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Title: The Role of the Basal Ganglia in Cognition and Language

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Submitted for the degree of Doctor of Philosophy by Research, June, 2001.

ABSTRACT

Discrete circuitry connecting the basal ganglia and cortical areas of the brain have received increasing attention as possible mediators of neuropsychological functions. Lesions of this circuitry among 25 right-handed people with various brain injuries (closed head injuries, cerebrovascular accidents and tumors) were verified by expert scrutiny of neuro-imaging. Their performance on measures of attention, performance of complex motor programs, executive functions, memory and language skills was compared to a control group of 11 subjects with spinal injuries and 13 right-handed people with early-stage Parkinson's Disease (PD). Data were analyzed according to an adaptation of classification tree analysis. Functions associated with this circuitry among the 25 brain injured subjects were dynamic allocation of attention between competing inputs (anterior cingulate circuit), problem solving that required consideration of several novel items of information in decision making and verbal elaboration of abstract phenomena (dorsolateral prefrontal circuit). Neither problem solving alone or working memory alone were associated with this circuitry. Significant differences between the lesion-subjects' and the PD subjects' performance were found. Mental processing associated with the basal cortical circuitry was orchestration of subprocesses (at the cortical level) and their integration, (at the subcortical level) to enable their fluid and effective synchronization for the person to complete more complex tasks.

Statement of Originality

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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Tim Connell

Date: 23/3/02

Acknowledgements

The completion of this work would not have been possible without generous assistance from a large number of people. They include:

Dr. Peter Delin, Senior Lecturer, Psychology Department at the University of Adelaide and the late Dr. Jo Wale, then Senior Clinical Neuropsychologist of the Royal Adelaide Hospital. I am grateful to them for providing the academic supervision of this project and Dr. Delin in particular for helping to finally bring this project to a conclusion through his friendly persistence and advice over 12 years.

Mr. Peter Oatey, then Staff Neurosurgeon of the Royal Adelaide Hospital and Dr. Chris Rowe, then Chief of the Nuclear Medicine Department, Queen Elizabeth Hospital of S.A. These two very skillful and very busy medical specialists sponsored my recruitment of research subjects, performed the critical analysis of brain scans and helped this project with other advice and support.

Dr. Richard Clark, Senior Psychology Lecturer, Psychology Department, Flinders University of S.A. who read an earlier draft of the manuscript and gave very helpful advice.

The 56 research subjects who gave up several hours each to perform the project test battery.

Mr. Bob Wilson of the Psychology Department of the university of Adelaide gave important assistance with the data analysis involved in the project.

Ms. Heather Trenorden, Project Officer of the Parkinson's Syndrome Society of S.A. Inc. sponsored my recruitment of research subjects with early-stage Parkinson's Disease.

Ms. Julie Grayston, Psychology Assistant of the Crippled Children's Association of S.A. Inc., gave assistance with graphic designs used in figures.

Library staff of the Crippled Children's Association of S.A. Inc., who obtained many items referred to in this thesis, with consistent efficiency and enthusiasm.

SYNOPSIS

The essential goal of this project has been to clarify the role of the basal ganglia in 'higher mental processes'. Some previous work has examined the function of individual basal ganglia structures in isolation (e.g. the caudate nucleus). However, this has not resulted in conclusive definition of their neuropsychological functions. In recent years another theory of their significance has emerged. It is based on their role as links within circuits connecting cortical and subcortical areas. These circuits are the dorsolateral prefrontal circuit, the lateral orbital frontal circuit and the anterior cingulate circuit (left and right for each), and Crosson's (1992), other language related circuitry. Various cortical areas within those circuits are already known to involve higher mental processing (for example the frontal lobes). Therefore an alternative, but untried, line of investigation is analysis of the function of those circuits, as unitary entities. No comprehensive investigation of the role of these circuits has previously been attempted. It is argued that lesions at any point in these circuits would result in more or less the same neuropsychological impairment. A very large amount of research data on the neuropsychological functions of individual structures within these circuits was reviewed. It was hypothesized that the complete set of skills associated with individual elements of a circuit corresponds to the functions of that circuit. In this way a separate list of possible functions was derived for each circuit. These hypothetical circuit functions were investigated with an analysis involving several phases.

A control group of 11 subjects with spinal injuries was given the test battery. This was to establish levels of test performance that could be expected among subjects who had comparable social and psychological disadvantage without brain injuries. The test battery covered a wide range of visual, motor, attention, memory and language skills. Another group of subjects included 25, right handed, people with various brain injuries (closed head injury, cerebrovascular accident and tumors). These were verified by expert scrutiny of neuroimaging to have involvement of any one of the six basal cortical circuits. The data gathered were complex, and addressing issues in relation to that data required a special, and elaborate, analysis in its own right before the analysis for remaining phases (2 to 6) could

proceed with confidence. This was the focus of the first phase (Phase 1), which actually dealt with two distinct data-related issues. In conclusion, the spinal injury, control group data was reasonably representative of the general population. The general accuracy, within limits, of the neuroimaging (CT & MRI) used to locate brain lesions was verified also.

The objective of Phases 2 to 4 was identification of tests, out of the pool identified from the literature (the test battery), which were sensitive to circuit lesions. A further part of this objective was checking for evidence of links between each of the so-identified tests and individual circuits. Such evidence would suggest possible differentiation of roles between the circuits. The numbers of subjects available with suitable lesions was inevitably small and rather heterogeneous, and consequently the commonly-used multivariate type of data analysis was not viable.

An adaptation of Godefroy et al.'s (1998) classification tree analysis was devised. All brain injured subjects were grouped according to circuits affected. Ten testing tasks were identified where a majority of one of these lesion groups showed a deficit and a majority of brain injured subjects outside the group did not. For each of these ten tasks in turn, lesion profiles of all brain injured subjects with a deficit on this measure were compared to lesion profiles of those without the deficit. This was to establish, for each task in turn, which of Godefroy et al.'s (1998) four modes of brain –behaviour relationships was most consistent with the data.

This resulted in nine out of the 31 testing tasks in the project battery being linked to five out of the seven circuits. Those nine test-tasks fell into three categories, firstly, conscious attention and performance of complex programs of motor activity, secondly, language functions and lastly executive functions. This provided the basis for further qualitative analysis. Tests in these categories (associated with lesions) were compared to other tests in these categories from the project battery, that were not associated with lesions. This resulted in a more precise qualitative definition of those aspects of testing tasks associated with the basal-cortical circuitry. This same qualitative analysis, combined with reference to other

published research findings, provided the basis for conclusions about the roles of individual circuits.

It is proposed that dynamic allocation of attention between competing inputs is associated with the anterior cingulate circuit, and that this is the main circuit affected in early-stage Parkinson's Disease. It is proposed that two other, related functions are linked to the dorsolateral prefrontal circuit. The first of these is the ability to manipulate several items of information at once to complete a task, when those items are novel, available to awareness from working memory only and not represented in concrete form (a critical element of executive functioning). The second of these is verbal expression of an abstract idea.

There is a common element to the analysis of mental processing involved in the three types of processing associated with lesions of the basal-cortical circuitry. This is the integration of several sub-processes to enable their fluid and effective synchronization, necessary for the person to perform more complex tasks. It is further proposed that there is a two-part differentiation within this area of cognition. The first element in this differentiation is the **orchestration** of sub-processes to complete a more complex mental processing event. This would correspond to a more complex type of processing linked to the frontal lobes under the heading of 'executive functions' by past research, although identification of the brain areas involved in executive functions is not yet conclusive. For example, the limitations on the evidence for this widely accepted proposition have been highlighted by some careful reviewers of the literature (e.g., Tranel, Anderson & Benton, 1994). The second of these two elements is the **integration** of outputs from these subprocesses. This includes the transmission of the orchestration to various subsystems, and feedback from its implementation, back to the 'conduction centre'. It is proposed that the second process (integration) is primarily mediated by subcortical sections of the basal-cortical circuitry.

Neural circuits have been characterized as a balance of excitation and inhibition. It has been argued (e.g., by Kapur, 1996) that lesions at different points within a circuit could result in different forms of imbalance, hence different forms of cognitive impairment. (See Section "2.3 Circuitry of the Basal Ganglia.") However, this concept has not been widely employed

in modeling of cognitive functions. Impaired performance of certain tests was linked to lesions of particular structures, within certain basal cortical circuits. This provided the basis for speculation about parallels between the inhibitory or excitatory functions of those structures and the subjective experience of performing those tests. The type of research methodology which might enable us to test such speculation is probably a refinement of the PET methodology.

Much more probably needs to be learnt about mental processing (including cognition and language) and neurophysiology before there can be a conclusive convergence of these two areas of knowledge. Clear shortcomings in our research methodology must be recognized. These involve psychometric instruments (imperfect reliability and diverse cognitive processing demands within individual tests), and inaccuracies of neuroimaging. Then there is our current conceptualization of mental processing; design of our present crop of psychometric instruments has been based on this. However, correspondence between contemporary theories of mental processing and brain activity is weak at best. The former is purely a manifestation of the latter after all. Thus this conceptualization must contain some errors and distortions. It is probably these combined limitations which prevent us achieving a more detailed knowledge of the functions of these circuits at the present time.

1. INTRODUCTION

1.1. The Research Question

"For both theoretical and practical reasons, our goal must be to identify fundamental cognitive systems, isolate and characterize their component mental operations and, finally, to link these components to the neural mechanisms which mediate them. ...[then] once clinicians understand an impairment in terms of the elementary operations involved, it may be possible to predict strategies which might usefully aid patients in understanding, adapting to, or overcoming their deficits." (Posner & Rafal, 1987, p 186-187). When they wrote these words, Posner and Rafal were explaining the purpose behind their work with attention deficits. It also describes, very well, the goal of this project.

Traditionally the basal ganglia were regarded as primarily motor structures (Schultz, Apicella, Romo & Scarnati, 1995). Lesions of their component structures have been associated with prominent motor deficits (Bhatia & Marsden, 1994), and the basal ganglia have an extensive output to the primary motor cortex and superior colliculus. However, 'despite our growing knowledge of the anatomical and physiological organization of the basal ganglia, the function of these structures remains an enigma.' (Jackson & Houghton, 1995, p 337) It has been shown that a major part of basal ganglia output is directed toward most parts of the frontal lobe. (Schell & Strick, 1984 and Ilinsky, Jouandet & Goldman-Rakic, 1985) This places the basal ganglia in direct functional association with a large area well known to serve higher cognitive processes.

