bilateral Left Hand/right face stimulation - right face imperception (BtactRF)
11. Bilateral Auditory Stimulation - right side imperception (BaudR)
12. Bilateral Auditory Stimulation - left side imperception (BaudL)

Table 10

Eigenvalues and Percentage of Variance Accounted for by the General Cognitive and Intellectual Factors

Factor	Eigenvalue	% of Variance
I	4.45	63.7
II	1.02	14.7
		78.4

Varimax Rotated Matrix

Factor Loadings

Variable	Verbal Abilities	Nonverbal Abilities
VIQ	.857	.197
PIQ	.728	.375
WRATR	.883	-.257
WRATS	.892	-.102
WRATA	.791	.199
MQ	.814	.356
AGE	-.003	-.058

loadings on the Performance IQ, the Memory Quotient and the arithmetic grade score from the Wide Range Achievement Test.

Factor analysis of the tests of adaptive abilities produced three factors which accounted for 66.3% of the variance. The eigenvalues and percentage of variance as well as the Varimax rotated factor matrix are presented in Table 11. The first factor was interpreted as reflecting left hemisphere functions with the highest loadings on tests of right left discrimination, speech perception and the Trail Making test. The second factor was felt to represent general adaptive functions by virtue of the highest loadings on the Category test, the Trail Making Test and the total time score of the Tactual Performance Test. The third adaptive factor was interpreted as representing right hemisphere functions in view of the highest loadings on the memory and localization components of the Tactual Performance Test.

The factor analysis of the measures of sensory-perceptual function yielded two factors with eigenvalues of greater than one which accounted for 65.2% of the variance. The eigenvalues, percentage of variance accounted for and the Varimax rotated factor matrix are presented in Table 12. The first factor was felt to reflect sensory abilities on the right body side because of the high loadings on most right side measures. Similarly, the second sensory factor was felt to reflect left sided sensory functions due to the high loadings on left side measures.

The tests of motor functions yielded four factors with an eigenvalue of greater than one which accounted for 82.7% of the variance. The eigenvalues, percentage of variance accounted for, and the Varimax rotated factor matrix are presented in Table 13.

Table 11

Eigenvalues and Percentage of Variance Accounted for by Adaptive Factors

Factor	Eigenvalue	% of Variance
I	3.386	37.1
II	1.475	16.4
III	1.150	12.8
		66.3

Varimax Rotated Matrix

Factor Loadings

Variable	Left Hemisphere	General Adapative	Right Hemisphere
Category	.142	.850	.230
IPT-I	.170	.542	-.417
IPT-M	-.286	-.334	.492
IPT-L	.029	.061	.811
Speech	.401	.272	-.136
Seashore	-.473	-.167	.202
Trails	.300	.575	-.281
Knox	-.883	-.291	.189

Table 12

Eigenvalues and Percentage of Variance Accounted for by Sensory-Perceptual Factors

Factor	Eigenvalue	% of Variance
I	3.925	49.1
II	1.289	16.1
		65.2

Varimax Rotated Matrix

Factors Loading

Variable	Sensory-R	Sensory-L
Fingag-R	.949	.025
Fingag-L	.621	.436
#Writing-R	.820	.422
#Writing-L	.285	.907
Roughness-R	.297	.308
Roughness-L	.339	.661
Tact Form-R	.479	.143
Tact Form-L	.038	.580

Table 13

Eigenvalues and Percentage of Variance Accounted for by Motor Factors

Factor	Eigenvalue	% of Variance
I	7.376	46.1
II	3.033	19.0
III	1.731	10.8
IV	1.097	6.9
		82.7

Varimax Rotated Matrix

Factor Loadings

Variables	Steadiness/ Coordindation (R)	Coordination (L)	Psychomotor	Steadiness (L)
Fingtap-R	-.872	-.209	-.015	.182
Fingtap-L	-.038	-.812	-.185	-.111
GRIP-R	-.594	-.488	.278	.332
GRIP-L	-.023	-.885	-.011	-.002
COORD-RT	.842	.062	.174	.156
COORD-RC	.897	.108	.217	.006
COORD-LT	.263	.705	.385	.330
COORD-LC	.314	.689	.340	.435
Stead-RT	.886	.113	.195	.311
Stead-RC	.683	-.117	-.125	.528
Stead-LT	.143	.391	.415	.739
Stead-LC	-.008	.173	.091	.891
Peg-RT	.880	.106	.348	-.023
Peg-LT	.149	.646	.589	.245
TPTR-T/B	.451	.139	.685	.241
TPTL-T/B	.115	.233	.876	.058

It can be seen that the first factor loaded most heavily on the scores derived from the right hand trials on tests of fine and gross motor coordination and steadiness. Consequently, this factor was interpreted as a right sided steadiness and coordination factor.

The second motor factor was felt to reflect left hand coordination while the fourth factor was interpreted as representing left hand steadiness. The third motor factor loaded most heavily on the left and right hand measures from the Tactual Performance Test and hence was regarded as a psychomotor factor.

Factor analysis of the scores from the Minnesota Multiphasic Personality Inventory produced five factors with an eigenvalue of greater than one which accounted for 80.2% of the variance. The eigenvalues and percentage of variance associated with each factor in addition to the varimax rotated factor matrix are presented in Table 14.

The first factor derived from this analysis loaded highly on scales typically associated with disordered personality functions, therefore the factor was felt to reflect psychopathology. Factor II loaded highly on MMPI Scales Hy, Hs, Pt and D which were felt to represent concern over somatic functions. The third factor from this analysis loaded most highly on two of the validity scales from the MMPI (L and K) and was therefore interpreted as a validity factor. The fourth factor was interpreted as reflecting depression and withdrawal while the fifth factor was felt to represent the general level of interest and activity.

The final factor analysis included the tests of sensory imperception and yielded five factors with an eigenvalue of greater than one which accounted for 71.4% of the variance. The eigenvalues, percentage of

Table 14

Eigenvalues and Percentage of Variance Accounted for by Personality Factors

Factor	Eigenvalue	% of Variance
I	4.172	29.8
II	2.478	17.7
III	2.053	14.7
IV	1.448	10.3
V	1.073	7.7
		80.2

Varimax Rotated Factor Matrix

Factor Loadings

Variables	Psycho-pathology	Anxiety	Validity	Depression	Extro-version
MMPIL	.042	-.048	.795	-.068	.031
MMPIF	.789	-.070	-.148	.339	.215
MMPIK	-.068	.153	.862	-.288	.031
MMPIHs	-.059	.856	-.001	.108	.249
MMPID	.159	.529	.098	.690	.106
MMPIHy	.180	.915	.032	-.058	-.145
MMPIPd	.505	.477	.170	-.155	.528
MMPIMf	.363	.080	-.241	.022	.621
MMPIPa	.875	.143	-.010	-.133	-.015
MMPIPt	.449	.658	-.120	.297	.152
MMPISc	.898	.197	.028	-.030	.028
MMPIMa	.215	.184	-.525	-.609	.279
MMPISi	.000	.070	-.314	.826	-.151
MMPIPn	.330	.175	-.411	.303	-.757

variance, and the varimax rotated factor matrix obtained from this analysis are presented in Table 15. The first factor loaded heavily on imperception of tactile stimuli on the left side with either unilateral or bilateral stimulation. The second factor loaded heavily on the two measures of unilateral auditory stimulation while the third factor loaded heavily on bilateral measures of tactile imperception. The fourth factor loaded heavily on the measures of right sided tactile imperception while the fifth factor was interpreted as representing bilateral tactile and auditory imperception.

The series of factor analyses were performed to reduce the number of variables to be incorporated in subsequent statistical procedures. A total of 66 test variables were entered into factor analysis and 21 factors were ultimately produced. A review of the amount of variance accounted for by the individual factor analyses suggested that relatively little data were lost by this procedure. The mean percentage of variance explained by these factors was 74.03% with the motor factors accounting for the highest percentage of variance and the sensory perceptual factors accounting for the least variance. The factor analyses yielded factor score coefficients which were employed to generate factor scores. These factor scores represented the combined results of several univariate measures and were utilized in the subsequent data analysis. It was also necessary to reduce the data from the second assessment. This was accomplished by applying the factor score coefficients to the test scores obtained from the second assessment. The generation of this second set of factor scores permitted an examination of changes in the factors between the two assessments.

Table 15

Eigenvalues and Percentage of Variance Accounted for by Imperception Factors

Factor	Eigenvalue	% of Variance
I	2.743	22.9
II	1.842	15.4
III	1.523	12.7
IV	1.318	11.0
V	1.136	9.5
		71.4

Varimax Rotated Matrix

Factor Loadings

Variables	Left Imper-ception	Unilateral Auditory	Bilateral Tactile	Right Imper-ception	Bilateral Tactile/ Auditory
UtactRF	.000	.062	-.047	.460	-.011
UtactLH	.854	.115	.115	.295	-.092
UAUDR	.038	.974	-.041	.187	.089
UAUDL	.207	.668	.210	.002	-.076
BTACTR	.017	.041	.165	.900	.312
BTACTL	.068	-.023	.681	-.140	.017
BTACTRH	.125	.006	.548	.396	.124
BTACTLF	.796	.117	-.123	-.041	.139
BTACTRF	-.015	.256	.565	.115	-.237
BTACTLH	.544	-.061	.328	.111	.716
BAUDR	-.037	.129	-.048	-.054	.215
BAUDL	.013	-.039	-.021	-.046	.237

Carotid Endarterectomy and Control Groups

In the initial stage of analysis, all five groups were included. The mean age of the total sample was 57.25 but there were differences between the groups in terms of age ($F = 15.90$, $df = 4,76$, $p < .001$). The ages of the various groups are presented in Table 2 where it can be seen that the control patients were younger than the endarterectomy patients. This difference arose primarily from the females in the normal (operated) control group whose mean age was 36.28 years. The males in this group had a mean age of 52 which was significantly different from the females ($t = 2.63$, $df = 7$, $p < .05$).

The groups also differed significantly on the basis of education ($F = 3.38$, $df = 4,75$, $p < .025$). There was no difference in the length of follow up which averged 6.14 months ($F = 1.32$, $df = 4,76$, $p > .10$).

Analysis of Change Scores

Multiple discriminant function analysis was employed to examine the null hypothesis of no overall multivariate differences between the groups. The stepwise method was employed which selected variables for inclusion into the anlysis on the basis of maximizing the differences between the groups (hence minimizing Wilks' Lambda).

The initial question to be addressed was whether the groups differed in their relative performance between the two assessments. In order to accomplish this, factor scores from the second assessment were subtracted from the corresponding factor scores derived from the initial assessment to yield change scores. These factor change scores were then entered into a stepwise multiple discriminant function analysis to determine

whether the groups differed in their respective change between the two assessments. This analysis yielded two discriminant functions which indicated that the groups could be significantly differentiated on the basis of changes in the factor score variables. The first function yielded a Wilks' Lambda of .0668 ($df = 40$, $p < .0001$) while the second function yeilded a Wilk's Lambda of .268 ($df = 27$, $p < .04$). These discriminant functions as well as the standardized discriminant function coefficients are presented in Table 16. It can be seen that the highest loadings on the first function were obtained on factors interpreted to represent nonverbal abilities, left hand coordination and psychopathology. The second function received its highest loadings on factors interpreted to represent right hemisphere functions and right and left side sensory-perceptual skills. This analysis suggested that there were differences among the groups in regard to changes over the test-retest interval. When the change scores were combined, the factors that contributed the most to the overall group difference were largely those interpreted to reflect right hemisphere function.

In view of the finding of multivariate differences over the test-retest interval, it was of interest to attempt to determine the source of these differences. To avoid the problems inherent with change scores, it was decided to abandon these scores for the remainder of the analysis.

Analysis of Initial Factor Scores

To elaborate on the differences obtained with change scores, it was decided to independently examine the results of the two assessments.

Table 16

Results of Stepwise Multiple Discriminant Function Analysis on Factor Change Scores

Standardized Discriminant Function Coefficients

Factor	Function I	Function II
Nonverbal Ability	1.140	0.142
Right Hemisphere	0.126	0.739
Sensory Right	-.511	1.091
Sensory Left	0.158	0.758
Psychopathology	0.816	0.630
Anxiety	-0.704	-0.324
Validity	-1.249	-0.067
Depression	-1.194	0.024
Right Steadiness/Coordination	-0.147	0.259
Left Coordination	0.578	-1.203

Discriminant Function	Eigenvalue	Canonical Correlation	Wilks' Lambda	df	p
1	3.007	.886	.0668	40	.001
2	1.534	.778	.2680	27	.037

Overall Correct Classification 45.12%

Discriminant analysis of the factor scores from the initial assessment produced two discriminant functions which indicated significant multivariate differences among the groups. The first function yielded a Wilks' Lambda of .1526 ($df = 40$, $p < .0001$) and the second function yielded a Wilks' Lambda of .3410 ($df = 27$, $p < .008$. (See Table 17.) The standardized discriminant function coefficients indicated that the highest loadings on the first function were the verbal intelligence factor, the left tactile imperception factor and the validity factor. The highest loadings on the second function were on the bilateral imperception factor, the verbal abilities factor, the general adaptive factor and the depression factor.