The search for links between individual components of the basal ganglia and particular neuropsychological functions has not been very fruitful (Afifi, 1994a, see Anatomy of the Basal Ganglia, Literature Review). The concept of neuropsychological functions being dependent on circuits that link together specific combinations of cortical and subcortical structures (including the basal ganglia) provides a new basis for interpreting research findings (Cummings, 1998). 'Any theory of basal ganglia function will ultimately have to attend to the role played by the corticothalamic projections.' (Goldman-Rakic, 1995, p. 142)

These connections could explain the similarity between cognitive impairments associated with the basal ganglia and with the frontal lobes. Alexander, DeLong and Strick's (1986) analysis of the pattern of neural fibers connecting several distinct combinations of structures led to wide acceptance by researchers that the integrity of this complete subset of interconnected structures was important to specific types of cognition.
This also suggests those circuits play a very important neuropsychological role. In the most comprehensive, recent review of frontal lobe research (Stuss, Eskes & Foster, 1994), the authors commented, 'to date, however, the functional significance of (basal cortical) circuits such as those proposed by Alexander et al. (1986) has not been fully delineated, and the relationship between the clinical symptoms and syndromes and various anatomical networks has not yet been established' (p 153). Another important commentator on the role of this circuitry (Cummings, 1998) wrote, 'The frontal subcortical circuit model has been extended to include aspects of schizophrenia and substance abuse as well neurobehavioural syndromes. No evidence disconfirming the frontal subcortical hypothesis has evolved although several issues remain to be settled... ..More studies on this issue are required.' (p 628). Clearly this concept needs to be tested. This project represents the most direct test so far.

The recognition that a set of connected brain structures (e.g., the basal cortical circuits), functioning in concert could be as important (if not more so) to specific mental activities as the component structures individually is not new. This idea is usually traced back to Hebb (1949), who described the concept of 'cell assemblies'. It is essentially what Alexsandr Luria (1973) was referring to with his concept of 'functional systems'. A more recent development of this idea involves cognitive processing units that directly reflect a corresponding neuroanatomical processing unit, or module (Bradshaw & Mattingley, 1995). Previously it was believed that functional systems including the basal ganglia were largely involved with motor functions only. Now there is some acceptance that the function of systems/circuits that include them may extend to mental activities of a 'higher' cognitive nature. Alexander et al.'s (1986) detailed elucidation of the neurological circuitry has led to considerable effort being spent trying to identify them. There have been three main approaches to this task.

1.1.1. Re-Analysis of Literature

One approach is more to do with re-examining published studies than with research in the usual sense. Typically this involves comparing established neuropsychological profiles of conditions known to affect different parts of the same circuitry. Cognitive impairments common to the different conditions arguably reflect disruption of the common circuitry, hence of the functions of that circuitry. Again this approach has not been fully explored. Crosson's (1992) contribution is probably the most significant one so far. He has clarified some parts of the picture, particularly as regards language and memory. Others have also contributed, (e.g., Penney & Young, 1983, 1986; Ballard, Hayhoe & Petz 1995).

However, while this process is important, at best the end result is only the formulation of hypotheses. These conclusions need to be tested through data gathering and analysis, subsequently replicated, before they can be considered facts (if that isn't too strong a word in this context). Given the subtle nature of some of the skills involved, hypothesis formulation should ideally proceed on the basis of the most comprehensive literature review. A very serious attempt has been made to perform such a review here, and to use it as the starting point for this project. Certainly, no more comprehensive reviews of this literature have appeared. A comprehensive set of possible functions (see section 4.1.6.) has now been identified for testing, and further tentative conclusions drawn about some more subtle underlying commonalities across various subgroupings of those functions.

1.1.2. Positron Emission Tomography (PET) Studies

A further approach has involved positron emission tomography (PET). Radionuclides introduced (e.g., by injection) into the bloodstream are then distributed through the brain (as they are through other bodily systems) by cerebral blood flow and oxygen and glucose metabolism. Such distribution in the brain is in direct proportion to the level of neuronal activity. The dynamic distribution of these radionuclides is displayed as an image by the PET device (Metter, 1987). Continuous improvement in the resolution of images produced by this technology has been achieved since it first appeared in the 1970s. Substantial investigation of brain function and attention, memory, language and motor function, has

been performed with PET (see respective sections of literature review). Some studies have shown coincident activation of the basal ganglia and cortical areas during test performance (e.g., attentional tasks, Posner & Dehaene, 1994). An important development of this technique is the 'subtractive or control paradigm'. This technique, pioneered by Petersen, Fox, Posner, Mintum and Raichle (1989) involves a series of tasks, each task in the series having a no more than one, very clear and well defined additional requirement, compared to the one before it. PET is performed for each task in the series and subtraction of the PET image for each task from the one for the task before it permits visualization of those areas that are uniquely active in the processing of the additional requirement alone. Examples of the application of this methodology to the study of memory have been described by Shallice, Fletcher and Dolman (1998).

However, the capacity for this technology to resolve questions about the role of the basal ganglia is limited. Coincident activation does not necessarily mean the different areas were functioning as a unitary system of interlinked structures, whose collective integrity is critical to performance of cognitive tasks. Petersen and Fiez (1993) have pointed out that a functional area is not necessarily a task mediating area. Factors intrinsic to the design of experimental tasks, such as practice, rate of stimulus presentation, task difficulty and attentional demands may all affect the distribution of activated regions.

Furthermore the high hopes held for this technology have been dampened by certain shortcomings. Crosson's (1992) comprehensive review of the literature on language and the basal ganglia identified discrepancies between results of PET studies. Some studies have revealed ambiguity in patterns of PET results during cognitive task performance (e.g., Haxby et al. (1986). Lack of anatomic landmarks (Damasio, 1991) and difficulty defining and establishing a 'resting state' for subjects being scanned (Lenzi & Padovani, 1994) are other unresolved issues in relation to this methodology. To this author's knowledge, no specialist has yet been able to reconcile consistent co-occurrence of deficits on task A and brain lesion B on the one hand, with the nonactivation of the lesion B area among intact subjects while performing task A during PET studies. Pulvermuller (1996) noted the difficulty reconciling two observations, language loss after focal lesion of a narrowly

defined region surrounding the left sylvian fissure (Wernicke's area) and widespread cortical activation (revealed by PET) during various language tasks. Another example, involving the very well studied verbal fluency task ('FAS'), is the discrepancy between Schlosser and Hutchinson's (1998) functional MRI findings of intact subjects, and Pendelton, Heaton, Lehman and Hulihan's (1982) findings with brain injured subjects. By itself this discrepancy suggests that conclusions of brain areas and task mediation should not be made on the basis of PET findings alone. There still seems to be an important place for methodologies other than PET (e.g., lesion studies). Further extensive discussion of the limitations of PET is provided by Lenzi and Padovani (1994).

1.1.3. Comparing Test Performance of Lesion Groups

A third approach has been to gather one group of subjects with basal lesions/pathology, and another with frontal lesions/pathology, and then compare their neuropsychological test performance. The degree of similarity between deficits presumably reflects the strength of their 'functional connectedness.' Groups compared in this way have included, for example, Parkinson's Disease (PD) groups and frontal cerebrovascular accident (CVA) groups (Owen, Downes, Sahakian, Polkey & Robbins, 1990; Owen, Doyon, Dagher, Sadikot & Evans, 1993; Wallesch, Karnath & Zimmerman, 1992). Another study compared basal ganglia CVAs with frontal CVAs (Eslinger & Grattan, 1993). Some general conclusions can be drawn. While some of the test tasks revealing impairment were the same for both the basal and frontal groups, the frontal subjects were more severely affected. One shortcoming of all those studies is that both the 'frontal lobes' and 'basal ganglia' were treated as unitary entities (albeit connected). First of all, they are clearly not 'unitary entities'; both involve a diverse set of component structures or subsections (see 'The Anatomy of the Basal Ganglia', and 'The Frontal Lobes' in the Literature Review). Not only that but, according to Alexander et al.'s (1986) widely accepted description of the circuitry, each circuit involves specific subsections of the frontal lobes and specific subsections of the basal ganglia only (see Figure 2). The affected basal cortical circuits of two subjects, one with a lesion in an unspecified section of the frontal lobes and another with an unspecified lesion in the basal

ganglia, need not be the same at all. This possibility may have accentuated the performance differences found between groups (i.e. basal ganglia group/frontal group comparisons).

In addition, the number of skills tested in comparing groups in this way has been small. Assessment tasks have been limited to a few traditional 'frontal lobe type' visual tasks. The Wisconsin Card Sorting Test (WCST, Owen, Roberts, Hodges, Summers, Polkey & Robbins, 1993; Eslinger & Grattan, 1993) and a computerized maze task (Wallesch, Karnath & Zimmerman, 1992). Clearly a much larger number of skills could be involved (see section 4.1.6.). The full potential of this approach has not been realized. From the data available so far, the idea that neuropsychological functions could depend on the integrity of the basal cortical circuits as much as on individual components seems plausible. A comparison of homogeneous lesion groups, where the lesions defining each group (while different) are part of the same basal cortical circuit, is probably the best test of this idea. The groups should perform equally poorly on tests of neuropsychological functions served by the circuit.

A major practical obstacle to doing this kind of research is the low incidence of the very specific kinds of brain injury that would be needed for such a study. This had in fact been this researcher's original goal. All hospital-based Neurosurgery and Neurology Departments in SA (Royal Adelaide Hospital, Queen Elizabeth Hospital, Flinders Medical Centre, Repatriation General Hospital) and various rehabilitation units (Julia Farr Centre and the Crippled Children's Association) were approached in an effort to recruit subjects between 1/2/89 and 28/7/95. This resulted in recruitment of 25 subjects with various lesions to the basal ganglia, adjacent subcortical areas, frontal lobes and some additional cortical areas (in addition to the subjects with Parkinson's Disease and controls with Spinal Injury). Any more extensive search for subjects (e.g., interstate or over a longer time period) was beyond this researcher's resources. The fact that no study like that has been published suggests that even researchers with considerably greater resources have found the task equally difficult.

An important general review of the literature by Bradshaw and Mattingley (1995) concluded that 'it is unclear whether lesions anywhere within this circuit(ry) produce exactly the same

behavioural deficits, or whether, as is perhaps more probable, there are subtle differences reflecting local information processing.' (p 284-5) The best test of the concept possible with these data involved grouping all subjects with lesions in a particular circuit (regardless of both which part of the circuit was involved and the presence of additional lesions) for comparison with controls. If these circuits have real neuropsychological significance then there must be substantial similarity of impairments among subjects with lesions anywhere along them. (Also any impairments apparently associated with a particular circuit must not be able to be explained by other common characteristics of those subjects, e.g., lesions elsewhere, diffuse effects.) No study involving this design has been published, let alone one attempting to examine a comprehensive set of skills all derived from a very extensive literature review. The current project considers a much more extensive set of skills than any previous one. Finally, results of the analysis allow some comment on recent models of information processing and in relation to the basal ganglia, and point the way for further model development.

2. LITERATURE REVIEW

2.1. Structure of Literature Review

The literature review begins with a detailed account of relevant neuroanatomy, as this determines the basic character of an associated neuropsychological system. Basal cortical circuitry being central to this project, it is described in some detail. Then the more complex elements within that circuitry (e.g., frontal lobes and thalamus) are also described. This forms the prelude for the main part of the literature review, cognitive deficits associated with lesions of the basal ganglia and associated circuitry.

Previous researchers have linked various functions to individual components of the basal cortical circuits. Indeed, some of these components would be among the most extensively investigated parts of the human brain, e.g., the prefrontal lobes. However because of the, now widely recognized, neurological circuitry connecting sets of basal ganglia and cortical areas, it is arguable that functions previously linked to components of these circuits may in fact depend on the complete set of circuit components, acting as an interlinked system.