The univariate F ratios for each of the factors which entered the discriminant analysis are presented in Table 18. This analysis revealed that there were significant differences between the groups on the verbal abilities and general adaptive abilities factors.

Pairwise comparisons were performed utilizing the Student Neumaq-Kuels procedure to limit the number of post hoc comparisons. On the verbal abilities factor it was revealed that the left carotid endarterectomy (LCE), the bilateral carotid endarterectomy (BCE) and the vascular control group (VC) all differed from the normal control group (NC) at the .05 level. On the general adaptive factor the three carotid endarterectomy groups differed at the .05 level from two control groups. There were no differences among the three endarterectomy groups on any of the initial factor scores. In order to confirm these differences as well as to examine the differences on the actual test variables, univariate F-tests were performed on the measures obtained at the initial

Table 17

Results of Stepwise Multiple Discriminant Function Analysis on Initial Factor Scores-All Groups

Standardized Discriminant Function Coefficients

Factor	Function I	Function II
Verbal Ability	.435	.371
Nonverbal Ability	-.629	-.190
General Adaptive	-.434	.318
Sensory-Left	-.399	-.561
Anxiety	.013	-.668
Validity	-.120	-.057
Depression	-.405	.327
Extroversion	-.539	-.002
Left Tactile	.214	-.517
Bilateral Imperception	-.032	.679

Discriminant Function	Eigenvalue	Canonical Correlation	Wilks' Lambda	df	p
1	1.234	.743	.152	40	.001
2	0.912	.690	.341	27	.007

Overall Correct Classification 56.10%

Table 18

Univariate F Ratios for the Factors Entered in the Stepwise Multiple Discriminant Function Analysis on Initial Assessment Factor Scores

Factor	F	df	p
Verbal Abilities	4.19	4,74	.004
Performance I.Q./Memory	.69	4,74	N.S.
General Adpative	6.60	4,63	.001
Sensory-Left	.86	4,73	N.S.
Anxiety	2.29	4,50	N.S.
Validity	.74	4,50	N.S.
Depression	2.13	4,50	N.S.
Left Tactile Imperception	.43	4,73	N.S.
Bilateral Imperception	2.40	4,73	N.S.

assessment. As can be seen in Table 19, there were significant differences between the five groups on several of the original test measures. Pairwise comparisons were again performed which revealed virtually no differences between the three endarterectomy groups. It was observed that the vast majority of the differences occurred between the normal controls and the remaining four groups. The results of this univariate analysis confirmed the findings of the multivariate analysis which demonstrated differences between the vascular disease groups (endarterectomy and vascular controls) and the normal controls primarily in the areas of verbal and general adaptive abilities.

Analysis of Second Testing Factor Scores

To determine how the initially derived factors had changed, the factor scores coefficients obtained from the original assessment data were applied to the second testing scores to produce another group of factor score dependent variables. These second factor scores variables were then entered into a multiple discriminant function analysis, the results of which again indicated significant multivariate differences between the groups. The first discriminant function yielded a Wilks' Lambda of .081 ($df = 44$, $p < .0001$) while the second function yielded a Wilks' Lambda of .255 ($df = 30$, $p < .02$). These two functions and the standardized discriminant function coefficients are presented in Table 20. The highest loadings on the first function were on the right steadiness and coordination factor, the verbal abilities factors, and the validity factor from the MMPI. The highest loadings on the second function were obtained on the anxiety factor from the MMPI, the right

Table 19

Univariate F Ratios on Test Variables
from First Assessment

Variable	F	df	p
WRATR	3.86	4,69	.006
WRATS	3.76	4,70	.007
WRATA	2.58	4,72	.044
TPTRHT	3.48	4,58	.012
TPTLHT	4.26	4.60	.004
TPT-TT	5.57	4,58	.007
TPT-Memory	4.23	4.61	.004
Trails A-credits	2.84	4,72	.029
Trails B-time	4.50	4,70	.002
Trails B-credits	10.69	4,70	.001
Trails Total-time	8.83	4,69	.001
Trails Total-credits	4.70	4,70	.002
Fingertap-L	2.89	4,72	.028
Peg-RT	3.94	4,70	.006
Peg Total-time	3.40	4,70	.013
MMPI-pt	2.85	4,50	.033
M.Q.	2.64	4,69	.040
Fingag-R	2.56	4.73	.045
#Writing-R	3.15	4.73	.018

Table 20

Results of Stepwise Multiple Discriminant Function Analysis on Factor Scores From Second Assessment

Standardized Discriminant Function Coefficients

Factor	Function I	Function II
Verbal Ability	.652	-.475
Nonverbal Ability	-.229	-.781
General Adaptive	-.441	.551
Right Hemisphere	-.299	-.347
Sensory-Left	.546	-.170
Anxiety	-.909	-.636
Validity	-.545	.285
Extroversion	-.804	-.186
Right Steadiness/Coordination	1.135	.449
Left Coordination	-.582	-.243
Right Tactile	-.531	-.666

Discriminant Function	Eigenvalue	Canonical Correlation	Wilks' Lambda	df	p
1	3.135	.825	.081	44	.001
2	0.505	.775	.255	30	.021

Overall Correct Classification 56.10%

steadiness and coordination factor and the right hemisphere factor. Univariate F-ratios were obtained on the factors which were included in the discriminant analysis. (See Table 21.) The results of these analyses revealed that there were significant differences between the groups at the second testing on intellectual, adaptive, personality and motor factors. Pairwise comparisons were performed utilizing the Student Newman-Kuels procedure to restrict the number of comparisons. On the verbal abilities factor the normal control group was found to be significantly different ($p < .05$) from the left and bilateral endarterectomy groups and from the vascular control group. These were the same pairwise differences which had been obtained on the initial factor scores. On the general adaptive factor the left and bilateral endarterectomy groups differed from the normal controls. These differences had also been obtained on the initial factors, but on the second factors, the right endarterectomy groups was no longer significantly different from the controls. The anxiety factor demonstrated differences between the right endarterectomy and vascular control groups while on the left coordination factor the left CE group differed from the normal controls. There were no significant pairwise differences on the validity or right steadiness/coordination factors.

As was the case with the initial assessment variables an attempt was made to determine differences between the groups on the basis of the actual test variables obtained at second testing. Univariate F ratios were obtained on these test variables and the results are presented in Table 22.

Table 21

Univariate F Ratios for the Factors Included in the Stepwise Multiple Discriminant Function Analysis of Factor Scores from Second Testing

Factor	F	df	p
Verbal Ability	3.87	4,60	.007
Nonverbal Ability	0.28	4,60	N.S.
General Adpative	3.44	4,49	.014
Right Hemisphere	1.76	4,49	N.S.
Sensory-Left	0.92	4,60	N.S.
Anxiety	3.18	4,42	.022
Validity	3.15	4,42	.023
Extroversion	0.76	4,42	N.S.
Right Steadiness/Coordination	2.58	4,60	.046
Left Coordination	2.63	4,60	.042
Right Imperception	1.34	4,61	N.S.

Table 22

Univariate F Ratios on Test Variables
from Second Assessment

Variable	F	df	p
VIQ	2.67	4,60	.040
WRATR	3.09	4,55	.022
WRATS	3.44	4,55	.013
WRATA	3.41	4,57	.014
TPT-LHT	3.13	4,48	.022
TPT-TT	2.87	4,46	.033
Fingtap-R	3.77	4,56	.008
Fingtap-L	3.83	4,58	.007
Trails B-time	3.33	4,58	.016
Trails B-credits	6.51	4,57	.001
Trails Total time	9.58	4,59	.001
Trails Total credits	5.48	4,59	.001
MMPI-K	4.61	4,41	.003
MMIP-Hy	3.26	4,42	.020
#Writing-R	3.26	4,56	.004
Pegboard-R	4.30	4,59	.004
Pegboard-L	3.29	4,60	.016
Pegboard Total	3.92	4,57	.007
Knox	3.48	4,62	.012
M.Q.	3.32	4,58	.016

It can be seen that many of the measures which significantly differed at initial testing also differ at the second assessment. There are some variables which were found only to differ at second testing, the most notable of which was the Verbal I.Q. ($F = 2.67$, $df = 4, 60$, $p < .05$). Pairwise comparisons were performed with the Student Newman-Kuels procedure to limit the number of comparisons. These comparisons revealed few pairwise differences, and where they did exist were distributed between all five groups. For example, the normal control group differed from all four other groups on the total credits score from the Trail Making Test ($p < .05$) while the vascular control group differed from all the others ($p < .05$) on the test of perception of numbers written on the right hand. In addition the left endarterectomy scored lower than three other groups on the right hand finger tapping test. (There was no difference between the LCE and VC groups on this measure.) It was also observed that some of the pairwise comparisons which had indicated differences between groups at initial assessment failed to do so on the second testing variables. For example, on the first assessment the reading subtest of the WRAT showed differences when the normal controls were compared with the left and bilateral endarterectomy groups as well as the vascular controls. On second testing only the bilateral endarterectomy and normal controls were found to differ ($p < .05$). At first testing all three endarterectomy groups differed from the normal controls on the left hand trial of the Tactual Performance Test while on second testing, only the left endarterectomy group differed.

A direct test of the group differences over the test-retest interval was accomplished by multivariate analysis of change scores derived from

factor scores. It was found that significant differences existed when the groups were compared on these change scores. This was interpreted as evidence that the groups differed in the changes that occurred over the six month intertest interval.

In addition, when the data from the two assessments were examined independently, certain indirect inferences were possible. For example, on some measures overall group differences were found only on first testing, while on other measures the groups differed only at second testing. Further suggestion of change was derived from the observation that many of the pairwise differences which existed at first testing were no longer apparent in the data obtained at follow-up testing. In view of the overall group differences, each group was examined separately in an attempt to determine the source of the intertest differences.

Independent Groupwise Analysis

The variables included in this aspect of the analysis were those 65 which had been employed in the factor analyses. For each group, comparisons were made between the first and second testing by the use of paired t-tests. The number of tests which showed significant improvement were tallied for each group and a comparison among the groups was made. Figure 1 reveals that the right carotid endarterectomy group improved on more tests than any of the other groups ($\chi^2 = 21.666$, df = 4, $p < .001$).

Only one instance of a significant decrement in performance occurred. At second testing, the vascular control group demonstrated greater concern about somatic function as reflected by an increased mean score on the hypochondriasis scale of the MMPI ($F = 3.21$, df = 8,

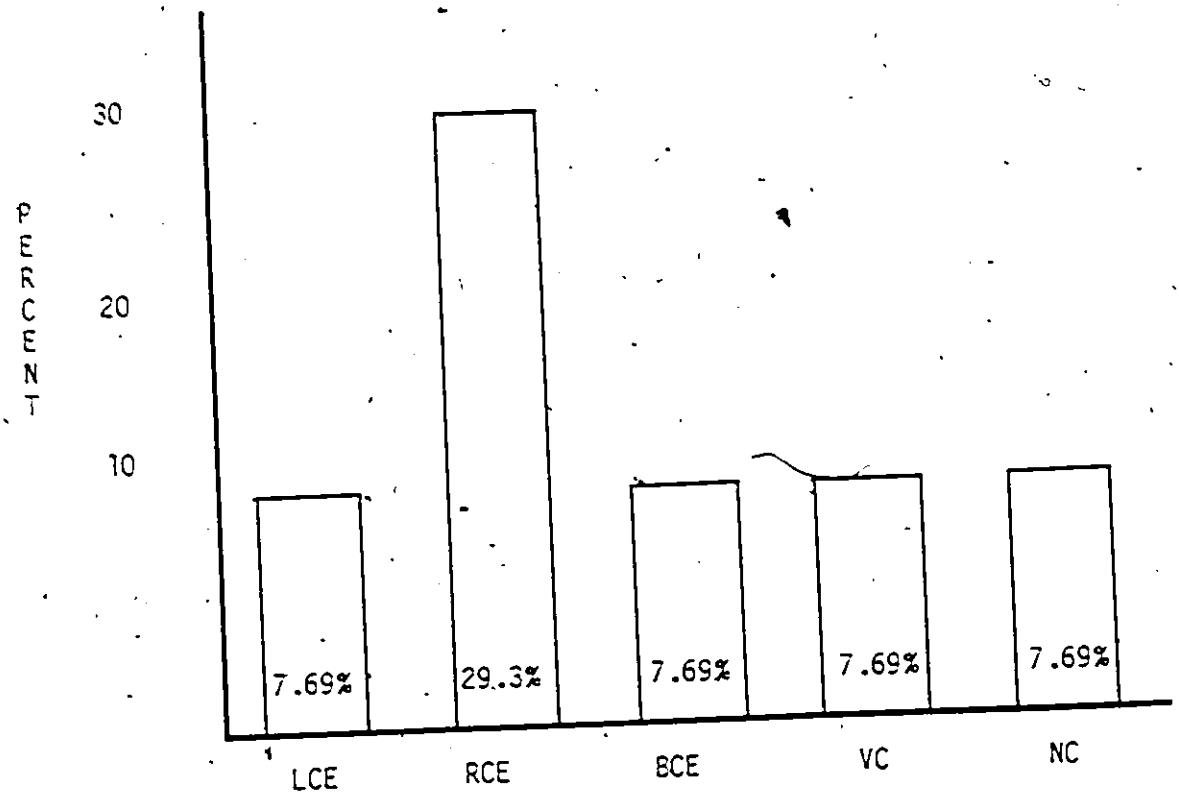

Figure 1: Percentage of tests improved for each group

$p < .01$). The test variables on which at least one group demonstrated significant change are presented in Table 23. As can be seen, all five groups improved on Performance IQ, while improvement was noted in four groups on the Memory Quotient. The left endarterectomy group closely approached significance on this measure ($F = -2.17$, $df = 12$, $p < .051$).