Therefore the complete set of all functions linked to any component of a circuit may in fact represent the set of functions served by that circuit. In this project, lists of possible functions of four key basal cortical circuits have been derived based on this reasoning. Three of those circuits (hereafter referred at as the dorsolateral prefrontal, lateral orbital frontal and anterior cingulate,) were among those identified by Alexander et al. (1986) in an article which has probably been more influential than any other in recent times about the basal ganglia. Another one which is also being investigated in this project is the other language-related circuitry defined by Crosson (1992).

This body of relevant literature is considerable. Sets of possible functions are examined for each circuit in turn. Functions associated with the cortical level of the circuit are examined first, followed by those associated at the level of the striatum, then the pallidum and the substantia nigra, concluding with the thalamus. At each level, to facilitate interpretation, functions are categorized according to traditional categories of cognition (e.g., memory and attention). This review provides the basis for conclusions about the role of each circuit. Models of information processing associated with these conclusions are then described, as they provide a basis for new, more integrated models of how each circuit plays its role in human cognition.

All this leads up to formulation of the three objectives of this project, which are presented at the conclusion of the literature review.

2.2. The Anatomy of the Basal Ganglia

How actions are planned and information processed by a neural system depends on what apparatus is available for these tasks. Furthermore, neuronal transmission of information occurs in only one direction along axons, and so the direction of information flow between structures limits the pattern of influence within the system (Crosson, 1992). Thus, it is important to start with a clear concept of the neuroanatomy involved. In fact, the much more detailed neuroanatomical and neurophysiological data that have become available over the past decade have had a profound influence on the development of information processing models (e.g., Houk, Davis & Beiser, 1995).

"The basal ganglia, a group of subcortical nuclei derived largely from the telencephalon, are among the most complex and least understood structures in the brain." (Afifi, 1994a, p. 249). Afifi has provided an extensive description of the main recent advances in our knowledge of their physiology (1994a, 1994b). "Early anatomists used the term "basal ganglia" to refer to all nuclear masses in the interior of the brain. Currently the term is used to refer to the following nuclei: caudate, putamen, globus pallidus, nucleus accumbens septi, and olfactory tubercle (Table 1)." (1994a, p. 249). There is also evidence of some differentiation of function among those nuclei. For a detailed analysis of studies reporting those data, see Rolls and Johnstone (1992), Bhatia and Marsden (1994), Kimura, Aosaki and Ishida (1993).

Table 1. Basal Ganglia Nomenclature

	Corpus Striatum	Striatum, Dorsal Striatum, neostriatum	Ventral Striatum	Pallidum, Paleostriatum	Lentiform Nucleus
Caudate Nucleus	+	+	-	-	-
Putamen	+	+	-	-	+
Globus Pallidus	+	-	-	+	+
Nucleus Accumbens	-	-	+	-	-
Olfactory tubercle	-	-	+	-	-

(From Afifi, 1994a, p 250)

2.3. Circuitry of the Basal Ganglia

In recent years substantial effort has gone into understanding the circuitry interconnecting basal ganglia structures and attempting to draw parallels between the neurocircuitry and models of information processing. The latest fruit of these endeavours is well summarized by Houk, Davis and Beiser (1995). Roughly three levels of circuitry have been proposed. The first relates to the overall circuitry between basal ganglia and cortical structures (Graybiel 1991). See Figure 1.

The projection of the whole cortex to the striatum, and at the striatum in turn to the smaller still pallidum, has led some writers (e.g., Percheron & Filion, 1990; Gerfen, 1992) to argue that the basal ganglia process information in a *serial* fashion like the cortex-striatum-thalamus-cortex, and that this results in a massive convergence of information at the site of the basal ganglia (Graybiel, 1991). However, this view has its critics. Alexander and colleagues (Alexander, DeLong & Strick, 1986; Alexander, Crutcher & DeLong, 1990; Alexander & Crutcher, 1990) have argued that the primary form of neural processing within the basal ganglia occurs within five identifiable, smaller *parallel* circuits. They have been named the motor circuit, the oculomotor circuit, dorsolateral prefrontal circuit, lateral orbitofrontal circuit and the anterior cingulate circuit (see Figure 2, also Cummings, 1993). This concept has been widely accepted and hailed as a major breakthrough in our understanding of the basal ganglia (Goldman-Rakic & Selemon, 1990). It is difficult to overestimate the influence of this over the development of theory and research about the basal ganglia (Houk, 1995; Cummings, 1998). Other authors have substantially elaborated on this concept to explain various phenomena observed in the presence of basal ganglia disease (e.g., Parkinson's Disease (PD), Saint,-Cyr, Taylor & Nicholson, 1995). The debate is not concluded yet, however. Joel and Weiner (1994) have proposed a qualification to the parallel view; that the various circuits are in fact "interconnected".

The circuits proposed by Alexander et al. (1986) follow a common general pattern. Each circuit receives output from several functionally related cortical areas that send partially overlapping projections to a restricted portion of the striatum. These striatal regions send further converging projections to the globus pallidus and substantia nigra, which in turn project to a specific region of the thalamus. Each thalamic region projects back to one of the cortical areas that feeds into the circuit, thereby completing the "closed loop" portion of the circuit.

The dorsolateral prefrontal cortex is the defining, cortical region of one circuit. Together with the arcuate motor area and the posterior parietal cortex, it projects to the dorsolateral head of the caudate nucleus. This structure then projects on to the lateral dorsomedial globus

pallidus and the rostrolateral substantia nigra, which in turn project to two specific regions of the thalamus (ventralis anterior pars parvocellularis). Finally these regions of the thalamus send projections to the dorsolateral prefrontal cortex. This constitutes the dorsolateral prefrontal circuit.

The second of Alexander et al's. (1986) three circuits is defined by the cortical section, namely the lateral orbitofrontal cortex. Together with the superior temporal gyrus, the inferior temporal gyrus and the anterior cingulate area, this cortical area projects to the ventromedial head of the caudate nucleus. From this structure, projections proceed to the medial dorsomedial globus pallidus and the rostromedial substantial nigra. Projections from this level of the circuit are to two separate regions of the thalamus (the medial ventralis anterior pars magnocellularis and the medialis dorsalis pars magnocellularis), which in turn project back to the lateral orbitofrontal cortex.

Then there is the third of Alexander et al's circuits of interest to this study. The anterior cingulate cortex is the defining cortical area, and together with the hippocampal cortex, the entorhinal cortex, the superior and inferior temporal gyri, it projects to the ventral striatum. From there projections are directed at the rostrolateral globus pallidus, ventral pallidum and the rostrodorsal substantia nigra. These structures project to the posteriormedial, medialis dorsalis section of the thalamus. Finally, this area projects back to the anterior cingualte cortex. The above three circuits are described diagrammatically in Figure 2.

The circuit concept has major implications for the interpretation of neuropsychological findings. From a review of the literature, Cummings (1993) argued that a particular circuit was involved in mediating a specific behaviour when three criteria were satisfied. These were (1) lesions in several circuit related structures produce a similiar behavioural disorder, (2) the behavioural syndrome is not commonly seen with lesions in other brain regions, and (3) simultaneous lesions in several circuit structures produce analogous rather than additive deficits. He argued that behavioural changes associated with subcortical lesions resembled those occurring with frontal lobe dysfunction because these anatomic structures are linked in discrete, parallel frontal-subcortical circuits. A further feature of these changes were specific

behavioural markers for particular circuits, including, (1) executive dysfunction and motor programming deficits for the dorsolateral prefrontal circuit, (2) irritability and disinhibition for the orbitofrontal circuit, and (3) apathy for the anterior cingulate circuit.

Cummings pointed out that syndromes with mixed behavioural manifestations due to involvement of several circuits are frequent with subcortical lesions and degenerative processes. While the precise anatomic correlates of mood disturbances and Obsessive Compulsive Disorder (OCD) require further study, the dorsolateral prefrontal or orbital frontal subcortical circuits are possibly involved in mediation of depression. Orbital frontal or anterior cingulate circuits were, Cummings argued, implicated in the mediation of OCD. Classic movement disorders (parkinsonism, chorea) were markers for involvement of the frontal subcortical circuits at the level of the basal ganglia. Furthermore, dysfunction of a circuit structure may produce symptoms by altering its effects on distant structures within the circuit. Disinhibition of the subthalamic nucleus by caudate dysfunction produces chorea (DeLong, 1990), and disinhibition of thalamocortical connections may be the common physiologic abnormality in both idiopathic OCD and OCD associated with caudate and globus pallidus lesions. As a further qualification, Cummings pointed out that circuit structures may have connections with noncircuit anatomic regions and may participate in non circuit related behavioural syndromes. For example amnesia is associated with thalamic lesions, and delusions occur with caudate dysfunction but these conditions are not seen with other frontal-subcortical circuit lesions. He concluded by calling for the testing of these hypotheses by experiment and observations.

However, the roles of these circuits in cognition are far from settled. A noteworthy elaboration on the contribution of this circuitry to language functioning has been contributed by Crosson (1992). The contribution of Broca's (sometimes referred to as the "anterior language area") and Wernicke's areas (sometimes referred to as the "posterior language area") to language functioning is well known. A comprehensive theory of neural substrates of language would be incomplete without some reference to these structures. The roles of these areas in verbal functioning are probably the earliest, and most enduring discoveries of modern research into brain-behaviour relationships.