Among the tests that contribute to the Impairment Index, improvement on the Category Test was observed in both the left and right endarterectomy groups as well as the normal controls. Only the right endarterectomy group demonstrated improvement on any of the other measures from the Index. It can be seen that the right operated group improved on the Time and Memory components of the Tactual Performance Test, the Halstead Speech Perception Test and the Total Credits score from the Trail Making Test. Further, the improvement of the right endarterectomy group appeared to be bilateral in that gains were observed on tests of motor function on both body sides.

These results argue that changes across the test-retest interval were not equal among the groups and that the right endarterectomy group improved to a greater extent than either of the control groups or the other endarterectomy groups. The fact that the left and bilateral endarterectomy groups did not differ from the control groups suggested that the improvement in these groups was no greater than would be expected due to practice effects or spontaneous recovery from vascular symptoms. Only the right operated group exceeded what might have been expected on the basis of the control group performance. These findings argue for the rejection fo the initial null hypothesis of no group differences over the intertest interval.

Table 23

Significance of Change in Test Variables
over Test-Retest Interval

Variable	LCE	RCE	BCE	NC	VC
VIQ		.000		.050	
PIQ	.005	.001	.005	.020	.025
WRATR		.003			
WRATS					.015
WRATA		.037			
Category	.006	.005		.010	
TPT-RHT		.001			
TPT-LHT		.050			
TPT-TT		.030			
TPT-M		.003			
Speech		.028			
Grip-R		.016	.002		
Grip-L		.005	.003	.010	
Footap-R	.031	.037			
Footap-L		.047	.037		
MMPIMf					.003
MMPIHs					.012*
MMPIF		.031			
#Writing-R	.037	.029			.004
Stead-RT		.016			
Peg-RT		.001			
Knox		.011			
M.Q.	(.051)	.000	.000	.004	.015
Total Positive Change	5+	19	5	5	5

(+ Does not include M.Q.)
(* Negative change)

TIA vs Completed Stroke

An attempt was made to determine possible sources of the group differences over the six month interval. There were no differences between the RCE group and the remaining two endarterectomy groups in terms of age, years of education, or initial level of impairment (as measured by the Impairment Index from the Halstead-Reitan Neuropsychological Test Battery ($F = .915$, $df = 3,35$, $p > .40$).

It was decided to examine any differences which might exist related to the initial level of presenting neurological symptoms (TIA vs completed stroke). To accomplish this, all endarterectomy patients with the presenting symptom of TIA were grouped and compared with those endarterectomy patients with completed stroke. There was considerable variability of symptoms in the completed stroke group. Some patients had very mild, circumscribed deficits (e.g. retinal occlusions with deficits restricted to vision) while other patients had extensive hemispheric damage with correspondingly extensive deficits). These two groups of endarterectomy patients were compared with the vacular control group to determine any difference in response as a function of the initial level of neurological deficit.

The vascular control group was somewhat younger than the two endarterectomy groups ($F = 13.26$, $df = 2,65$, $p < .001$) but they did not differ in regard to years of education or initial level of neuropsychological impairment (see Table 24). There was also considerable variation in regard to initial severity of symptoms in the control group. There were 25 subjects in the TIA group (9 females, 16 males), 30 subjects in the stroke group (8 females, 22 males) and 14

Table 24

Age, Education and Level of Impairment for TIA and Stroke Groups and Vascular Control

	TIA	Stroke	Control	F	df	p
Age	63.79	60.96	50.78	13.265	2,65	.001
Education	10.16	10.06	10.38	.035	2,64	.965
Impairment	.68	.71	.76	.757	2,48	.474

vascular controls (4 females, 10 males). The groups did not differ in sexual representation ($X^2 = 3.22$, df = 2, $p > .35$).

Analysis of Factor Change Scores

The data analysis was approached in the same manner as was presented previously. As before, the initial question to be addressed was whether the groups differed in regard to the change over the test-retest interval. To examine this question, the factor change scores (as described in a previous section) were entered into a stepwise multiple discriminant function analysis as a multivariate test of the group differences over the intertest interval. This analysis yielded one discriminant function which significantly discriminated between the groups (Wilks' Lambda = .042, df = 30, $p < .001$). The single function correctly classified 68.12% of the subjects. These results and the standardized discriminant function coefficients are presented in Table 25 where it can be seen that the highest loadings were obtained on the nonverbal ability factor, the left tactile imperception factor and the left steadiness factor. These results indicated that when subjects were grouped according to the severity of presenting neurological symptoms, there were differences in the changes observed over the six month intertest interval. As was the case in the initial group comparisons, the factors that contributed most highly to the discrimminant function were those interpreted as largely reflecting right hemisphere function.

This analysis suggested that when the change score variables were combined, group differences existed in regard to changes over the test-retest interval. It again was of interest to attempt to determine

Table 25

Results of Stepwise Multiple Discriminant Function Analysis for TIA, Stroke and Controls on Factor Change Scores

Standardized Discriminant Function Coefficients

Factor	Function I
Verbal Abilities	-0.622
Performance/Memory	1.831
Right Hemisphere	0.450
Sensory Right	1.697
Sensory Left	-1.510
Validity	-1.452
Depression	-1.302
Extroversion	0.551
Right Steadiness/Coordination	-0.686
Psychomotor	0.460
Left Steadiness	1.503
Left Tacticle Imperception	1.511
Bilateral Tactile Imperception	-0.617
Bilateral Right Tactile	-1.577
Bilateral Left Tactile	1.156

Discriminant Function	Eigenvalue	Canonical Correlation	Wilks' Lambda	df	p
1	7.172	.936	.042	40	.001

Overall Correct Classification 68.12%

the source of these differences, and furthermore it was again desirable to avoid the difficulties inherent in the use of change scores. To avoid these difficulties and to gain further inferences about the source of group differences, the data from the two assessments were examined independently.

Analysis of Initial Testing Factor Scores

The factor scores from the initial assessment were used in a multiple discriminant function analysis to examine overall multivariate differences between groups. The results of this analysis are presented in Table 26 and reveals that one discriminant function was obtained which significantly separated the groups (Wilks' Lambda = .401, df = 14, $p < .003$). The standardized discriminant function coefficients revealed that the highest loadings on the discriminant function were found with the general adaptive, verbal abilities, and right imperception factors.

The univariate F ratios for the factors which were included in the discriminant function are presented in Table 27 which shows that there were differences between the three groups on the general adaptive factor ($F = 6.72$, df = 2,52, $p < .003$), the anxiety factor ($F = 3.88$, df = 2,42, $p < .03$) and the psychomotor factor ($F = 3.89$, df = 2,61, $p < .03$). Pairwise comparisons were performed employing the Student Newman-Kuels procedure to limit the number of comparisons. The vascular control group differed from both endarterectomy groups on the general adaptive factor ($p < .05$). On the anxiety and psychomotor factors the stroke/endarterectomy group differed from the control group ($p < .05$). To further assess the nature of these differences, univariate F tests

Table 26

Results of Stepwise Multiple Discriminant Function Analysis for TIA, Stroke and Controls on Initial Factor Scores

Standardized Discriminant Function Coefficients

Factor	Function I
Verbal Abilities	0.355
General Adaptive	0.809
Right Hemisphere	-0.493
Anxiety	-0.763
Psychomotor	-0.569
Left Tactile Imperception	-0.786
Bilateral Right Imperception	0.205

Eigenvalue	Canonical Correlation	Wilks' Lambda	df	p
.999	.707	.401	14	.003

Overall Correct Classification 56.52%

Table 27

Univariate F-Ratios for the Factors Included in the Stepwise Discriminant Function Analysis (TIA, Stroke and Controls) First Testing

Factor	df	F	p
Verbal Abilities	2,63	0.35	N.S.
General Adpative	2,52	6.72	.002
Right Hemisphere	2,52	1.52	N.S.
Anxiety	2,42	3.88	.028
Psychomotor	2,61	3.89	.025
Left Tactile	2,62	1.39	N.S.
Right Imperception	2,62	0.13	N.S.

were performed on the actual test variables from the initial neuropsychological assessment. The results of this analysis revealed that the groups differed on several measures at initial assessment (see Table 28).

Pairwise contrasts were computed employing the Student Newman-Kuels procedure. The endarterectomy stroke group was different from either one or both of the remaining groups in all cases of significant pairwise differences. The differences occurred on a variety of measures of motor, sensory and cognitive functions. For example, it can be seen that the endarterectomy stroke group performed poorly relative to the other groups on tests measuring left sided abilities of coordination, fine manipulative skills, nonverbal abilities and visual attention. On the other hand, the endarterectomy-stroke group achieved better scores on right foot tapping rates and lower scores on three scales from the MMPI.

Analysis of Second Testing Factor Scores

In order to further evaluate the changes in the factors over the six month interval, the factor scores derived from the second testing were utilized in a stepwise multiple discriminant function analysis. This procedure was regarded as a multivariate test of the difference between groups at second testing and the results yielded one discriminant function which separated the groups (Wilks' Lambda = .301, df = 14, $p < .001$).The standardized discriminant function coefficients revealed that the highest loadings on the discriminant function were the nonverbal ability factor, the depression factor and the right imperception factor (see Table 29). Univariate F tests were performed on the factors which

Table 28

Univariate F Ratios on Original Test Variables
TIA, Stroke and Controls at First Testing

Variable	$\bar{X}$TIA	$\bar{X}$Stroke	$\bar{X}$Control	F	df	p
PIQ	99.84	86.60	95.07	4.81	2,64	.011
Trails A-t	50.84	106.20	74.21	3.86	2,61	.026
Trails A-c	7.96	5.08	6.21	5.38	2,61	.007
MMPI-Pt	58.14	55.60	66.66	3.30	2,42	.046
MMPI-Hy	60.00	56.33	67.88	3.83	2,42	.029
MMPI-Pn	5.19	4.30	12.00	3.73	2,38	.032
Footap-R	34.66	41.30	39.27	4.36	2,39	.019
Coord-RC	12.36	36.62	7.16	5.00	2,56	.010
Coord-LT	3.09	43.30	16.41	4.58	2,57	.014
Fingag-L	1.08	2.87	1.42	3.89	2,60	.025
Roughness-R	0.66	1.27	0.0	3.40	2,38	.043
Peg-Lt	90.24	154.64	88.92	5.52	2,63	.006
Peg-Total	118.12	263.75	160.87	3.89	1,59	.025
Knox	11.86	9.18	11.64	4.11	2,66	.020

Table 29

Results of Stepwise Multiple Discriminant Function Analysis: TIA, Stroke and Controls on Second Testing Factors

Standardized Discriminant Function Coefficients

Factor	Function I
Nonverbal Ability	.928
Right Hemisphere	-.393
Sensory-Right	-.234
Anxiety	-.987
Depression	.621
Right Steadiness/Coordination	-.014
Right Imperception	.493

Discriminant Function

Eigenvalue	Canonical Correlation	Wilks' Lambda	df	p
1.561	.780	.301	14	.001

Overall Correct Classification 60.87%

were included in this second discriminant analysis and as can be seen in Table 30, only the anxiety factor from the MMPI significantly differed between the groups ($F = 3.80$, $df = 2,35$, $p < .033$). It was of interest that the absolute value of the standardized discriminant function coefficient for the anxiety factor was the highest obtained on the discriminant function. Pairwise comparisons indicated that the vascular control group differed from the endarterectomy/stroke group as had been the case on initial testing. Only two factors were included in both first and second discriminant analyses (anxiety and right imperception).

To further examine the differences between the groups at second testing, univariate F tests were performed on the actual test variables obtained at that assessment. Table 31 reveals that there were much fewer differences between the groups at second testing (15 at first testing versus only 3 at second testing). With the exception of the hysteria scale from the MMPI these variables had not differed at initial testing. Pairwise comparisons were performed employing the Student Newman-Kuels procedure to limit the number of comparisons. The vascular control group differed from the two endarterectomy groups in having significantly higher scores on the hysteria scale of the MMPI and in making a greater number of errors on a test of perception of numbers written on the fingertips ($p < .05$). The endarterectomy stroke group made significantly more errors of roughness discrimination with the left hand than either the TIA or the control group.

A direct test of the group differences over the six month intertest interval was accomplished by a multivariate analysis of change scores derived from the factor scores obtained at first and second assessment.

Table 30

Univariate F Ratios for Factors Included in Stepwise Discriminant Function Analysis (TIA, Stroke, Controls) Second Testing

Factor	df	F	P
Nonverbal Ability	2,51	2.25	N.S.
Right Hemisphere	2,40	1.00	N.S.
Sensory-Right	2,51	2.25	N.S.
Anxiety	2,35	3.80	.032
Depression	2,35	1.12	N.S.
Right Steadiness/Coordination	2,51	0.62	N.S.
Right Imperception	2,52	0.99	N.S.