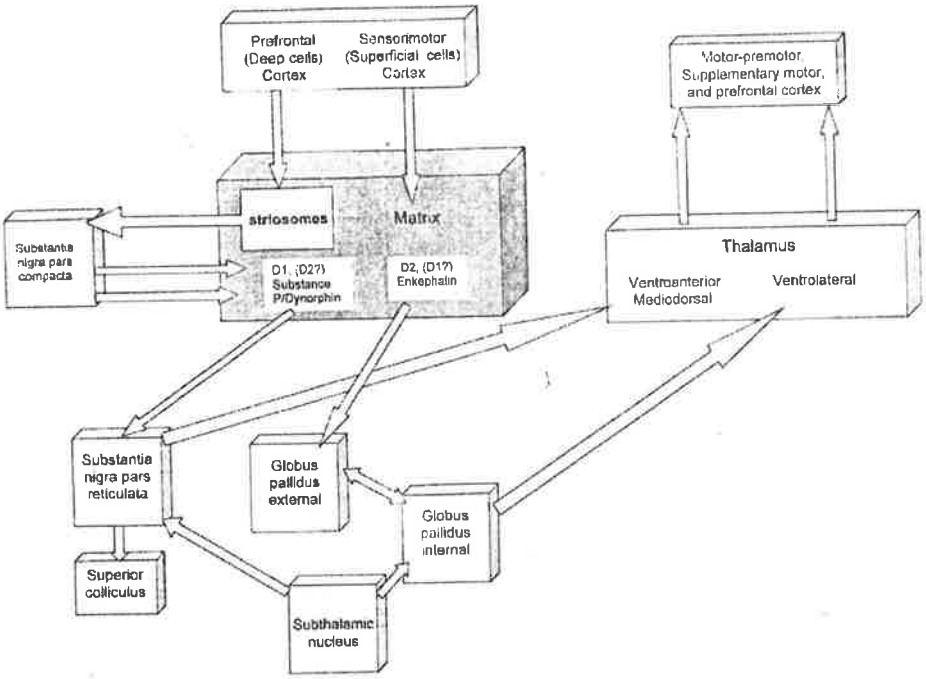

Figure 1
General Basal-Cortical Circuitry

A diagram of the principal pathways interconnecting the cortex and the basal ganglia. The cortex projects massively to the striatum (shaded box). Different cortical areas (and deep versus superficial layers) project differentially to the striosomes (S) and the matrix (M). Different areas of cortex also project primarily to the caudate nucleus and the putamen (not separately illustrated). The major outputs of the striatum lead to the substantia nigra pars compacta (SNpc), substantia nigra pars reticulata (SNpr), and to the globus pallidus external (GPe) and internal (GPi) segments. Dopamine (D1) receptors, and the neuropeptides substance P and dynorphin, have been associated with the paths to the SNpr and GPi. Dopamine D2 receptors, and the neuropeptide enkephalin, are associated with the path the GPe. Striosomes project to the SNpc; some cells in striosomes may project to the SNpr and/or the globus pallidus (not shown). The subthalamic nucleus (Sth.N) receives the main outputs of the GPe and modulates firing in the SNpr, GPe and GPi. A smaller subthalamic path to the SNpc also exists (not shown). Pathways leaving the basal ganglia arise mainly in the GPi and the SNpr and lead to the thalamus and lower brain stem. The ventrolateral (VL), ventroanterior (VA) and medialdorsal (MD) thalamic nuclei project to different parts of the frontal cortex. A large projection from the GPi to the centromedian is not shown. Of the paths to the lower brain stem only the one from the SNpr to the superior colliculus (SC) is shown. (Figure and Explanation adapted from Graybiel, 1991, p 645).

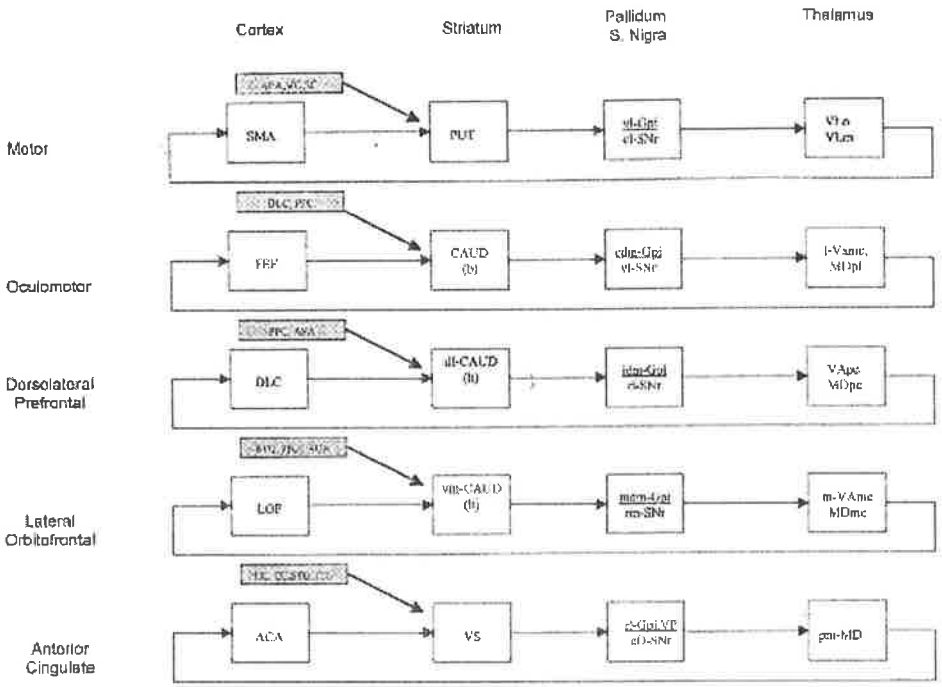

Figure 2
Proposed Basal Ganglia-Thalamocortical Circuits.
Parallel organization of the five basal ganglia-thalamocortical circuits. Each circuit engages specific regions of the cerebral cortex, striatum, pallidum, substantia nigra, and thalamus. Abreviations are as follows: ACA: anterior cingulate area; APA: arcuate premotor area; CAUD: caudate, (b) body (h) head; DLC: dorsolateral prefrontal cortex; EC: entorhinal cortex; FEF: frontal eye fields; Gpi: internal segment of globus pallidus; HC: hippocampal cortex; ITG: inferior temporal gyrus; LOF: lateral orbito frontal cortex; MC: motor cortex; MDpl: medialis dorsalis pars paralamellaris; MDmc: medialis dorsalis pars magnocellularis MDpc: medialis dorsalis pars parvocellularis; PPC: posterior parietal cortex; PUT: putamen; SC: somatosensory cortex; SMA: supplementary motor area; SNr: substantia nigra pars reticulata; STG: superior temporal gyrus; VAmc: ventralis anterior pars magnocellularis; Vapc: ventralis anterior pars parvocellularis; VLm: ventralis lateralis pars medialis; Vlo: ventralis lateralis pars oralis; VP: ventral pallidum; VS: ventral striatum; c/-: caudolateral; cdm-: caudal dorsomedial; dl-dorsolateral; l-: lateral; ldm-: lateral dorsomedial; m-: medial; mdm-: medial dorsomedial; pm: posteromedial; rd-: rostrodorsal; rl-: rostrolateral; rm-: rostromedial; vm-: ventromedial; vl-: ventrolateral. (Figure and explanation adapted from Alexander, DeLong & Strick 1986, p 364)

Wallesch and Papagno's (1988) model involves all three cortical areas in an elaboration of the cortical-striatal-pallidal-thalamic loop described by Alexander et al. (1986). Essentially this postulates that Broca's and Wernicke's areas (which themselves have considerable exchange of input in the course of verbal processing) also have input to the striatum, along with the anterior cingulate cortex. Crosson has argued that this more extensive set of circuitry is involved in regulating the release of language segments that are formulated in the cortex. He further argues t the thalamus is involved in tonic arousal of the anterior language cortex, and the cortico-thalamo

cortical pathways transfer information from anterior to posterior language cortex and vice versa (Crosson & Early, 1990).

Another important addition to theories about these circuits comes from Baxter (1992). He has argued, on the basis of an extensive review of neuroimaging studies, that Obsessive Compulsive Disorder involves a disruption to the balance of excitatory and inhibitory connections making up the loop of orbital prefrontal cortex, caudate nucleus, globus pallidus, thalamus, and back to the orbital prefrontal cortex.

This points to another critical feature of neural circuits which needs addressing as we try to tease out exactly how they are involved in mental processing. The interplay of neural structures, (manifested as mental processing) is sometimes described as a balance of inhibitory/excitatory outputs across varying combinations of those structures (Kapur, 1996). The broad balance of inhibitory/excitatory inputs is described in a diagram (Figure 3) from Houk (1995).

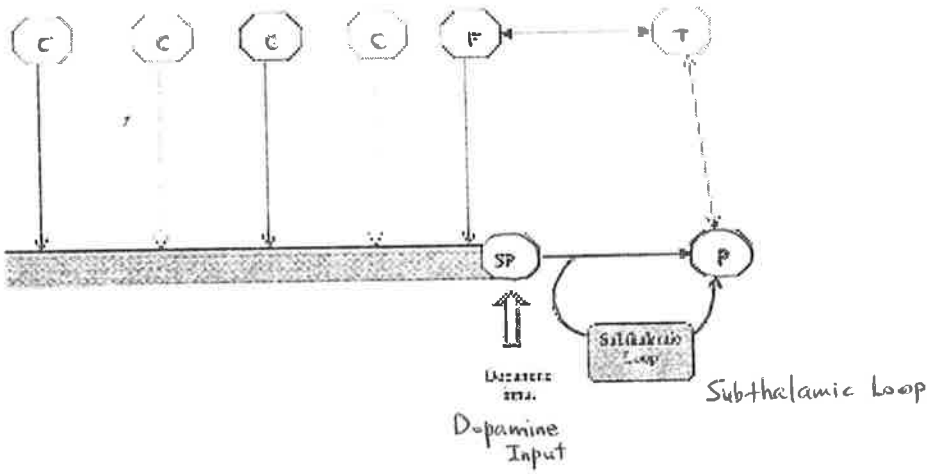

Figure 3
Schematic Diagram of a Cortical-Basal Ganglionic Module.
Thin arrowheads signify net excitation; the solid black arrowheads in the direct SP to P projection and in the P to T projection signify net inhibition; the triangular arrowhead for the dopamine input signifies neuromodulation. C, cerebral cortical neuron; F, neuron in frontal context; SP, spiny neuron of the striatum; P, pallidal neuron; T, thalamic neuron. (Houk, 1995, p. 5)

This has important implications for our understanding of circuit/mental processing relationships. For example, Figure 4 shows a hypothetical area (*L)* in the ventral anterior thalamus related to language, and inhibitory fibres traversing other portions of the ventral anterior thalamus to reach *L*. Lesion *X* within the ventral anterior thalamus would interrupt the inhibitory input to *L*, decrease the inhibitory input to *L* at times when the input to *L* from the pallidum would normally be active and lead to increased output to *L* at these times. On the other hand a lesion *Y* within *L* itself would interrupt the source of output from L, thereby reducing output at times when L would normally be active (Crosson, 1992). It has even been proposed that alterations in the balance of inhibitory and excitatory structures can facilitate behavioural functions. A number of instances of skill improvement after direct or indirect neural damage ('paradoxical functional facilitation') have been reported (Kapur, 1996). For example, Miller et al. (1998) described five patients with frontotemporal dementia who acquired new artistic skills in the setting of dementia. The deterioration of one brain area was thought to have removed inhibition from visual perceptual areas, thereby enabling new artistic expression.

If the cortico-striatal-pallidal-thalamic circuits operate in this way (as a dynamic balance of inhibitory/excitatory inputs), it would follow that lesions at different points in a circuit could disrupt different processes (i.e. excitatory versus inhibitory) hence produce different types of deficits. Whether such variation would be only minor and qualitative, or substantial is also unknown. As Kapur (1996) points out, how this micro-level of neural processing relates to neuropsychological processing is right at the frontier of our knowledge at the present time. Not enough is known about the role played in cognition by subsections of these structures, or the micro level neurophysiological processes, to know which form of cognition is being interrupted by lesions. For example, our advancing knowledge of these neurophysiological processes (Houk, Davis & Beiser, 1995) may be extended to how they are manifest as behaviour. This is an issue for future generations of researchers.

Other areas receiving attention in relation to circuitry definition include the different sections of the thalamus involved in each circuit (Groenewegen & Berendse, 1994; O'Leary, Schlaggar & Tuttle, 1994; Bolz, Gotz, Hubener & Novak, 1993) and the fine-grained neurophysiology involved (Smith & Bolam, 1990; Parent & Hazrati, 1993). Studies of people with Parkinson's disease have also pointed to critical roles played in the operation of those circuits by dopamine (Gotham, Brown & Marsden, 1988) and cholinergic activity (Dubois, Pillon, Lhermitte & Agid, 1990). The observations providing the basis for these conclusions only became possible with the arrival of fine-grained physiological analysis and reliable anatomical tracing techniques.

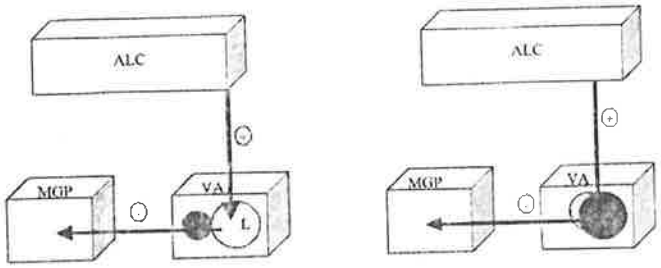

Figure 4
Two Depictions of a Hypothetical Area L within the Ventral Anterior Thalamus.
A lesion X involving the inhibitory pallidal input to area L would have the opposite impact of a lesion Y to area L itself under circumstances in which the inhibitory pallidal input would normally be active (Adapted from Crosson, 1992, p 56). Explanation of abreviations: anterior language cortex (ALC), medial globus pallidus,or medial pallidum (MGP) and ventral anterior thalamus (VA).

In addition, there are the much more speculative, and still more detailed proposals of specific circuitry underpinning particular cognitive and/or motor skills, all involving different subsets of neurological structures drawn from the basal ganglia, other subcortical structures and the cortex. These are discussed later, in the respective sections of this review.

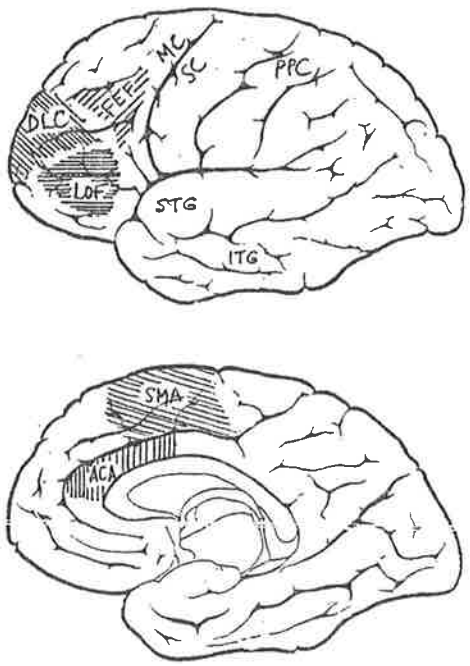

Figure 5
Frontal Cortical Targets of Basal Ganglia Output.
Schematic illustration of the five cortical areas that contribute to the "closed loop" portions of the basal ganglia-thalamocortical circuits disclosed in this review. Abreviations are as follows: ACA: anterior cingulate area; APA: arcuate premotor area; DLC: dorsolateral prefrontal cortex; FEF: frontal eye fields; ITG: inferior temporal gyrus; LOF: lateral orbitofrontal cortex; MC: Motor Cortex; PPC: posterior parietal cortex; SC: somatosensory cortex; SMA: supplementary motor area; STG: superior temporal gyrus. (Adapted from Alexander, DeLong & Strick 1986, p 359).

2.4. Anatomy of Associated Brain Structures

The circuits described by Alexander, DeLong and Strick (1986) included two other main structures. Those were the frontal lobes (Figure 5) and the thalamus. As their interconnections with the basal ganglia are so extensive, investigation of the basal ganglia's role could not proceed without consideration of their involvement in the same functions. Thus, these additional regions are also a part of the 'apparatus' which limits the way that associated information processing can occur, and a clear description of that apparatus is also important.

2.4.1 The Frontal Lobes

In discussing findings relating to the frontal lobes, the subdivisions advocated by Damasio (1985, 1991), Grattan and Eslinger (1991) will be used. The subdivisions are motor,

premotor, limbic (including the anterior cingulate and the posterior sector of the orbital frontal surface) and prefrontal sectors (dorsolateral, mesial and orbital prefrontal). The sections of particular interest to this project, the dorsolateral prefrontal cortex, anterior cingulate cortex and the lateral orbital frontal cortex are all shown in Figure 5.

2.4.2 The Thalamus

The Thalamus is divided into three nuclear groups by a band of fibres. Those fibres are known as the internal medullary lamina of the thalamus, and the three nuclear groups are known as the anterior, the medial and lateral nuclear groups. A very thorough list of functions of each significant subdivision of the thalamus is laid out in a table compiled by Tasker and Kiss (1995). In summary they were:

Nuclei Set	**Functions**
Lateral group, ventral tier	–preparation for, initiation of movement;
lateral group, dorsal tier	–language function;
medial group	–memory;
intralaminar group	–motor control, pain ;
posterior complex	–visual and auditory functions, somatic sensation;
anterior nuclei	–directed attention to sensory stimuli;
ventral thalamus	–recurrent inhibition to thalamic sensory relay nuclei.

5. Cognitive Deficits Associated with Lesions of the Basal Cortical Circuitry: Preliminary Issues

People suffering any of a range of basal ganglia conditions (cerebrovascular accidents[CVAs] and traumatic haematomas, brain tumors, Parkinsons Disease[PD] and Huntington's Disease[HD], Ballism, Tardive Dyskinesia, Wilson's Disease, Dystonia Musculoram Deformans) have been found to perform less well on a wide range of tasks. See Dubois, Defontaines, Deweer, Malapani and Pillon (1995) for review. These conditions each involve a different subset of basal ganglia structures and possibly a subset of subcortical and cortical structures. With some (e.g., CVAs and brain tumors), there is wide variation in neurological involvement across people with ıse conditions. Much of the data that will provide the basis for the objectives of this project comes from studies of these kinds of conditions. Consequently the neurological

impact of those conditions providing the bulk of the data will be described. Conditions most studied are Cerebrovascular Accidents (CVAs), Parkinson's Disease (PD) and Huntington's Disease (HD).

Cerebrovascular Accidents (CVAs)

This term denotes any abnormality of the brain resulting from a pathologic process of the blood vessels (Adams & Victor, 1985, p. 569). For a pathologic process in a blood vessel to cause brain damage it must disrupt the supply of oxygenated blood to the territory served by that blood vessel. The substantia nigra is served by the paramedian arteries in the circular (or proximal) segment of the posterior cerebral artery. The caudate nucleus and the putamen are both served by the middle cerebral artery. Therefore CVAs in those locations would result in basal ganglia damage.

Parkinson's Disease (PD)

The main pathophysiological findings associated with this condition include the degeneration of the dopaminergic projection from the substantia nigra to the striatum. (Barbeua, 1986; Cote & Crutcher, 1985). This degeneration specifically involves the neurons containing melanin in the substantia nigra, and (to a lesser degree) in the globus pallidus. One result, first recognized by Hornykiewicz (1966), is a reduction in the amount of dopamine in the caudate nucleus and putamen. The significant decrease of dopamine in the mesocortical limbic projection indicated by post mortem studies also suggests degeneration of dopamine producing neurons in the ventral medial tegmentum (Javoy-Agid & Agid, 1980; Javoy-Agid, Taquet, Plosko, Cherif-Zahar, Ruberg & Agid, 1981; Scatton, Rouquier, Javoy-Agid & Agid, 1982; Barbosa, Limongi & Cummings, 1997). CT, MRI and PET findings from people with this condition are reviewed by Lenzi and Padovani (1994).

Huntington's Disease (HD)

The focus of this condition is the caudate nucleus. Among those people who have inherited this autosomal dominant trait, neuronal death commences in the dorsomedial aspect of the head and tail of the caudate nucleus. Next to be affected are the putamen

and the globus pallidus. Eventually the impact of the disease spreads to the cortex, the subcortical gray and white matter and the cerebellar and brainstem nuclei (Jacob & Huber, 1992; Haddad & Cummings, 1997). CT, MRI and PET findings from people with this condition are reviewed by Lenzi and Padovani (1994).

A challenge to the interpretation of this amorphous set of data is finding a valid theoretical framework; one which accounts for the full range of human cognition. Elements of such a framework that were dysfunctional in this population could then give some indication of the role(s) played by the set of structures making up the basal ganglia. At least they could provide a starting point for further investigation. But theory construction is an imperfect art. As well as broad frameworks covering the full range of cognition, there are frameworks for significant subareas, e.g. language and memory. In some areas, e.g. visual processing, broad theoretical integration of all relevant research findings is far less advanced. Further attempts are simply beyond the scope of this project. Therefore, qualified use will have to be made of the best attempts of others, while acknowledging their shortcomings.

Another problem is that anatomical processes involved in some basal ganglia disorders are known to extend well beyond the basal ganglia with progression (e.g., PD and HD). Studies of people with those disorders frequently fail to specify disease progression (Marsden, 1982b). Giles (1988), Perlmutter and Raichle (1985) have presented evidence suggesting that frontal involvement among PD sufferers often occurs when their condition has reached Stage 3 of the Hoehn & Yahr scale. Godefroy, Rousseaux, Leys, Destee, Scheltens and Pruvo, (1992) observed a similiar phenomenon among a set of patients who had suffered basal ganglia strokes (unilateral lenticulostriate infarcts). MRI scans detected additional cortical infarcts not detected by initial CT scans, and only the patients with the cortical infarcts displayed 'frontal lobe' style neuropsychological deficits.

Therefore, studies of PD subjects that reveal deficits will only be considered when Stage 3 or higher sufferers have been excluded. Studies failing to exclude will only be

considered if they did not find specific deficits, as this would suggest that all brain areas impaired among their subjects (including the basal ganglia) were uninvolved. Jellinger (1986) has pointed to a further behavioural indicator able to identify frontally impaired PD sufferers. This is the presence of 'dementia'. Unfortunately the criteria used for diagnosis of dementia were not specified. The DSM III criteria are the most likely (McLean, 1987). However, patients with either cortical or subcortical dementia would probably satisfy the DSM III definition (as described by McLean). Additional problems of data interpretation are posed by other phenomena. For a number of years controversy has persisted about the possibility of "remote affects" (Cappa & Vallar,1992; Metter, 1987, 1992). After Cappa and Vallar, they are:

1. The possibility of small additional cortical lesions, undetected by CT (especially, see Godefroy et al. 1992) or MRI assessments.

2. Mass effects due to compression which could be direct, or indirect due to compression of the vascular supply by the primary lesion, resulting in remote effects.

3. In the case of acute arterial occlusions, blood flow in areas adjacent to the infarction may be sufficient for viability, but not sufficient for normal function (ischaemic penumbra: Astrup, Siesjo & Symon, 1981). A related mechanism, which also bears some resemblance to possibility 1., could be a partial ischaemic neuronal loss (incomplete infarction: Lassen, Olsen Hojgaard & Skriver, 1983)." (Cappa & Vallar, 1992, p 14)

4. Damage in one region can result in metabolic changes in a distant region, due to damage to messages sent from the first to the second region, (dendritic activity). Thus the distant effect can be direct (loss of neuronal firing) or indirect (decreased dendritic activity) and it is very difficult to establish the occurrence, or relative strength of these two processes. Damage to white matter tracts can result in a disconnection, leading to remote effects. Metabolic changes at sites that were

> connected by the white matter tracts seem more likely. Thus, lesions in the cortex could result in remote changes based on the contribution of the damaged region to the remote region... (sometimes referred to as 'diaschisis'). The effect of a remote metabolic change on behaviour may be distinctly different from effects of direct structural and local metabolic damage (Metter, 1987).