Table 31

Univariate F Ratios on Original Test Variables
TIA, Stroke and Controls at Second Testing

Variable	$\bar{X}$TIA	$\bar{X}$Stroke	$\bar{X}$Control	F	df	p
MMPIHY	59.78	58.15	68.45	3.45	2,35	.043
#Writing-R	1.82	1.63	5.46	5.77	2,49	.006
Roughness-L	0.0	1.27	0.20	5.56	2,31	.009

When these change scores were combined, the groups were found to differ, and the factors that contributed most to the discrimination were those interpreted as reflecting right hemisphere function. These findings were regarded as evidence that the groups differed in the changes that occurred over the test-retest interval.

Indirect inferences regarding these changes was obtained by an independent evaluation of the data from the two assessments. The fact that different factors entered the discrimination analyses at first and second testing was interpreted as evidence of change over the test-retest interval. Further evidence of some change was drawn from the observation that considerably fewer measures distinguished between the groups at the second assesssment than had been the case originally. To further analyze the possibility of significant change, each group was considered separately and the extent of change between the two assessments was examined.

Independent Groupwise Analysis

The variables included in this aspect of analysis were the 65 test variables which had been utilized in the initial factor analyses. For each group, performance on the first and second assessments were compared by paired t-tests. A count was made of the number of measures which showed significant improvement, and the groups were compared on this frequency count. Table 32 presents the measures and level of significance for each group in the measures which signficantly changed. There were no instances of reduction in the level of performance. Figure 2 demonstrates that the endarterectomy group with completed stroke

Table 32

Significance of Change in Test Variables
over Test-Retest Interval

Variable	TIA	Stroke	Control
VIQ	.003	.013	
PIQ	.001	.001	.025
WRATS			.015
WRATA		.018	
Category	.007	.006	
TPT-RT		.004	
TPT-LT	.047		
TPT-TT	.035	.005	
TPT-M		.002	
Trails (time)		.033	
Grip-R		.001	
Grip-L	.006	.022	
Footap-R	.003	.045	
Footap-L	.018		
Coord-RC		.024	
Coord-LT		.049	
#Writing-R		.001	
#Writing-L		.018	.004
MMPI-Mf			.003
Stead-RT		.050	
Stead-LT		.028	
Peg-RT	.024	.038	
Peg-LT		.024	
Knox		.007	
M.Q.	.001	.001	.015
Total	10	21	5

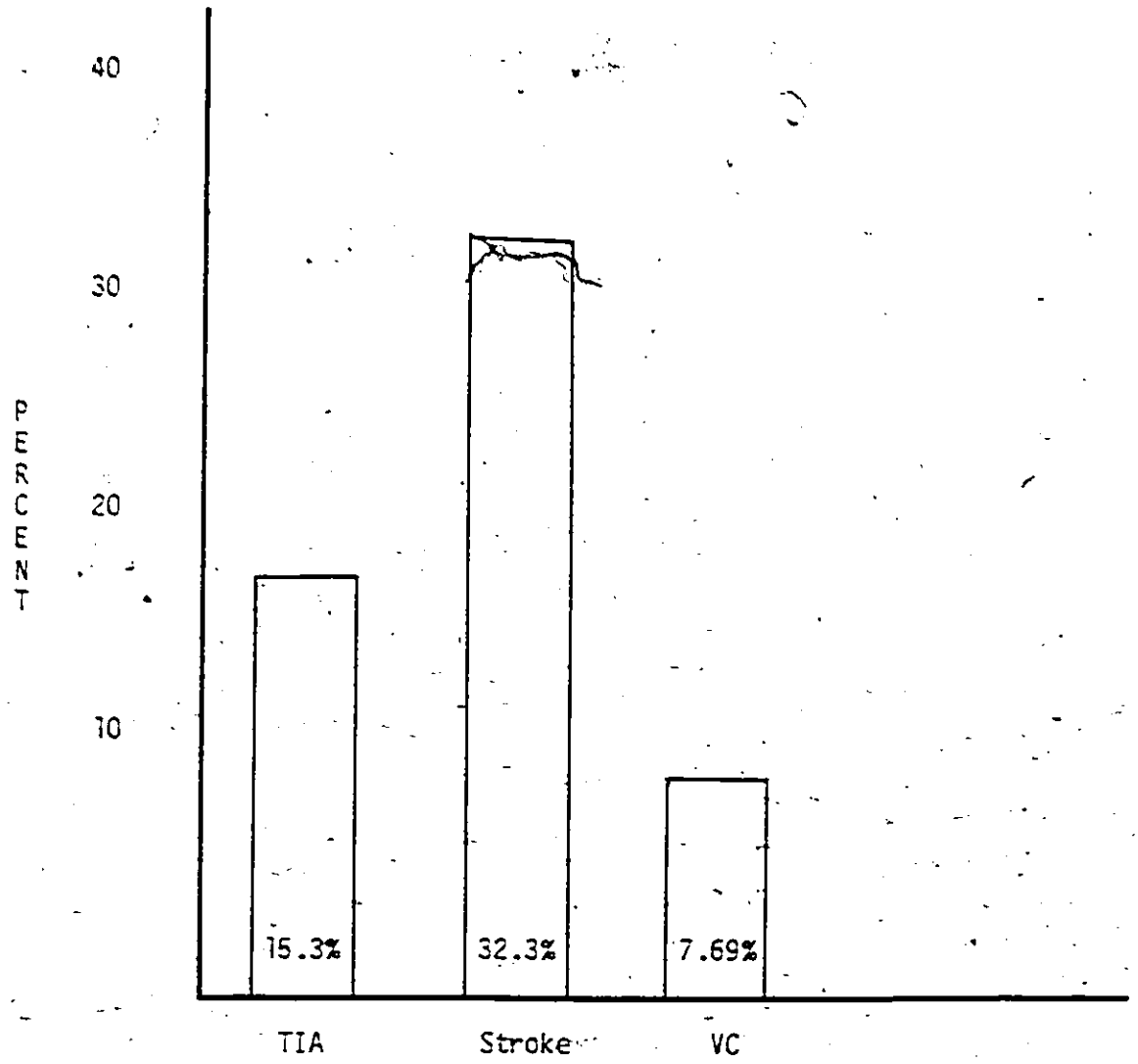

Figure 2: Percentage of tests improved for operated TIA and stroke patients and vascular controls

improved on significantly more tests than either the vascular controls or the TIA endarterectomy group (χ^2 = 13.69, df = 2, $p < .01$). As can be seen in Table 32, all three groups showed significant gains on Performance I.Q. and the Memory Quotient. There were several instances in which only the two endarterectomy groups improved and the endarterectomy/stroke group is observed to improve on a broader range of motor and sensory measures than either of the other groups.

It had been initially hypothesized that the TIA group would demonstrate greater improvement by virtue of the fact that there was no clinical evidence of cerebral infarction. These results failed to confirm this initial hypothesis in that it was found that patients with completed stroke and subsequent endarterectomy improved more than either the vascular controls or the TIA group with subsequent endarterectomy.

All groups improved on some measures and it was considered likely that practice effects could account for the improvement observed on these measures. Spontaneous recovery of function was considered to be an unlikely explanation of these results for two reasons. First, although the stroke-endarterectomy group performed somewhat poorly on some motor and sensory measures, there were no differences between the groups in the overall level of performance (Impairment Index). Secondly, a greater improvement would be expected in the vascular control group if spontaneous recovery alone were accounting for the observed changes. These results then were interpreted as evidence that carotid endarterectomy contributed to improved performance in patients with completed stroke as the presenting neurological condition.

Right vs Left Endarterectomy - Stroke Patients

When these results of greater change in the endarterectomy/stroke group were considered in light of the previous finding that the right endarterectomy group showed a greater improvement than either of the control groups or the other endarterectomy groups, it was considered to be of importance to determine whether differences existed between the patients with completed stroke in the right and left endarterectomy groups. In order to accomplish this, the stroke patients in the right and left endarterectomy groups were compared on the original test variables obtained at both first and second testing.

There were more stroke patients in the RCE group but the difference did not attain statistical significance ($X^2 = 1.81$, $df = 1$, $p > .175$). In addition, as seen in Table 33, the two groups did not differ in age, years of education, or initial level of impairment as assessed by the Impairment Index (computed from the Halstead-Reitan Neuropsychological Test Battery). There were very few differences between these groups on initial testing. The differences occur on measures of intelligence, memory, and a few motor tests, mainly with the right hand (see Table 34). In all cases of significant differences the LCE group was inferior to the RCE group.

When the two groups were compared on the test variables from the follow-up assessment, it was observed that, to a large extent, the groups differed in the same tests on which they had differed initially. As was the case at initial assessment, all of the differences obtained on the second assessment varibles were in the direction of superior performance by the RCE group. Examination ot Tables 34 and 35 reveals that the

Table 33

Age, Education and Level of Initial Neuropsychological Impairment: Stroke Patients with Left and Right Endarterectomy

	$\bar{X}$LCE	$\bar{X}$RCE	t	df	p
Age	64.62	61.06	1.09	16	.290
Education	9.37	11.26	-1.50	14	.157
Impairment	0.75	0.70	0.31	9	.809

Table 34

t Tests on Original Variables from Initial Assessment: Stroke Patients in LCE and RCE

	$\bar{X}$LCE	$\bar{X}$RCE	t	df	p
VIQ	86.62	104.53	-2.30	21	.032
PIQ	75.37	93.00	-2.87	19	.009
WRATA	3.12	5.93	-2.36	19	.029
TPT-LT	9.93	8.36	2.56	10	.028
TPT-TT	29.80	25.03	2.70	10	.022
Fingtap-R	26.75	41.42	-2.70	8	.027
Trails-Credits	3.50	9.53	-2.72	17	.014
Grip-R	18.78	30.02	2.57	21	.018
Pegboard-R	202.28	98.87	2.53	7	.039
Mem. Quot.	78.12	104.26	-2.84	21	.010

Table 35

t Tests on Original Variables from Second Assessment: Stroke Patients in LCE and RCE

	$\bar{X}$LCE	$\bar{X}$RCE	t	df	p
VIQ	87.66	109.84	-2.76	17	.013
WRATR	8.12	12.47	-2.37	16	.031
WRATA	3.32	7.80	-3.44	15	.004
Seashore	19.50	25.87	-2.66	8	.029
Trails-Credit	6.60	12.16	-2.36	15	.032
Grip-R	22.52	35.00	-2.88	17	.010
Pegboard-R	144.33	71.46	3.19	5	.024
Knox	8.83	11.92	-2.55	17	.021
Mem. Quot.	81.50	115.06	-3.47	17	.003

groups ceased to differ in the Performance I.Q., right hand finger tapping, and the left hand and memory scores from the Tactual Performance Test. In addition, differences were obtained on second assessment variables on which no preoperative differences had existed (i.e. WRATR, Seashore and Knox).

To further pursue the examination of these two groups, each was considered separately in comparing the relative performance on the two assessments by use of paired t-tests. The variables included in this stage of the analysis were the 65 test variables which had been employed in the original factor analyses. When this analysis was applied to the LCE stroke patients, only the Performance I.Q. was shown to significantly improve from first to second testing ($t = 2.66$, $df = 5$, $p < .048$). The results of this analysis for the RCE stroke patients is shown in Table 36 and reveals that this group improved on a signficantly larger number of measures including three of the ten measures which comprise the Halstead Impairment Index ($X^2 = 13.96$, $df = 1$, $p < .001$). Figure 3 presents the relative percentage of tests improved upon by the completed stroke patients in the left and right carotic endarterectomy groups.