Cappa and Valla go on to discuss situations when these alternative explanations (to the proposition that subcortical, or basal ganglia lesions are the cause of a cognitive deficit) are unlikely. However, quite sophisticated and costly investigations often seem necessary to check for these.

Cummings (1993) made several important points about the relationship of circuitry to behavioural deficits (see '3. Circuitry of the Basal Ganglia', above). Deficits associated with the non basal ganglia sections of basal ganglia circuitry (the thalamus and frontal lobes) will thus also be reviewed. Any similarities across the deficits linked to the separate elements of the one circuit may indicate the role of that circuit, which can then be tested against the data gathered in this project. This approach to the identification of the role of a circuit as a whole is not new. Various researchers have alluded to this, but then stopped far short of the comprehensive literature analysis, and testing of the conclusions of such analysis, which is to be attempted in this project. An example of the application of this approach is from Gabrieli (1995). See Table 2 below:

Table 2

Memory Impairments common to frontal lobe and Parkinson's disease (PD) patients and older subjects

	Study		
Memory Impairment	Frontal Lobe Patients	PD Patients	Older Subjects
Temporal Order	Milner, 1971	Sagar et al. 1988	Naveh-Benjamin, 1990
Source	Janovsky et al. 1989	Taylor et al. 1990	McIntyre & Craik, 1987
Conditional associative learning	Petrides, 1985	Gotham et al. 1988*	
Self ordered pointing	Petrides & Milner, 1982	Gotham et al. 1988*	Shimamura & Juric in press
Recall relative to recognition	Jetter et al. 1986	Taylor et al. 1986	Craik & McDowd, 1987

* On levadopa only.

(From Houk, Davis & Beiser, 1995, p 287.)

A cautionary note. The nonbasal ganglia sections of basal ganglia circuitry are themselves complex. Significant subdivisions have been documented within the thalamus and frontal lobes. Usually a particular circuit will only involve one or more discrete subdivisions, rather than the whole structure. However, Damasio (1991), for example, has pointed out that boundaries of sections of the frontal lobes lack precise definition. Groups assembled in many lesion studies may be homogeneous in terms of one such brain structure (e.g., left frontal lobe) but be quite diverse in terms of the subdivisions of that structure involved (e.g., motor, premotor or prefrontal cortex). Furthermore, imaging (e.g., CT) used to identify the extent of lesions frequently has limited resolution. More recently developed scanning methods (e.g., PET) do not have anatomic landmarks, and a large amount of guesswork is involved in localizing brain areas highlighted by them. Different patients with apparently identical lesions have sometimes been found to show different deficits, for example in relation to language deficits (Caplan, 1994), and in relation to frontal lobe functions (Stuss, Eskes & Foster,

1994). Godefroy et al. (1998) have contributed a very lucid description of the complexity involved when researchers attempt to draw conclusions about the relationship between a lesion and neuropsychological deficits (see further description of their approach in 5.3.1 Data Analysis and Rationale). All things considered, drawing conclusions from this literature sometimes seems like little more than educated guesswork. But, imperfect as it is, it is all we have to build on.

Alexander, DeLong and, Strick (1986) in their highly acclaimed article, proposed that certain subdivisions of the frontal lobes were linked to the basal ganglia (see Figure 5, '2.3. Circuitry of the Basal Ganglia' above). Specific attention will be paid to those subdivisions, which were dorsolateral pre-frontal, lateral orbital frontal, anterior cingulate cortex.

2.6. Functions Associated with the Basal Ganglia

2.6.1 Attention

Research data linking individual elements of the basal ganglia to attention skills seems limited to animal studies of monkeys and rats in particular (Rolls & Johnstone, 1992). Elements of the basal ganglia so-linked include the head and tail of the caudate nucleus and the posterior ventral putamen. The ventral striatum (which includes the nucleus accumbens) has been linked to responding to emotion provoking or novel stimuli. The most significant theoretical development in regard to (visuospatial) attention and the basal ganglia has come from Jackson and Houghton (1995). Essentially they have postulated a model of information flow between subcortical and cortical structures. While not the same as Posner's theory (e.g., Posner & Rafal, 1987; Posner & Dehaene, 1994) it is nonetheless compatible with it.

Connolly and Burns (1995) attempted to derive mathematical formulae to explain the pattern of 'firing' by striatal neurons when a person shifts between physical activities, e.g., when a motor system (arm, body etc) "must make its own way from the current state to one or more goal states, avoiding undesirable states along the way" (p. 163).

They argued that this function is served by the striatum. Jackson and Houghton (1995) have interpreted this conclusion in the context of Posner and Peterson's (1990) theory of attention (see Table 3 below), suggesting that this corresponds to an attentional shift, and that the striatum plays a key role in such an event.

Investigations of PD patients have used various measures of attention (e.g., Brown & Marsden, 1988 –Stroop test; Globus, Mildworf & Melamed, 1985; Wolfe et al. 1990 –Paced Auditory Serial Addition Task; Frith, Bloxhaum & Carpenter, 1986; Montgomery & Neussen, 1990; Zappia, Colao, Montesanti, Puccio, Valentin & Quattrone, 1990 –word list recall, with and without recurrent task demands; Wright et al. 1990; Bennett, Waterman, Scarpa & Castiello, 1995 –special personal computer presented tasks; Vieregge, Verleger, Wascher, Stuven & Kompf,1994; Sharpe, 1986 –dichotic listening tasks etc; Goldenberg, 1990 –special concurrent visual memory tasks). With three exceptions (Bennett et al.1995; Yamada, Izyuuinn, Schulzer & Hirayama, 1990; Sharpe, 1986), none of them took care to exclude PD patients beyond stage II on the Hoehn & Yahr scale. Thus any findings of attention deficit in the first set of studies are not clearly attributable to basal ganglia impairment.

Table 3
Posner's Model of Attention

Component	Response	Function
I Alertness		
A. Tonic Arousal		Diurnal fluctuation in wakefulness and performance
B. Phasic Arousal	Generalized speeding of reaction time. Physiologic indices: heart rate, GSR, pupillary changes	Instantaneous generalized facilitation of performance induced by warning signal
II Selective Attention		
A. Pre-conscious	Mental shifting of attention to target. Facilitatory Component: disengage from a current focus of attention (parietal lobe), move across a visual field (midbrain), engage. Inhibition of return (midbrain)	Facilitation of selected information. Parallel processing of multiple-input codes and simultaneous pathway activation.
B. Conscious	Movement of head, eyes and body to target	Voluntary allocation of attention. Sequential processing. Limited capacity.
III Vigilance		Investment of conscious mental effort into a given act

Willingham, Treadwell, Koroshetz and Bennett (1995) found that subjects with Parkinson's disease (PD) or Huntington's disease (HD) all showed a benefit in reaction time, at the same level as intact control subjects, if they were told beforehand which signal would appear. This seems to correspond to level IB ('Phasic arousal') of Posner's theory. Thus this component does not seem to be impaired by PD or HD. Sharpe found that Stage I and II PD sufferers took longer to cease responding to the irrelevant channel in a dichotic listening task. However, they were not different from controls when stimuli used (including distractors) were visual. That is, they had no difficulty selectively attending to a designated visual stimulus (component IIA in Table 3 above). However, they were slower to orient their attention toward a visuo-spatial target than the normal controls (a different aspect of component IIA in Table 3 above).

This was independent of mood and intellectual status. Yamada et al.'s (1990) study was essentially a confirmatory replication of the latter finding, also among Stage I and II PD sufferers. Crosson (1992) has pointed out that patients with Parkinson's Disease (PD) were impaired on attending tasks requiring deliberate orientation to the object of attention, but unimpaired on those where external cuing occurred (p 311). Bennett et al. (1995) found their sample of people with Parkinson's disease (at Hoehn & Yahr stage 1 & 2 only) had difficulty modulating their attentional focus or managing more than one attentional task (component IIB in Table 3 above).

Sprengelmeyer, Lange and Homberg (1995) found that the components of Posner's model most disturbed among their sample of Huntington's patients were simultaneous monitoring of different input channels in a divided attention task, response flexibility involving internal cued shifts, and vigilance (components IIA, IIB and III respectively in Table 3 above). Their experimental tasks were presented on a personal computer and were very deliberately modelled on Posner's theory. Other attention related skills impaired by HD identified in a review by Jacobs and Huber (1992) were the kind of mental tracking entailed in counting backwards by 7s from 100 and WAIS-R Digit Span.

2.6.1.1 *Visual Neglect*

Further light is cast on the role of the basal ganglia in attention by data and theories relating to another type of neurological deficit, visual neglect. The right caudate nucleus and the putamen have been consistently associated with visual neglect. Hier, Davis and Richardson (1977) found visual neglect in four patients with a right sided haemorrhage of the putamen. Damasio, Damasio and Chang Chui (1980) found visual neglect in two CVA patients with lesions in the caudate nucleus and putamen (one patient's was on the left, the other's was on the right). A similiar case with left sided lesions in the caudate nucleus and putamen following CVA was reported by Healton, Navarro, Bressman and Brust (1982). Ferro, Kertesz and Black (1987) studied in detail 15 patients with right hemisphere subcortical infarcts. These patients had considerable basal ganglia involvement, as well as involvement of some other adjacent subcortical

structures. Varying degrees of visual extinction and hemispatial neglect were revealed by their series of special assessment tasks. A less precise study by Levine, Lagresse, Dobkin and Turski (1988) reported a comparable conclusion. Fromm, Holland, Swindell and Reinmuth (1985) reported visual neglect among a substantial proportion of their sample with right hemisphere 'basal ganglia' lesions. Villardita, Smirni and Zappala (1983) investigated this same phenomenon among 31 PD sufferers. They only found visual neglect among the bilateral and left sided sufferers.

2.6.2 Motor Function

Motor symptoms were the first to be associated with basal ganglia disorders. The types of motor disorders now recognized as due to basal ganglia damage are impaired voluntary movements, abnormal muscle tone, involuntary movements, and abnormal postures and reflexes (Bhatia & Marsden, 1994). The incidence of motor difficulties in various populations with basal ganglia disorders has been surveyed. For example two thirds of a sample of cardiovascular accident sufferers (Levine et al. 1988) and 54% of 240 patients identified in a meta-analysis of patients with focal, basal ganglia lesions (Bhatia & Marsden, 1994). The latter study also revealed that lesions in the putamen and the globus pallidus were more likely than other basal ganglia lesions to result in motor deficits.