These findings indicated that there were initial differences between the stroke patients in the left and right endarterectomy groups. The differences at second testing were largely the same as those that had existed initially. In spite of the fact that the differences between the groups remained relatively constant, it was observed that the stroke patients in the RCE group improved on a vastly greater number of measures than the stroke patients in the LCE group. Since the RCE group (including TIA patients) demonstrated improvement on more measures than

Table 36

Significance of Change for Test Variables over Test-Retest Interval: Stroke Patients LCE and RCE

Variable	LCE	RCE
Verbal I.Q.		.006
Performance	.045	.005
WRAT-R		.005
WRAT-A		.023
Category		.046
TPT-RHT		.018
TPT-TT		.024
TPT-Memory		.022
GRIP-R		.013
GRIP-L		.038
Coord-RC		.008
#Writing-R		.031
Steadiness-R		.018
Pegboard-R		.004
Mem. Quot.		.000
Total	1	15

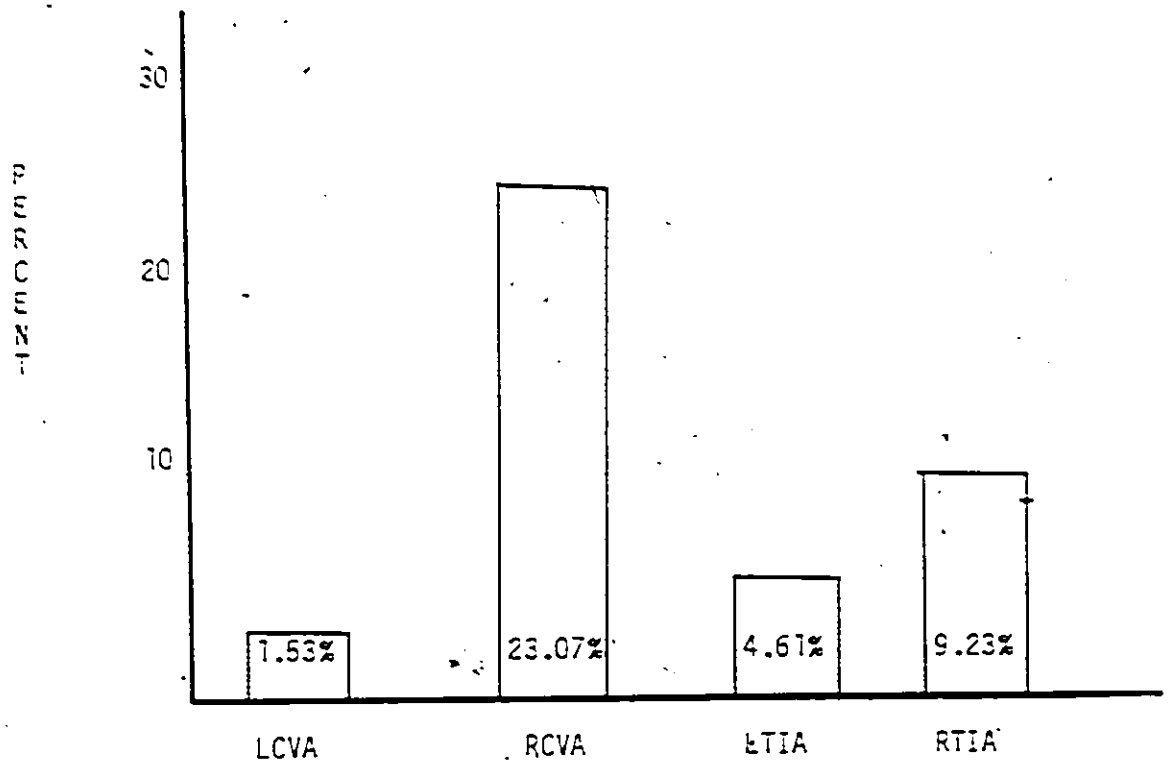

Figure 3: Percentage of tests improved Stroke and TIA patients from RCE and LCE

those in Table 36, it was suggested that the improvements obtained by the RCE group could not be attributed solely to the changes observed among the stroke patients in this group.

Right versus Left Endarterectomy - TIA Patients

However, when the TIA patients from the right and left endarterectomy groups were compared, there were virtually no differences between the groups. It can be seen in Table 37 that the patients in the right operated group were older than those in the left operated group ($t = 2.55$, $df = 16$, $p < .04$) but there were no differences in terms of education or initial level of neuropsychological impairment. In addition, there were very few differences between the groups on the preoperative assessment. The variables on which the groups differed are presented in Table 38 where it can be seen that in each case the right operated group performed more poorly than the left operated patients. In view of the number of comparisons performed, this small number of differences may be due to chance. A comparison of the groups on the postoperative data failed to produce any significant differences. These findings suggested that the two groups of TIA patients were highly similar and that little differential change occurred over the intertest interval.

In fact, very little change was observed for either group. Table 39 presents the measures on which the groups improved. There was no difference on the percentage of tests which improved, 4.61% for the left operated patients versus 9.23% for the right operated group ($\chi^2 = .89$, $df = 1$, $p > .30$). It was of interest that the left operated group improved on Verbal IQ but not Performance IQ while the reverse was true

Table 37

Age, Education and Neuropsychological Impairment in TIA Patients from Right and Left Endarterectomy Groups

	LCE	RCE	t	df	p
Age	63.00	68.14	-2.25	16	.039
Education	10.33	11.29	-0.45	17	.662
Impairment	.63	.78	-1.83	16	.085

Table 38

t-Tests on Original Tests Variables from Initial Assessment: TIA Patients from LCE and RCE

	LCE	RCE	t	df	p
TPT-M	5.9	4.0	2.53	15	.023
Btact RH	0.25	1.25	-2.49	9	.016
Roughness-R(time)	43.2	62.0	-2.22	14	.043

Table 39

Significance of Change over Intertest Interval
Right and Left Operated TIA Patients

Variable	LCE	RCE
VIQ	.031	
PIQ		.040
Category	.017	.022
TPT-RT		.013
TPT-M		.033
Trails T		.035
MMPIF	.041	
MQ		.047
Number Improved	3 (4.61%)	6 (9.23%)

true for the right operated patients. In addition to the measures in Table 39, it was found that left hand finger tapping rates decreased in the left operated group ($t = 2.50$, $df = 6$, $p < .05$).

In summary, when stroke and TIA subgroups of the right and left operated groups were compared, no differences were found for the TIA patients in terms of the relative level of performance or the amount of change over the intertest interval. However, a different pattern was obtained with the stroke patients. There were a few scattered differences on preoperative assessment and essentially the same differences postoperatively. The most pronounced finding was the improvement of the patients in the right operated group, and the conspicuous lack of improvement in the left operated group.

Comparison of Endarterectomy Groups on Medical Variables

In addition to the neuropsychological data, the endarterectomy groups were also compared on a number of variables obtained from their medical chart during their hospitalization. These included length of hospitalization, duration of symptoms, history of cigarette smoking habits, and a number of clinical laboratory values obtained during routine blood analysis.

The left, right and bilateral endarterectomy groups were found not to differ on the major milestones of their hospitalization. These included the day of hospitalization on which the angiogram, neuropsychological examination or first operation were performed. The bilateral group had significantly longer stay in hospital ($F = 9.83$, $df = 2,52$, $p < .0002$) due to the fact that they underwent two operative procedures. There were no differences between the groups in terms of the duration of symptoms

($F = 1.27$, $df = 2,52$, $p > .25$). Over 49% of the subjects had experienced symptoms for less than three months prior to admission and more than 83% had experienced symptoms for less than 12 months. No differences were found between the groups in regard to the number of cigarettes smoked ($\bar{X} = 21.9$, $F = .534$, $df = 2,52$, $p > .55$) or the number of years smoked ($\bar{X} = 34.63$, $F = .766$, $df = 2,52$, $p > .47$). In addition, no differences were found between the groups on systolic or diastolic blood pressure, and blood levels of cholesterol, glucose, hemoglobin and hematocrit. These results are summarized in Table 40. The only significant differences on the medical varibles examined occurred on the angiographic estimates of arterial stenosis.

It was found that the right endarterectomy group had a higher degree of stenosis in the right carotid artery than the left endarterectomy group ($F = 4.949$, $df = 2,46$, $p < .01$) and that the bilateral group occupied an intermediate position. The estimates of stenosis in the left carotid artery revealed the opposite situation in which the left endarterectomy group had a higher estimate of stenosis than the right group ($F = 11.85$, $df = 2,45$, $p < .0001$). The bilateral endarterectomy group also differed from the right operated group. The mean right sided stenosis for the right group did not differ from the mean left sided stenosis for the left group ($t = 1.79$, $df = 37$, $p > .20$). This suggested that comparable degrees of pathology on the operated side existed for the right and left endarterectomy groups. The degree of stenosis on the unoperated side also did not differ ($t = .631$, $df = 31$, $p > .20$). Table 41 presents the angiographic estimates of stenosis in both carotid arteries for the left, right and bilateral endarterectomy groups. Also presented are the duration of the carotid artery clamping (required for

Table 40

Comparison of Carotid Endartectomy Groups
on Medical Variables

Variable	LCE	RCE	BCE	F	df	p
Angiogram (day)	4.10	3.82	3.23	.30	2,52	N.S.
Neuropsych (day)	7.31	9.13	8.92	.44	2,52	N.S.
Operation	10.00	11.52	12.00	.45	2,52	N.S.
Discharge	19.21	22.52	31.76	5.71	2,52	.005
Cigarettes/day	19.21	22.52	24.76	.53	2,52	N.S.
Smoking (# years)	31.36	37.08	35.07	.76	2,52	N.S.
Symptom Duration (mo.)	11.06	5.34	6.69	1.27	2,52	N.S.
Systolic B/P	148.44	158.68	145.64	.88	2,48	N.S.
Diastolic B/P	82.77	90.31	87.27	.95	2,48	N.S.
Cholesterol mg%	223.08	223.95	235.72	.39	2,40	N.S.
Glucose mg%	123.22	131.36	117.09	.27	2,48	N.S.
Hemoglobin G/DL	24.58	14.68	15.47	1.44	2,42	N.S.
Hematocrit	41.83	42.31	43.39	.47	2,41	N.S.

Table 41

Estimates of Stenosis and Arterial Clamping Times for Endarterectomy Groups

Variable	LCE	RCE	BCE
% Stenosis-R	53.67	86.86	73.25
% Stenosis-L	87.88	44.44	85.23
Cannulation-R (sec)		78.5	96.46
Decannulation-R (sec)		108.5	111.92
Cannulation-L (sec)	82.15		86.91
Decannulation-L (sec)	101.66		105.58

the insertion and removal of the intraluminal shunt). The cannulation and decannulation times for the right group (on the right carotid artery) were compared with the comparable times from the left endarterectomy group (i.e., the left carotid artery). There were no differences on either the cannulation time ($t = -.32$, $df = 37$, $p > .25$), decannulation time ($t = .67$, $df = 36$, $p > .25$), or total time of artery clamping ($t = .47$, $df = 31$, $p > .25$).

In summary, the endarterectomy groups did not differ on a wide range of medically based measures including blood pressure, blood levels of cholesterol, hemoglobin, hematocrit and glucose and other variables such as course in hospital and smoking habits. When a number of aspects of the surgical procedure were compared, the right and left groups again did not differ when comparable measures were examined.

It was also of interest to determine whether among the endarterectomy patients there were differences between those patients with TIAs and those with completed strokes. No differences were found in terms of the course of hospitalization or cigarette smoking habits. The groups also failed to differ in terms of symptom duration ($t = .92$, $df = 44$, $p > .35$). In addition, there were no differences between the groups on systolic or diastolic blood pressure, or blood levels of cholesterol, glucose, hemoglobin or hematocrit. The only medical variables on which the TIA and stroke groups differed were the angiographic estimates of stenosis. The TIA group had a mean 58.28% stenosis on the right side as compared with the stroke group mean stenosis of 84.67% ($t = -2.89$, $df = 47$, $p < .006$). However, on the left side the TIA group had a mean

stenosis of 83.38%, while the stroke group had a mean stenosis of 61.14% ($t = 2.26$, $df = 46$, $p < .03$).

It was considered a possibility that the amount of plaque material removed might in some way have influenced the differential effects observed among the right and left endarterectomy subjects. Following surgery, the material removed was routinely sent to pathology where measures of the length and maximum transverse diameter were recorded.

A random sample of pathology reports (11 right and 11 left) were reviewed and a global estimate of the amount of plaque removed was calculated. The estimate was derived by multiplication of the length of the specimen by the maximum transverse diameter. There was no difference between the right and left plaque estimates ($t = .376$, $df = 21$, $p > .20$). This suggested that there was no difference in the amount of plaque removed in right, as compared with left carotid endarterectomy. It was therefore unlikely that the quantity of plaque removed could account for the improvements observed in the right endarterectomy group.

The possibility was also considered that the timing of surgery during the course of hospitalization could have been different depending on the side of operation and the nature of presenting symptoms. The stroke and TIA patients from the RCE and LCE groups were examined in regard to the day on which endarterectomy was performed. It was found that the left TIA group was operated upon most promptly (mean operated day = 8.27) while the group with the longest delay before surgery (mean operated day = 12.38) was the left stroke group. The difference between the left stroke and TIA groups was significant ($t = -1.96$, $df = 17$, $p < .05$). There were no differences between the stroke patients from the LCE and

RCE groups (t = .088, NS), nor were there differences between the stroke and TIA patients within the RCE group. The difference between the TIA patients in the RCE and LCE groups approached significance (t = -1.09, df = 17, p > .15). These data in regard to day of operation are summarized in Figure 4. It appeared that the nature and severity of presenting symptoms influenced the decision to operate only among those patients who underwent left endarterectomy.