Ideomotor apraxia has been associated with the basal ganglia (Heilman & Rothi, 1993). They argue that impairment of basal cortical circuits, which included the putamen, were most likely to result in apraxia. These circuits do not include the ones being examined in this project, i.e., dorsolateral prefrontal, orbitofrontal and the anterior cingulate circuits, see Figure 2). However, impairment of voluntary movements (traditionally known as 'akinesia') has attracted the most neuropsychological research attention. Performance of well learned sets of motor acts, sometimes referred to as 'motor programs' has been classically considered the main neuropsychological function of the basal ganglia (Marsden, 1982, 1984a). Research studies have employed a variety of visuo-motor tasks. The overwhelming majority of these studies have examined sufferers from Parkinsons' Disease. HD and PD movement disorders result from the

interplay of the spared neurological structures with the distinctive set of impaired ones. These complex processes were well reviewed by Bradshaw and Mattingley (1995).

A rich variety of visuo-motor tasks have revealed deficits in the presence of basal ganglia lesions (Bradshaw & Mattingley, 1995). First there are those tasks with a greater emphasis on the motor component, such as sequential finger tapping (Taylor, Saint-Cyr & Lang, 1987; Benecke, Rothwell, Dick, Day & Marsden, 1987; Robertson & Flowers, 1990; Godefroy, Rousseaux, Leys, Destee, Scheltens & Pruvo, 1992; Jones, Phillips & Bradshaw, 1992) various ideo-motor apraxia assessment tasks (Della Sala, Basso, Laiacona & Papagno, 1992) and sequential left/right hand clenching (Horstink, Berger, van Spaendonck, van den Bercken & Cools, 1990). A second type involves paper and pencil tasks, such as writing and drawing (Lie-Ganchia & Kinsbourne, 1987; Mohr, Juncos, Cox, Litvan, Fedio & Chase, 1990; Kertesz, 1992), drawing in between a series of numbered circles, in order, at speed (Trail Making Test, Taylor, Saint-Cyr & Lang, 1987; Katz, Alexander, Seliger & Bellas, 1989; Matthews & Haaland, 1979; Mayberg et al. 1990; Globus, Mildworf & Melamed, 1985). The third involves various combinations of visual and motor elements, such as reaction time (Rafal, Posner, Walker & Friedrich, 1984, but not by Howard, Binks, Moore & Playfer, 1994), microcomputer presented visual tracking tasks (Frith, Bloxhaum & Carpenter, 1986, Yamada, Izyuuinn, Schulzer & Hirayama, 1990), simultaneous performance of two separate motor tasks, and use of a driving simulator (Madeley, Hulley, Wildgust & Mindham, 1990).

The degree of impairment on these tasks has been found to vary with the condition, and with the stage of the condition. A distinctly more complex role for the striatum in motor function has been proposed by Connolly and Burns (1995). They attempted to derive mathematical formulae to explain the pattern of 'firing' by striatal neurons when a person shifts between physical activities. A motor system (arm, body etc) 'must make its own way from the current state to one or more goal states, avoiding undesirable states along the way.' (p 163). They argued that this function is served by the striatum. Other authors (Jackson & Houghton, 1995) have interpreted this conclusion in the

context of Posner and Peterson's (1990) theory of attention (see Table 3), suggesting that this corresponds to an attentional shift, and that the striatum plays a key role in such an event..

Two closely related types of impaired voluntary movements have aroused special interest. These are perseverative and stereotypical behaviour. Ebersbach, Hattig, Schelosky, Wissel and Peowe (1994) demonstrated that this is one of the distinctive consequences of Parkinson's disease. In a major review, Ridley (1994) concluded that stereotyped behaviour in animals seemed to be related to excess dopaminergic activity in the basal ganglia, while perseverative behaviour could be produced by lesions to the frontal lobes.

Research with PD sufferers has cast some light on the physiological mechanism underlying basal ganglia motor disorders (Marsden, 1984a). While the selection of muscles and relative timing of their activation is intact, errors (at least in the first agonist burst) occur in the number of motor neurons activated, and how often they are activated. A positive correlation been found between severity of akinesia and the decrease of dopamine (and its metabolite homovanillic acid) in the caudate nucleus. Alterations to dopamine function are believed to play a critical role in this process (Jenner & Marsden, 1984). Willingham and Koroshetz (1993) contributed a thoughtful analysis of data on Huntington's disease (HD) and motor skills. Essentially, the main motor impairment was in the learning of a repeated motor sequence (e.g., key pressing). In a later study Willingham and Koroshetz (1995) reported the further finding that subjects with HD showed slowed reaction time when they did not have warning of which kind of signal they would be reacting to.

The possibility that cognitive and motor deficits associated with basal ganglia lesions may have a common cause has been raised. Mortimer, Pirozzolo, Hansch and Webster (1982) reported significant correlations between severity of akinesia and impairment of visual-spatial reasoning and psychomotor speed. Viitanen, Mortimer and Webster (1994) reported bilateral, as opposed to unilateral, decline of arm movement speed

predictive of more cognitive impairment, and a faster rate of decline in that motor indicator was predictive of memory difficulty.

In another summary of research into the basal ganglia and motor control, Brooks (1995) listed 8 aspects of motor control linked to the basal ganglia. They included (1) determination of movement parameters, (2) preparation for movement, (3) enabling movements to become automatic, (4) facilitation of sequential movement, (5) inhibition of unwanted movements, (6) adaptation to novel circumstances, (7) facilitation of rewarded actions, and (8) promotion of motor learning and planning. Brooks went on to test these propositions with a PET scanner. This new device has allowed researchers to collect a different kind of data about brain areas involved in motor function. He tested the significance of regional cerebral activation among neurologically intact people while they operated a joystick. He concluded that it is unlikely that the basal ganglia play a primary role in determining basic parameters of movement. Furthermore, the cerebellum, and not the basal ganglia, were most likely to be the structures directly involved in motor skill acquisition or in promoting automaticity of movement. However, this suggestion was not supported by PET data reported by Jueptner and Weiller (1998). These researchers reported that the dorsolateral prefrontal cortex and striatum (Caudate Nucleus and anterior putamen) were activated during new learning. They also found that it was the sensorimotor cortex and posterior putamen that were activated during automatic (overlearned) movements.

Brooks also concluded that, as the basal ganglia are not differentially activated by performance of complex sequences of movements compared with stereotyped actions, facilitation of sequential movement was unlikely to be their primary purpose. Neither were they directly involved in decisions regarding direction or timing of movement. However they were, he argued, equivalently activated during imagination and performance of actions, which suggests that they play a role in movement preparation and execution. This role could conceivably be to monitor and optimize the pattern of muscular activity employed by a limb to reach its target most efficiently once a motor decision is taken. He further proposed that the basal ganglia suppress unwanted

movements during motor tasks and play a role in adapting to novel circumstances or facilitating rewarded actions; to date, no PET studies have addressed these questions.

In another PET study of PD patients during movement activities, Playford, Jenkins, Passingham, Nutt, Frackowiak and Brooks (1993) reported that PD subjects (unlike controls) showed no significant activation in the contralateral putamen, and impaired activation of the anterior cingulate, supplementary motor and dorsolateral prefrontal areas.

2.6.3. Visual Processing

A number of studies included reports of significant visual processing deficits. For example a meta-analysis of 70 studies of people with Parkinson's Disease (PD) by Waterfall and Crowe (1995) reported deficits in complex visuo-spatial functions and multifactorial spatial functions. However, interpretation is made difficult by their failure to specify PD progression. It is possible the neuropathology might have extended beyond the basal ganglia.

Giles (1988), and Perlmutter and Raichle (1985) have presented evidence suggesting that frontal lobe involvement among sufferers of PD does not occur until their condition has reached Stage III on the Hoehn and Yahr Scale. Only Giles (1988) and Taylor, Saint-Cyr and Lang (1987) have administered visual processing tasks to groups made up solely of people whose condition had not progressed beyond Stage II. Both studies used the Wisconsin Card Sorting Test (WCST). It involves sorting cards according to regularly changing criteria (categories'), which must be learnt by deduction. Both studies found a significantly low number of categories were learnt by by the mildly affected Parkinson's sufferers. Giles also reported a high degree of perseveration. Other visual processing tasks used by Taylor et al. were Money's road map test (identifying right and left turns on an imaginary group walk, Money, 1976), and a test of numerical reasoning in space (the Block Test, Terman & Merrill, 1973). Hollander at al. (1993) also reported impaired performance by PD subjects on the WAIS-R Block Design subtest.

Owen et al. (1993) compared frontal and PD patients on the WCST. They found both had impaired performance, although there were some subtle differences in the character of that performance between the two groups. A similar study by Eslinger and Grattan (1993) compared patients with cardiovascular accidents resulting in discrete lesions either to the basal ganglia or the frontal lobes. Their findings closely followed those of Owen et al. Wallesch, Karnath and Zimmerman (1992) also compared subjects with frontal lesions and others with PD, only they used a computerised maze task instead. However, the pattern of results was similar. Both groups showed deficits, but with important qualitative differences. Generally, in all studies the impairment displayed by the frontal groups was in some respects more severe. An important implication of these results is support for Cummings's (1993) contention that patients with lesions at different points in the one circuit could be expected to present with similar cognitive deficits, that is assuming the different lesions affected the one circuit.

However, other studies of WCST performance with PD sufferers and HD sufferers failed to find significant deficits (Mohr et al.1990, Mayberg et al. 1990 [both PD] and Josiassen, Curry, Mancall, Shagass & Roemer, 1986 [HD]). Sharpe (1986) found slowing of visual attention across the visual field among Stage I and Stage II PD sufferers, suggesting that apparent deficits on visual tasks may be due to more basic difficulties in simple attention.

Saint-Cyr, Taylor, Trepanier and Lang (1992) further investigated the nature of the performance deficit in another category of assessment tasks among people with PD, often described as demanding the same category of cognition (i.e. 'an executive function'), those tasks being those called "Tower of Hanoi" and the "Tower of London". Essentially, these tasks require the subject to placed certain numbers of balls on specified pegs. (E.g., in task 1, Tower of Hanoi: S must transfer a stack of 3 balls from the left-most to the right-most peg of a three-peg stand, the constraints being that only light coloured balls can be put on dark coloured ones, and that only one ball can be

moved at a time.). Their conclusion was a particularly lucid description of a very subtle process and seems to shed significant new light on the issue.

> "The obvious contributions of conscious operations in complex tasks are not superceded or replaced by the so-called nonconscious procedural system but rather supported by it. The unique role of the basal ganglia in this respect is to limit the field of operations (i.e., potential strategies) at an intuitive level, thus liberating the conscious processes to be appropriately focused on salient context dependent stimuli and contingencies. It seems logical that the interplay between cortical and striatal systems would function in parallel as suggested by Alexander and his colleagues (Alexander & Crutcher, 1990a, 1990b; Crutcher & Alexander, 1990)." (Saint-Cyr, et al. 1992, p. 218)

Reviews of cognitive deficits associated with Huntington's Disease have identified a range of visuospatial impairments (Brandt, 1991; Jacobs & Huber's, 1992; Lange, Sahakian, Quinn, Marsden & Robbins, 1995). They have included pattern and spatial recognition, simultaneous matching to sample, visuospatial paired associates, the Tower of London test of planning, spatial working memory, visual discrimination learning, and reversal paradigm, and perception of position or movement in relation to the observer. Cope, Georgiou, Bradshaw, Iansek and Phillips (1996) reported further findings of distinctive, slowed processing of more complex spatial stimuli (the "Simon Effect' task). Jacobs, Shuren and Heilman (1995) reported further deficits in the area of perception of facial identity and facial affect.