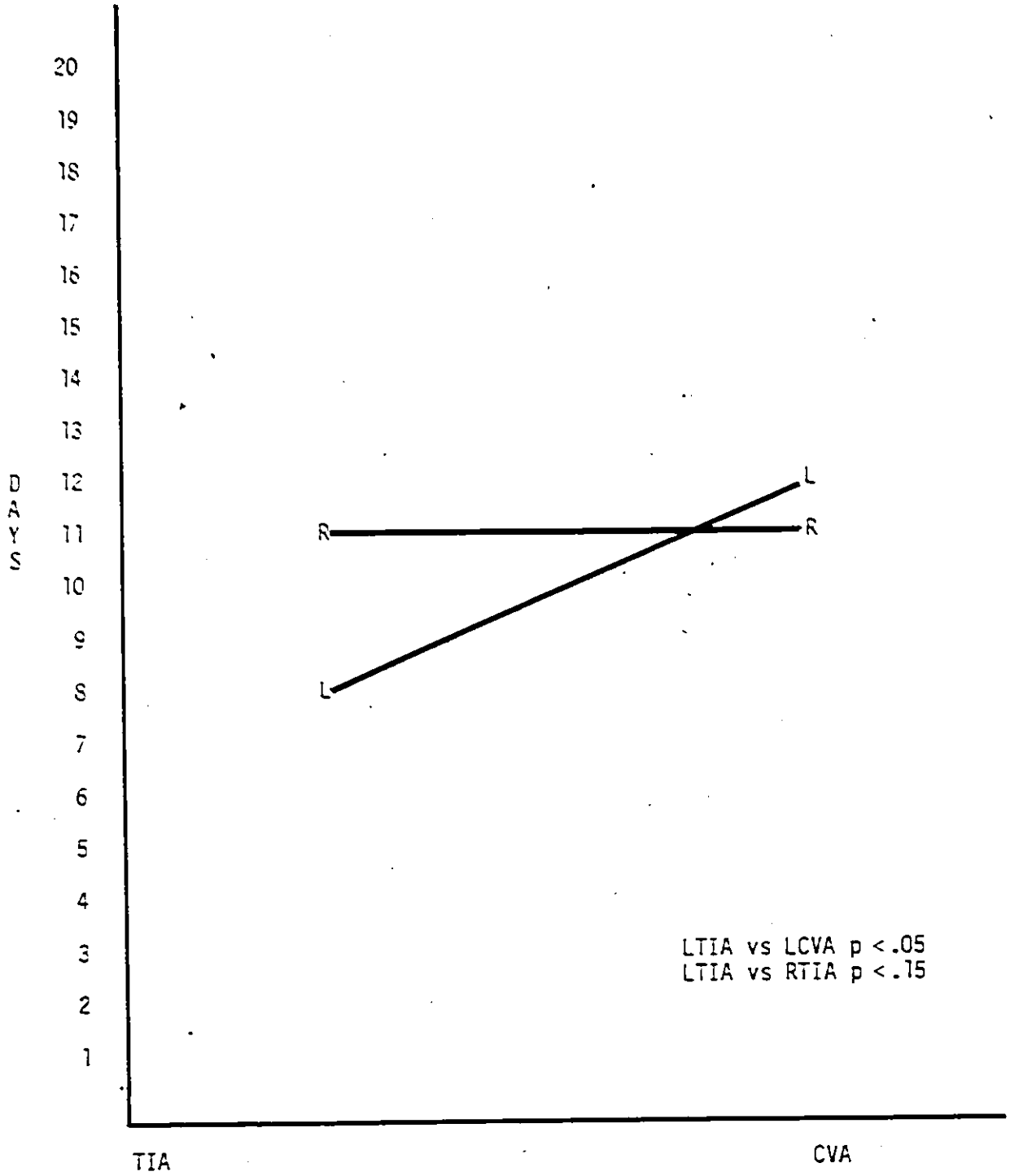

Figure 4: Comparison TIA and Stroke Patients from RCE and LCE on hopsital day of surgery.

CHAPTER IV

DISCUSSION

Carotid endarterectomy was first introduced 25 years ago, and has been shown to be an effective method for reducing the probability of subsequent cerebrovascular accidents. Conventional medical and surgical opinion holds that endarterectomy is a prophylactic measure, and does not result in restoration of abilities. During the past 15 years, however, several investigators have argued in favor of some restorative changes subsequent to endarterectomy. These changes presumably would be attributed to increased blood flow in areas of the brain which prior to surgery had flow sufficient to maintain tissue viability, but insufficient to support normal function.

Several studies have employed objective measures of behavior in the attempt to document improvement subsequent to endarterectomy. The investigations reported in the literature to date have suffered from a number of methodological and theoretical weaknesses which have resulted in the failure to clearly resolve the prophylactic versus restorative debate in regard to carotid endarterectomy. The flaws in previous studies have recently been reviewed by Asken and Hobson (1977). These authors point out that previous investigators have used inapproprite or no control groups and have neglected potentially important variables relating to the nature of symptoms; location and severity of disease and certain aspects of the operative procedure. In addition, synthesis of results from previous studies is limited by variations in the duration of the inter-test interval, the measures employed and the subject population.

The present investigation has addressed many of the problems outlined by Asken and Hobson. The findings reported here indicated that carotid endarterectomy may be considered as more than a prophylactic measure for a select subgroup of the patients who undergo this procedure. In this study, the primary evidence is derived from a comparison of endarterectomy subjects (grouped according to the side of operation) with control subjects who have vascular symptoms but do not undergo endarterectomy and a group of normal subjects who receive an operation not involving the cerebral vasculature.

Data from the pre- and postoperative neuropsychological assessments were subjected to factor analytic techniques for the purpose of data reduction. Change scores on these factors were then computed and subsequently employed to determine if there were group differences in the change over the intertest interval. Significant differences were obtained and it was observed that the factors which made the highest contributions to the overall differences were those that were felt to reflect right hemisphere function.

When each group was examined individually, it was found that the right endarterectomy group improved on a significantly greater number of measures than any other group. This difference could not be attributed to age, education, or the initial level of neuropsychological impairment. In addition, no differences existed between the endarterectomy groups on a large number of medical varibles including blood pressure, serum glucose and cholesterol levels, and a number of operative measures including the duration of arterial clamping. Of considerable interest was the finding that the right and left endarterectomy groups failed to

differ on the angiographic estimates of stenosis of both the operated and unoperated carotid arteries. Furthermore, the amount of material removed from the right and left carotid arteries was not different. These findings of greater improvement among the right operated subjects cannot therefore be attributed to greater arterial pathology or the existence of other contributing disease processes. Since the goal of endarterectomy is to restore the patency of the lumen, the degree of stenosis was considered more likely to be an important factor than the amount of material removed at operation. The failure to find any difference between the right operated group and the other endarterectomy groups on angiographic and pathological estimates of disease would argue that in the present sample, the degree of arterial disease was not related to improvement following endarterectomy. The lack of a relationship between stenosis and improvement was not totally unexpected in view of the findings of Perry et al. (1974) which failed to find a correlation between the Halstead Impairment Index and changes in carotid blood flow.

The superiority of the right endarterectomy group cannot be attributed to practice effects since neither the control groups or the other endarterectomy groups approached the same magnitude of improvement. In particular, there was no difference in the amount of improvement among the other groups in this study. This suggested that the improvements of the left and bilateral endarterectomy patients were likely due to practice effects, the recovery from vascular symptoms that might have occurred spontaneously or a combination of both.

Practice effects or spontaneous recovery cannot, however, completely account for the dramatic improvement demonstrated in the right operated

group. The available estimates of medical pathology and behavioral impairment revealed no differences between the endarterectomy groups. Since all three groups had behavioral deficits with vascular etiology, spontaneous recovery would be a possible explanation for some of the improvements observed. The mechanism of spontaneous recovery cannot easily account for all the differential improvements observed in the present data. Since the intertest interval was equal for all groups, the possibility of practice effects would seem to be equalized.

Several authors have suggested improvement in personality function following endarterectomy. King et al. (1977) and Haynes et al. (1976) presented evidence of reductions on scales of the MMPI measuring suspiciousness and withdrawal. Hayes et al. presented evidence of reductions in anxiety after endarterectomy. On the other hand, Asken and Hobson (1977) raised the possibility that preoperative personality factors such as anxiety and depression, and postoperative reductions of these factors might explain the previous reports of improvements on psychological tests. As Asken and Hobson point out, one possible solution would be to use a control group of patients scheduled to undergo some other type of surgery who theoretically would be subject to stresses similar to those in patients preparing to undergo endarterectomy. The present data, however, did not provide support for either improved personality function, or for personality factors as a basis for the improvement on behavioral measures.

When the groups were compared on the MMPI at initial assessment, the vascular controls were more anxious than the normal operated controls, but no other differences were found. The only personality measure which

significantly changed over the intertest interval indicated that the vascular control group was more concerned about somatic function than they had been at initial assessment. The lack of any difference on personality factors between the operated controls and endarterectomy subjects would support the argument that the stresses of their respective situations are similar, but does not support the contention that anxiety reduction can account for the improvements of the endarterectomy patients. In particular, since the right operated subjects were not different from any other operated group (endarterectomy or control) on MMPI measures of anxiety and depression, it was unlikely that the improvements observed in this group could be attributed to the alleviation of stress. The lack of any significant change over the intertest interval further argues against personality factors as the underlying source of the observed behavioral improvement.

Another possibility that might account for the improvements observed in the right endarterectomy group might be the composition of the groups in regard to the relative percentage of patients with completed strokes versus transient ischemic attacks. There were no differences between the endarterectomy groups in this regard. It was considered however, that among endarterectomy patients, differences in the degree of postoperative improvement might exist between patients with TIA and those with completed stroke. In spite of the differences in the initial persistence of neurologic deficit, the groups did not differ in regard to level of preoperative neuropsychological impairment.

The presence of behavioral impairment in patients with ostensibly transient neurovascular symptoms may seem inconsistent. This lack of

consistency between behavioral and neurological data may be resolved by studies of regional cerebral blood flow (rCBF). Several authors have reported reductions in cerebral blood flow in TIA patients who are clinically asymptomatic. These reductions in rCBF may last for only a few hours (Paulson, 1971) or may persist for a considerable time (Skinhoj, Hoedt-Rasmussen, Paulson and Lassen, 1970; Rees, DuBoulay, Bull, Marshall, Russell and Lyman, 1971). It is possible, therefore, that similar reductions in the present TIA group may have been present at the preoperative assessment and may provide the neurological basis for the deficits observed in the TIA patients.

When the groups were examined independently it was found that the stroke group who underwent endarterectomy improved on a greater number of measures than either the TIA group with endarterectomy or the vascular control group. This indicated that the improvement in the stroke endarterectomy group could not be attributed to simple practice effects or spontaneous recovery of function. The amount of improvement shown by the TIA group was not different from the controls which suggested that for those patients endarterectomy did not lead to significant improvement of neuropsychological function beyond what might be expected from practice effects or spontaneous recovery of function.

The TIA and stroke groups undergoing endarterectomy were also compared on the medical variables. It was found that the stroke patients had a higher degree of stenosis on the right, while the TIA patients had a higher degree of stenosis on the left. The differences in angiographic estimates of stenosis could be explained in two ways. Even though there were no differences in regard to the relative percentage of completed

strokes versus TIAs in the endarterectomy groups, it was observed that 73% of the stroke group received a right endarterectomy while 68% of the TIA group was operated on the left side. This high percentage of right operated patients in the stroke group and left operated patients in the TIA group may account for the differences in angiography. Alternatively the angiographic findings could be viewed as evidence that stenoses of comparable degree have different consequences as a function of the side involved. Since the right and left operated groups did not differ on estimates of stenosis of the operated and unoperated artery, it seemed possible that comparable degrees of stenosis were more likely to lead to TIA in the left hemisphere and more persistent neurological deficit (at least initially) in the right hemisphere.

To examine whether the performance of the stroke patients with subsequent endarterectomy could be explained by the high percentage of right operated patients, subjects with completed stroke from the left and right endarterectomy groups were compared. It was found that these groups were not different in terms of age or preoperative level of neuropsychological impairment. This suggested that in general a completed stroke leads to comparable levels of neuropsychological impairment regardless of the hemisphere affected. The few preoperative differences that did exist indicated greater cognitive and right sided motor impairments among the left operated stroke subjects.

Some of these differences might be explained by the fact that the right operated group was somewhat better educated (9.3 vs 11.2 years). The greater level of education in the RCE stroke group may have contributed to their superiority on measures such as Verbal and Peformance IQ,

Memory Quotient and WRATA. The presence of aphasic symptoms in some of the LCE stroke patients could also have influenced these measures.

However, the remainder of the tasks on which there were differences were motor tasks. Even though both groups demonstrated bilateral deficits, the fact that the right sided deficits in the left operated group were more pronounced than the corresponding left sided deficits in the right operated group suggested the possibility of more severe neurological impairment among the left operated stroke patients. In spite of possible differences in the degree of neurological deficit, the groups did not differ on a summary measure of behavioral impairment (Halstead Impairment Index).

Although the difference between the RCE and LCE stroke groups on the Impairment Index (.75 vs .70) did not reach significance, this would not necessarily be consistent with the argument that the groups were equally impaired on behavioral measures. In fact, it was observed that most of the measures on which there were significant differences were not those that comprised the Impairment Index.

The fact that most of the differences between the two groups were stable, and that new differences post surgery were due to improvements by the RCE stroke group suggested that the level of impairment was greater initially, and that the impairment was more permanent among the left operated stroke patients. This was supported by the fact that the left operated stroke group improved on only one measure while the right operated stroke group improved on significantly more measures. The argument of more persistent impairment in the left operated stroke group was supported by the fact that the mean Impairment Index was virtually

unchanged over the intertest interval. On the other hand, the mean Impairment Index for the right operated stroke group significantly decreased over the intertest interval.

It seemed clear then that there was a pointed contrast between the considerable improvement demonstrated by the right operated stroke patients and the negligible improvement observed among the left operated stroke patients. The basis for this difference was not immediately clear. One possibility was that the patients in the left operated group reached or surpassed some critical level which precluded any substantial improvement. This could be supported by the fact that this group of patients failed to show even the minimal change that might have been expected on the basis of practice effects or spontaneous recovery. The possibility existed that the critical level could be related to the presence of aphasia, hemiparesis or both. This possibility could not be examined in the present data due to the small number of stroke patients in the LCE group.

In view of the differential response of right and left operated stroke patients, it was decided to examine TIA patients from the right and left endarterectomy groups. This analysis revealed virtually no differences between the groups at either pre- or postoperative assessment. Further, the groups did not differ on the number of measures showing improvement.

The lack of differences between the right and left operated TIA patients in conjunction with the clear differences among the operated stroke groups seemed to support the argument of differential improvement following endarterectomy as a function of the side of operation and

severity of symptoms. Specifically, endarterectomy appeared to be related to improved function only in the right operated stroke group.

It was of interest that both right and left endarterectomy groups demonstrated bilateral behavioral deficits. These bilateral effects may be related to recent reports of disturbances of cerebral blood flow in the hemisphere contralateral to a unilateral ischemic infarct. Hoedt-Rasmussen and Skinhoj (1964) were the first to describe the phenomenon of "diaschisis" in patients with unilateral cerebrovascular disorders. These investigators reported that CBF may be depressed for as long as three weeks in the noninfarcted hemisphere. The cerebral blood flow gradually returns to normal in the noninfarcted hemisphere while the reductions in the infarcted hemisphere persisted for longer periods. These findings have subsequently been confirmed by others (Meyer, Shinohara, Kanda, Fukuuchi, Ericssen and Kok, 1970; Lavy, Melamed and Portnoy, 1975; Slater, Reivich, Goldberg, Banka and Greenberg, 1977). Further, Lavy et al. reported no differences in the effects of right versus left cerebrovascular lesions on CBF in the noninfarcted hemisphere. Although there were no data on CBF alterations in the present investigation, this may provide an explanation for the bilateral behavioral deficits observed in both right and left operated patients.

The possibility existed that the differences between the stroke patients in the right and left operated groups may have been related to the manner in which the cases were managed.

Patients presenting with cerebrovascular symptoms were typically initially referred to a neurologist who then had the option of a further referral to a neurosurgeon. It was possible that the neurologist

involved may have been less likely to refer a patient with a completed stroke of the left hemisphere for angiographic investigation. Since the present data were obtained from patients actually referred for angiographic investigation, the possibility of pre-screening cannot be ruled out. Although the present sample may not be representative of the cerebrovascular disease population in general, there was no indication that it was not representative of that subgroup of patients who are treated surgically.

In the present group of subjects the criteria for operation and the performance of the procedure itself did not appear to differ among the three endarterectomy groups. The duration of the operation and the time of carotid occlusion for insertion and removal of the intraluminal shunt did not differ. Angiographic estimates of stenosis in both the operated and unoperated arteries were equal in the left and right operated groups and the amount of material removed at operation did not differ. Therefore differences in the surgical procedure itself or the extent of arterial pathology would not be likely explanations for the differences observed between the left and right endarterectomy subjects.

However, another possibility was that the differences between left and right operated stroke patients was due to the timing of the operation during the course of hospitialization. Specifically it was considered that the decision making process regarding surgery was different with respect to right and left carotid endarterectomy. The possibility existed that there may have been somewhat greater reluctance in performing a left sided operation, ostensibly because of the risk to language function. From the opposite viewpoint, however, it could be argued that

the presence of left hemisphere symptoms might serve as an indicator for more prompt surgical intervention.

In light of the reports by Whisnant, et al. (1973) that a high percentage of patients with TIA proceed to stroke within a short time from the initial onset of symptoms, the presence of left hemisphere symptoms could lead to an early decision to operate (particularly in the patients with left hemisphere TIA). In the event that a cerebrovascular accident had already occurred, the variables weighing on the decision to operate could change. In that instance it might be desirable to insure a stable neurologic condition and thus result in a more cautious approach toward proceeding with surgery.

These possibilities were examined by comparing the TIA and CVA patients from the RCE and LCE groups on the hospital day on which endarterectomy was performed. It was observed that the subgroup with the earliest day of operation was the TIA patients from the LCE group, while the group with surgery at the latest point in the hospitalization was the stroke patients from the LCE group. The difference between the TIA and stroke patients was significant within the LCE group but a similar comparison among subgroups from the RCE group did not achieve significance. A comparison of stroke patients from the RCE and LCE groups did not reach significance, but the comparison of TIA patients from the two groups approached significance (the left TIA group being operated upon earlier).

These findings related to the timing of operation may bear upon the differential improvement observed among the patient groups. It appeared that among the left operated subjects, an early decision was made for

those patients presenting with TIA as compared to those presenting with completed stroke. The difference between right and left TIA approached significance while there was clearly no difference between the right and left stroke patients.

It will be recalled that the left and right TIA patients did not differ in terms of the number of tests which improved while there were large differences between the stroke patients. In view of the data pertaining to the day of operation it may be that patients with left hemisphere symptoms should be operated upon sooner than patients with right hemisphere symptoms. The left TIA patients were operated upon earlier than the right TIA patients, and there was no difference between these two groups in terms of the extent of postoperative improvement. On the other hand, the left stroke patients did not undergo endarterectomy at a correspondingly earlier time in their hospitalization. In fact, the left stroke patients were operated upon significantly later in their hospital course than the left TIA patients, while this was not evident among the right operated patients.

It was of particular interest therefore, to note that the left stroke group failed to demonstrate the marked improvement demonstrated by the right operated stroke patients. These data may indicate that the decision to perform left carotid endarterectomy in patients with completed stroke was delayed too long. It may be necessary to expedite the decision making process regarding endarterectomy in patients with left hemisphere symptoms. This argument would tend to be supported by the fact that the left TIA patients were operated sooner than the left stroke patients and obtained improvement equal to right TIA patients.

The left stroke patients were not operated sooner than the right stroke patients (in fact an average of almost one day later) and failed to show improvement similar to the right operated stroke patients.

Although there were no apparent differences in the degree of arterial pathology, the possibility existed that differences in cerebral blood flow changes could underlie the differences between the left and right operated subjects. The facilities required to examine cerebral blood flow were not available to the present study, but several studies have reported data pertaining to the effects of carotid endarterectomy on cerebral blood flow.

Previous studies of psychological changes following endarterectomy have suggested that these improvements occurred by virtue of an increased blood supply to cerebral tissue previously deprived of the metabolic requirements sufficient for normal function. However, there has been considerable disagreement in the literature as to whether or not endarterectomy results in increased cerebral blood flow.

Waltz, Sundt and Michenfelder (1972) reported increases in cerebral blood flow in 50% of their patients immediately following carotid endarterectomy. These authors cautioned that these postoperative increases could be transient effects and might not indicate permanent increases. In a subsequent study (Sundt, Sharbrough, Anderson and Michenfelder, 1974) it was reported that cerebral blood flow increased only when the preoperative stenosis was greater than 90%. Some caution in interpreting these results is required in view of the fact that the cerebral blood flow measurements were obtained following the use of Halothane anesthesia. This agent is a vasodilator which acts to increase

cerebral blood flow. It is difficult to attribute the findings of Sundt et al. to vasodilaton because the increases in blood were seen only in those patients with a stenosis of 90% or more.

A similar pattern of results was reported by Engell, Boysen, Ladegaard-Pedersen and Henriksen (1972). These authors also reported a measure of blood flow in the cervical internal carotid artery. It was reported that in the ten cases with more severe stenosis there was a significant increse in cerebral blood flow whereas a similar increase did not occur in those 59 patients with less severe stenosis. Engell et al. also calculated a ratio which was believed to represent the amount of brain tissue supplied by the artery being studied. As had been the case with cerebral blood flow, this ratio was increased only for those patients with a more severe stenosis.

In addition to these studies of blood flow immediately after endarterectomy, there have been a few reports of long term postoperative changes. Bregentz, Haggendal and Nilsson (1969) measured cerebral blood flow at a one month postoperative interval. It was found that cerebral blood flow had increased in patients who had improved clinically, but flow was decreased in the groups who had not improved.

A more recent study (Herrschaft, Durrs, Gleim, and Ungeheuer, 1975) reported blood flow changes 4-6 weeks after surgery. Twenty-four of the thirty cases showed significantly improved flows which ranged from ten to fifty percent. The group with severe stenosis had a mean increase of 33% over preoperative flow while a group with kinking of the vessel showed a mean improvement of 26%. In addition a small group of unoperated patients showed no change in blood flow after three to six months. The

authors argued that this lack of improvement in unoperated subjects supported the contention of long term improvements in blood flow as a consequence of carotid endarterectomy.

Jennett, Miller and Harper (1976) reviewed the literature on cerebral blood flow changes after endarterectomy and concluded that when stenosis was less than 70% blood flow was not impeded. However, when the stenosis surpassed 90%, the distal blood flow was impaired even at rest and in these cases normal cerebral blood flow was restored by endarterectomy. Although the present investigation did not include any measure of cerebral blood flow, it was regarded as likely that increases had occurred in this series of cases.

In the current study, the mean arterial stenosis on the operated side approached 90% for both right and left endarterectomy groups and approximately two thirds of both groups had a stenosis of 90% or greater in the operated artery. Therefore, a large percentage of the subjects in the present study had patterns of arterial stenosis similar to those patients reported in the literature to have obtained improved cerebral blood flow following endarterectomy. When the stroke patients from the RCE and LCE groups were compared, it was found that nearly three fourths of the patients in the RCE group had stenosis of at least 90% while only one half of the patients in the LCE group had stenosis of comparable severity. This difference approached, but did not attain statistical significance.

Even if it had been found that the right operated stroke group had a higher percentage of patients with severe stenosis, there is no evidence from the literature that changes in blood flow are related to neuropsy-

chological improvement. In fact, only one study has investigated this relationship and reported negative results. Perry et al. (1975) measured increases in internal carotid artery blood flow and reductions of neuropsychological impairment as reflected by a significantly lower impairment index. It was found, however, that there was no significant correlation between the change in the impairment index and the change in internal carotid artery flow.

In spite of these negative findings, it cannot be concluded that improvement in psychological functions following endarterectomy are unrelated to changes in cerebral blood flow. Although Perry et al. have been the only investigators to directly examine the relation between psychological changes and blood flow, improvements in their procedure might have yielded different results. For example, measurement of cerebral blood flow as opposed to internal artery flow could be employed. Since non-invasive inhalation techniques are now available it would be possible to obtain postoperative blood flow measurements at the same interval used with neuropsychological assessment. Furthermore, in view of the findings of the present study, it would be of interest to determine whether differences in blood flow changes existed after right as compared with left carotid endarterectomy.

Another possible explanation for the present data was that these findings were an expression of hemispheric differences in the changes produced by cerebrovascular accidents. Several investigators have presented data in support of such a differential hemispheric response.

Reitan (1970), for example presented data that patients with right, left or diffuse cerebrovascular disease were equally impaired on a

battery of neuropsychological tests with the exception of a test of finger tapping rates which showed the expected pattern of performance among patients with lateralized lesions. Patients with right vascular lesions, however, obtained lower scaled scores on measures of non-verbal intelligence, while lower verbal scores were obtained in the group with left hemisphere lesions. Several other studies have also confirmed the presence of verbal deficits associated with left hemisphere lesions and nonverbal deficits associated with right hemisphere lesions (Reitan, 1962; Bauer and Becka, 1954; Fitzhugh, Fitzhugh and Reitan, 1961; Reitan, 1955).

These differences are what might have been expected in view of what has become known about differences in hemispheric specialization of function. Other evidence, however, has been presented which extends beyond these basic functional differences. For example, Gainotti (1972) has reported that emotional reactions differ in relation to the hemispheric laterality of cerebral lesions. Patients with left hemisphere lesions were more likely to suffer catastrophic reaction while patients with right hemisphere lesions showed indifference. It was noted that more than 60% of both groups had suffered cerebrovascular lesions.

Reitan and Fitzhugh (1972) compared the performance of groups of patients with right, left and diffuse cerebrovascular disease. The lateralized lesions groups did not differ in the extent to which motor as compared to intellectual functions were impaired. In both lateralized lesion groups, motor functions were more adversely affected than sensory or intellectual functions.

It was reported, however, that of the intergroup comparisons on a number of sensory and motor tests, the significant differences involved the left hand in almost all cases. These authors felt that their data suggested that lesions of the right cerebral hemisphere were more likely to produce contralateral motor or sensory deficits than lesions of the left hemisphere. The tendency in the present data for a higher percentage of the right operated patients to present with residual neurological symptoms may be viewed a support of Reitan and Fitzhugh's findings.

Boll (1974) presented further evidence of differences in the deficit pattern following lateralized cerebral lesions. Three measures of tactile perception identical to those used in the present investigation were employed on groups with lateralized cerebral lesions of mixed etiology. One third of each group suffered cerebrovascular lesions. It was reported that patients with right sided cerebral lesions made more errors of tactile perception with the hand both ipsilateral and contralateral to the lesion. The author concluded that lesions of the right hemisphere produced greater overall impairment of tactile perceptual skills than did similar lesions of the left cerebral hemisphere. These findings would seem to be consistent with those of Reitan and Fitzhugh.

Most of the previous investigations of behavioral changes following carotid endarterectomy have failed to examine potential differences between right and left operated patients. The only study that has addressed this question (Duke, et al.) found the same pattern of results on the Wechsler Adult Intelligence Scale as in the present study. That is, the left operated group improved on Performance IQ and Full Scale IQ, while the right operated group improved on these measures as well as the

Verbal IQ. Duke, et al. rejected the possibility of differential responses of the cerebral hemispheres to endarterectomy on the basis that at that time, there were no known biological differences between the hemispheres. Those authors stated "There is an absence of evidence for basic differences between the left side of the brain and the right side of the brain either in structure or neural function". Several studies (to be discussed later) have demonstrated that such asymmetries do exist in regard to morphology and perhaps neurochemistry. These recently discovered asymmetries of structure, in conjunction with the evidence for functional asymmetry, argue in favor of basic hemispheric differences. The data of Duke et al. which supports the data from the present investigation may constitute further evidence of hemispheric asymmetries in regard to recovery of function following cerebrovascular damage.

The comparability of the patient group in the Reitan and Fitzhugh study to the current subjects is unknown since little information about the former group was provided. Furthermore, those authors acknowledged the possibility of differences between the lateralized lesion groups in the type or location of vascular lesions. These sources of variability do not appear to have been a problem in the present study. In regard to the type of vascular lesion, all but one of the endarterectomy subjects were judged to have suffered an ischemic infarction with atherosclerotic carotid artery disease as the likely etiological factor. A precise localization was virtually impossible, but all subjects were judged to have vascular disturbances in the internal-carotid-middle cerebral artery distribution. Further, there were no apparent differences in the presence of other complicating medical conditions such as diabetes,

hypertension or heart disease. Even though the subject population in the current investigation may not be completely comparable with that of Reitan and Fitzhugh, the present findings would seem to support and extend the conclusions of the latter investigators. That is, right operated patients had a tendency to present with completed stroke, and furthermore improved on a greater number of measures than the left operated subjects.

These differential changes in the right and left operated stroke patients may be a further reflection of hemispheric differences in the response to cerebrovascular lesions. As has been pointed out by Baker and Meier (1970) in regard to behavioral changes in cerebrovascular disease "Resulting transient or permanent behavioral changes then depend upon the configuration of interacting pathophysiological events which produce reversible ischemia or irreversible infarction," and "There does not appear to be a a simple linear relation between changes in the vessels and behavioral or neurological changes."

The endarterectomized groups were found to not differ on several indices of potential "interacting pathophysiological events" such as occurrence of complicating medical conditions, family history of disease, or duration of symptoms. If the present findings and reports of previous authors are in fact indicative of some basic hemispheric difference in the response to cerebrovascular disturbances, or to cerebral lesions in general, then there must be some neuropsychological or neuroanatomical basis for these differences.

Indeed, recent investigations have postulated the existence of just such differences. LeMay and Culebras (1972) reported that anatomic

differences between the cerebral hemispheres could be detected through arteriography. Geschwind and Levitsky (1968) were the first authors to demonstrate a larger planum temporale in the left hemisphere of most adult brains. This asymmetry has been confirmed by others in children as well as adults (Wada, 1969; Wittleson and Pallie, 1973; Wada, Clarke and Hamm, 1975). Unfortunately, these data were based on brains obtained at autopsy, but the report of LeMay and Culebras constitutes the first in vivo evidence of anatomic hemispheric asymmetries. These authors argued that a larger parietal operculum in the left hemisphere produced a different arterial pattern on arteriography than is normally observed in the right hemisphere. Specifically they reported that the arches formed by branches of the middle cerebral arteries as they left the sylvian fissures were narrower in the left hemisphere arteriograms in 86% of their right-handed patients. The characterization of these differences in the arterial patterns was entirely subjective, and no statistical analysis was reported. The consistency of the findings however, lends some support to the validity of these results. LeMay and Culebras concluded that in view of the different arterial patterns, arteriography might offer a method of investigating anatomic hemispheric differences.

These results may also be viewed from the perspective of the current investigation. Specifically, these hemispheric asymmetries in the arterial pattern or degree of angulation may have direct or indirect influence in the etiology of cerebrovascular symptoms. The different arterial patterns imposed by the anatomic asymmetries could lead to a greater or lesser tendency for the formation of atherosclerotic disease. It was previously noted that points of angulation are prime sites for the

formation of atherosclerotic plaques, and the vascular asymmetries described by LeMay and Culebras might produce a difference in the atherogenic potential of the cerebral hemispheres. In the present series of cases, all endarterectomy patients suffered extracranial arterial disease and intracranial stenoses were extremely uncommon. It is unlikely, therefore, that the different angles of the middle cerebral artery branches has influenced the current findings by an increased incidence of intracranial stenoses. The asymmetry of branches of the middle cerebral artery reported by LeMay and Culebras may be the first of other as yet undetected differences in the hemispheric vascular system. These hypothetical differences would also be imposed by the anatomic differences in the planum temporale. Regardless, however, of whether other differences are found, it is possible that different degrees of angulation of the arterial branches could affect the ultimate point of vascular occlusion and subsequent infarction. For example, emboli from a carotid plaque might lodge at different sites as a function of the degree and pattern of angulation in the arterial systems. Likewise, asymmetric arterial patterns could lead to differences in the potential efficiency of the collateral circulation.

Evidence for hemispheric asymmetry has also been provided by studies of cerebral blood flow. Several investigators have examined mean hemispheric and regional cerebral blood flow in normal volunteers and a variety of patient populations. In normal subjects, it has been shown that the mean hemispheric flow is equal in the two cerebral hemispheres (Risberg, Halsey, Wills and Wilson, 1975). Further, the typical "hyperfrontal" resting pattern has also been shown to be equal in the two

hemispheres (Larsen, Skinhoy and Lassen, 1978). Abnormal patterns of cerebral blood flow, both at rest and in response to activation have been demonstrated in patients with cerebrovascular disease (Kohlmeyer, 1975: Goldberg, Miller and McHenry, 1975).

The techniques developed to analyze the cerebral blood flow yield measurements which are purported to be indices of the relative flow in grey and white matter. Most studies of the effect of mental activation in cerebral blood flow have examined grey matter blood flow particularly since white matter blood flows have not been shown to change during mental activation (Ingvar and Risberg, 1967; Risberg and Ingvar, 1973).

Some investigators also compute a measure which is believed to represent the relative weight of perfused grey matter as a percentage of the total weight of the perfused tissue. A recent study utilizing this measure (Gur, Packer, Hungerbuhler, Reivich, Obrist, Amarnek and Sackheim, 1980) has suggested hemispheric differences in the relative amount and distribution of grey and white matter. These authors found that the ratio of grey matter to white matter was greater in the left hemisphere, primarily in the frontal and pre-central regions. A larger grey to white matter ratio in the left hemisphere has also been reported in temporal and occipital lobe measurements by Meyer, Ishihara, Deshmukh, Naritomi, Sakow, Hsu and Pollack (1978). Gur et al. suggested that from their results it could be argued that because of the relatively greater amount of grey matter in the left hemisphere, functions subserved by that hemisphere were performed via a neural organization based largely on transfer or processing within regions. On the other hand, the relatively greater white matter weight in the right hemisphere was interpreted as

suggesting that those functions were subserved by a neural organization involving a greater degree of transfer across regions.

The results of the present investigation could be partially explained by the results of Gur et al. If in fact the right hemisphere can be characterized by a neural organization that emphasizes transfer across regions, then damage of equal degree might lead to a more diffuse pattern following right hemisphere lesions. The results of Boll which showed greater ipsilateral and contralateral tactile perceptual deficits following right hemisphere lesions would seem to support this argument.

A similar pattern of neural organization founded on different patterns of motor and sensory deficits has also been proposed by Semmes (1968). The patients studied were war veterans who had sustained penetrating missile wounds of the brain. Based on patterns of motor and sensory deficits, she concluded that the representation of both ipsilateral and contralateral sensorimotor functions tended to be focal in the left hemisphere and more diffuse in the right hemisphere. The fact that the subjects in this study were relatively young and that the nature of their injuries were markedly different from cerebrovascular disease patients limits to a considerable extent the generalizability of those findings to the present data.

In addition to these studies suggesting morphological or organizational differences between the right and left cerebral hemispheres, recent investigations have produced evidence of neurochemical asymmetries. Robinson (1979) examined the effects of occlusion of the right or left middle cerebral artery in the rat. It was found that following right middle cerebral artery occlusion the animals became

hyperactive and there was a depletion of norepinephrine in several brain regions, and depletion of dopamine in the substantra nigra. Neurochemical depletions were found only in the hemisphere ipsilateral to right artery occlusion. On the other hand, left middle cerebral artery occlusions did not produce similar behavioral or neurochemical changes. The left occluded animals were not more active in comparison with their own baseline activity levels or with sham operated controls, and there was no evidence of catecholamine depletion in any brain region studied. In the right occluded animals, the depletions were observed only in those that were sacrificed at the fifth postoperative day. The hyperactivity was also transient, but was observed until the seventeenth postoperative day. Dennenberg, Garbanti, Sherman, Yutzey and Kaplan (1978) have also reported increased activity following right but not left hemispheric lesions in rats, but those investigators performed entire hemispheric ablations as opposed to the focal vascular lesions produced by Robinson. The latter author argued that the finding of generalized behavioral and biochemical disturbances only after right hemisphere lesions was indicative of some underlying anatomical or physiological asymmetry of the catecholaminergic pathways, or of a noncatecholaminergic feedback loop. Robinson argued further that the results of Oke, Keller, Mefford and Adams (1978) supported the argument for asymmetry of the catecholaminergic pathway.

Oke et al. found that the levels of norepinephrine differed between the right and left thalamus. It was reported that the left pulvinar was relatively rich in norepinephrine while the right thalamus was relatively rich in norepinephrine in the area of the ventro-posteromedial and

ventro-posterolateral nuclei. The fact that this is a somatosensory input area is particularly interesting in view of Boll's finding of greater tactile perception deficits in patients with right hemisphere lesions.

Although there has been no comparable demonstration of differential effects on neurotransmitter systems following lateralized lesions in humans, the evidence of asymmetrical pathways from Oke et al. would favor this possibility. Furthermore, the findings of Robinson, Denenberg et al. and Oke et al. would suggest a different behavioral response following lateralized cerebral lesions. The data of these investigators would therefore seem consistent with the results of Reitan and Fitzhugh, Boll and the present investigation.

The data of Boll and Reitan and Fitzhugh produced evidence of greater motor and sensory deficits following right hemisphere lesions. In light of the present data, it was particularly interesting that Robinson's data gave evidence of transient but generalized behavioral disturbances following right arterial occlusion. It is possible that the performance of the right operated group in the present study can be reviewed with respect to these previous data. Specifically it was shown that the right operated group was different from the left operated group in the improvement on those measures of bilateral or contralateral hemispheric function. There was no difference between these groups on measures of hemispheric function ipsilateral to the operation. This seems to suggest that following right hemisphere lesions, there is a transient generalized behavioral disturbance which affects the function of both cerebral hemispheres, whereas a comparable disturbance does not occur after left

hemisphere lesions. The fact that at six month follow-up the right operated group showed improvement on tests of bilateral and contralateral hemispheric function might reflect a resolution of this transient general disturbance.

CHAPTER V

SUMMARY AND CONCLUSIONS

It seems unlikely that any one factor can completely explain the present findings. The statement by Baker and Meier regarding interacting pathophysiological events underlying the expression of behavioral deficits following ischemic lesions may be expanded in view of the current data. There seems to be evidence of morphological and physiological differences between the cerebral hemispheres that in all likelihood do not exist in isolation from each other. The interaction of these factors with pathophysiological factors and other factors presently undetermined likely produced the pattern of results obtained in the current investigation.

It seemed clear that the right operated group improved on more measures than any other group, and that improvement was observed on variables that appeared to be related to the function of both cerebral hemispheres. A similar pattern was not observed with the left operated patients. This finding could suggest that the improvement of the right operated group is related to recovery from a more generalized behavioral disturbance produced by right but not left cerebrovascular lesions. The biological mechanism for this disturbance may be related to asymmetries in neurotransmitter pathways, hemispheric differences in neural organization, variations in arterial pattern or degree of angulation, or patterns of cerebral blood flow.

Carotid endarterectomy will continue to be performed primarily as a prophylactic measure, but the present findings suggest that an improvement in mental function may also be achieved. Although the right operated group demonstrated significant gains, the mean performance continued to fall in the impaired range in comparison with normal controls. This suggests that the restorative role of this surgical procedure is only partial.

The timing of the procedure during the course of hospitalization may be an important factor. The attempt to protect language function by delaying surgery in patients with left hemisphere stroke may have precluded the restorative effects for that group. This would suggest that there is some critical period during recovery from cerebrovascular symptoms during which the extent of recovery may be influenced by endarterectomy.

The present study was unable to resolve the question of whether the different responses of the right and left endarterectomy groups were related to the timing of the procedure or to basic hemispheric differences. One clearly indicated study would be to examine groups of patients who undergo endarterectomy at similar points in their hospitalization. Continued superiority in that study by the right operated patients would provide further evidence of a basic hemispheric difference in recoverability from cerebrovascular lesions.

A further study to clarify the mechanisms underlying the changes observed in the present data would be to include an examination of cerebral blood flow at the same post-operative interval as the behavioral evaluation. In particular, it would be interesting to employ this

technique in groups of patients undergoing right or left endarterectomy. This could provide further clarification of the mechanism underlying the improvements observed in the current investigation.

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