In a study investigating a very different aspect of visual processing, Varney and Risse (1993) reported an association between colour association (ability to identify colour normally associated with an item presented as a black and white drawing only) and left hemisphere basal ganglia lesions.

2.6.4. Memory

Research evidence concerning the basal ganglia and memory has already been well reviewed by Tranel and Damasio (1995) and Crosson (1992). Tranel and Damasio concluded that the basal ganglia (along with the cerebellum) are linked to nondeclarative memory, more specifically, *procedural memory,* unlike the medial temporal region, (hippocampal complex) which is linked to an independent form of memory, *declarative memory*. The central evidence for this conclusion was the finding that this kind of memory was spared in people with Alzheimer's disease. In this condition, the basal ganglia and cerebellum are typically spared while sufferers will have severe cortical neuropathology. They can still perform complex motor activities (e.g., dancing or playing golf) and even learn new ones (*procedural memory*), but they are unable to give any factual information about the context in which those skills were acquired (*declarative memory*). A more recent review by Gabrieli (1995) advanced a consistent conclusion that the basal ganglia are important for working memory. Crosson (1992) has pointed out that patients with Parkinson's Disease (PD) were impaired when attending tasks required deliberate orientation to the object of attention, but not when external cueing occurred (p. 311). However, his speculation that therefore the basal ganglia may have a role to play in deliberate (i.e., declarative) acts of memory seems tenuous. Crosson's (1992) review of the PD and memory literature concluded that people with this condition have a retrieval deficit, possibly due to an inability to generate responses based on an internal data base.

Crosson's review of studies of Huntington's Disease (HD) and memory concluded 'Huntington's patients either fail to initiate or cannot devise effective strategies for searching long term memory stores when recall is required, resulting in faulty retrieval' (Crosson, 1992, p. 276). He raised additional possibilities, such as that HD patients may not store as much in long term memory as nonimpaired people, that they may have faulty registration of material in long term store, and that long term traces are weaker. They also show deficient acquisition of motor skills. This general picture of retrieval deficits in relation to basal ganglia damage is confirmed by studies of another basal ganglia condition, progressive supranuclear palsy (Pillon et al.1995). This is a

degenerative disease involving the basal ganglia, the cerebellum and the brain stem nuclei.

2.6.4.1. New 'Micro'-Models of Memory Function and the Basal Ganglia

Some much more speculative, and still more detailed models of specific circuitry underpinning particular cognitive and/or motor skills have been proposed, all involving different subsets of neurological structures drawn from the basal ganglia, other subcortical structures and the cortex.

Golman-Rakic (1995) has proposed a circuit model of working memory. She argued that physiological and anatomical data support the notion that the motor component of working memory functions (spatial and nonspatial) are carried out by multiple dedicated and parallel networks of corticosubcortical structures that make up the prefronto-striato-thalamo-cortical loop. Directional information is presumably conveyed to the basal ganglia via the cortico-striatal pathway whenever the memory field of a preforntal neuron in layer V is activated. Arbib and Dominey (1995) have gone on from the basis provided by Goldman-Rakic's work to postulate a parallel information processing model of working memory for motor movements; in particular, 'memory' for the particular patterns of eye movements required to direct the eyes to a target and scan it. Memory for those eye movement patterns is proposed as being represented by the concerted action of groups of subcortical neurons.

Another model for basal ganglia mediated memory function has been proposed by Ballard, Heyhoe and Pelz (1995). They speculated that 'the basal ganglia' as a unitary entity, control the loading and use of short term visual memory. They suggest that the context of a memory task (e.g., for recall of various configurations of block pattern images) determines how identical retinotopic images are processed, and a potential keeper of such context is the basal ganglia. Such a structure must somehow send that context to the perceptual circuitry.

2.6.5. Language

A noteworthy representation of the comparative contributions of different brain areas to important aphasic syndromes was provided by Metter (1992). Broca's aphasia showed the greatest global hypometabolism with the lowest values in the head of the caudate nucleus. The frontal regions are the most markedly depressed in Broca's aphasia as compared to Wernicke's and conduction aphasias. Wernicke's aphasia occupies a middle ground between Broca's and conduction aphasia with some left prefrontal metabolism that tends to be mild to moderate in severity. Metter concluded from these studies that the temporo-parietal cortex is primarily responsible for the language abnormalities associated with these types of aphasia, and the subcortical-frontal system seems to be associated with the modulation and modification of the underlying language problems.

Theory of the role of the basal ganglia in language is more advanced than theory development in any other area of mental processing in relation to the basal ganglia. In fact there is not one but three rival theories in relation to the basal ganglia and language. These are described, compared and evaluated most eloquently by Crosson (1992).

One model is the *Subcortical Pathways Model.* This holds that certain neural pathways connecting cortical areas involved with language travel through the subcortical region of the brain. Hence, damage to those pathways can disrupt functioning of cortical regions involved in language, but the striatum itself is not involved in language in any significant way. Key proponents of this view are Alexander, Naeser and Palumbo (1987).

Another model is that of *Lexical Decision Making.* Wallesch and Papagno (1988) have proposed that the striatum (among other subcortical structures) is involved in lexical decision making between alternatives generated within cortical areas. Following a very balanced and detailed evaluation of these alternatives, Crosson (1992) still felt the need to advance a third model ('*The Response-Release/Semantic-Feedback Model of*

Language '). This model is developed across several publications (Crosson, 1985; Crosson & Early, 1990; Crosson, 1992). Crosson's synthesis is probably by far the most important single contribution to this literature, and is worth describing in some detail.

Crosson's view (which he describes as '*The Response-Release/Semantic-Feedback Model of Language* ') is that cortico-striato-pallido-thalamo-cortical loops are involved in regulating the release of cortically formulated segments, that the thalamus is involved in tonic arousal of anterior language cortex, and that the cortico-thalamo-cortical pathways serve to transfer information from anterior to posterior language cortex and vice versa. (Crosson & Early, 1990). It is well summarized in Crosson and Early's diagram. (See Figure 6.)

Crosson's review included an extensive discussion of research up to that date. His conclusions from CVA studies were that lesions to the head of the caudate nucleus and the globus pallidus tended to result in nonfluent aphasia and severe reduction in verbal comprehension. Lesions to the globus pallidus tended to produce the additional result of impaired repetition and semantic paraphasia. Other important work has been performed with Parkinson's (PD) and Huntington's Disease (HD) subjects. Key differences between these two conditions involve the basal ganglia structures where most deterioration occurs, the caudate nucleus in HD and the substantia nigra in PD. This work has been summarized and extended by Murray (2000). She summarized previous studies reporting high level comprehension impairments such as difficulties processing sentences with metaphoric, ambiguous or implied information or with complex grammar, among HD and PD subjects. However, her comparison of the spoken language output from HD, PD and control subjects found significant differences between the two experimental groups. While the only distinctive feature of the PD subjects' output was a smaller proportion of grammatical sentences, the HD subjects produced shorter utterances, a smaller proportion of grammatical utterances, a larger proportion of simple sentences, and fewer embeddings per utterance.

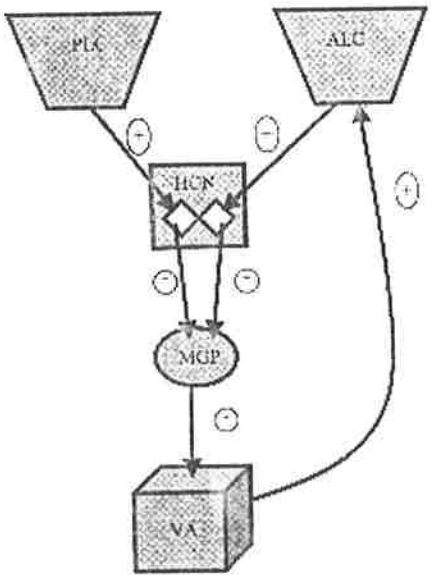

Figure 6
Crosson and Early's Conceptualization of the Cortico-Striato-Pallido-Thalamo-Cortical Loop in Language.
Fibres from anterior and posterior language cortices converge upon adjacent areas of the striatum, which act to convert patterned input to qualitative output. Spatial summation of this quantitative output from adjacent striatal areas occurs in disc-shaped dendritic fields within the medial globus pallidus. This spatial summation is inhibitory and decreases the inhibitory output from the globus pallidus to the ventral anterior thalamus, resulting in greater excitation of the anterior language cortex by the ventral anterior thalamus. Normally, a balance in lateral inhibition within the striatum prevents high levels of inhibition over the pallidum by the striatum. However, this lateral inhibition is overcome during release of a language segment by focused input from the cortex. Pluses and minuses in circles indicate excitatory and inhibitory neurotransmitters, respectively. (Adapted from Crosson, 1992, p 134.) Explanation of abbreviations: Anterior Language Cortex (ALC), the Posterior Language Cortex (PLC), the Head of the Caudate Nucleus (HCN), the medial globus pallidus (MGP) and the Ventral Anterior Thalamus (VA).

The HD group also produced utterances that were shorter and syntactically simpler than those of the PD group, despite similar performances on the motor speech and cognitive tests. The greater impairment in the group with caudate degeneration (HD) would tend to support Crosson's conclusions regarding its importance in verbal expression.

Results of PET studies are less clear. While there is some confirmation of the importance of the head of the caudate nucleus to language production, it is unclear just

what type of language function is involved. Nor have PET studies provided unequivocal indications of the role played by other subcortical structures in language.

Crosson made a call for 'Future studies to explore the use of complex syntax in nonthalamic subcortical aphasias' (Crosson, 1992, p. 78). HD subjects have shown the additional deficit of below-normal performance at word-list generation. A final comment by Crosson on the data, with interesting implications for the circuit concept, was that 'it would appear that small lesions limited to one structure of the basal ganglia do not cause severe or lasting aphasia... One pertinent question to be addressed is whether the nervous system compensates easily for small lesions in the cortex, white matter, or basal ganglia, or whether some other process explains these phenomena.' (pp. 78-79). A possible explanation is that connections between one circuit and another may allow a damaged circuit to continue to function through bypassing its defective elements by means of longer, alternative chains of linked structures.

Starkstein, Federoff, Price, Leiguard and Robinson (1994) investigated a different aspect of the basal ganglia and language. They found right hemisphere basal ganglia lesions associated with impaired comprehension of the emotional tone of spoken language.

2.6.6. Personality Changes Associated with Basal Ganglia Lesions

2.6.6.1. Depression

A large number of studies have reported significant depression. Several measures of depression have been used, especially the Beck Depression Inventory (BDI), the Hamilton Rating Scale (HRS) and the Present State Exam (PSE). Starkstein Robinson, and Price (1987), Starkstein, Robinson, Berthier, Parikh and Price (1988) and Starkstein, Preziozi, Berthier, Bolduc, Mayberg and Robinson (1990) have also found an association with side of motor impairments (right), strongly suggesting that left basal ganglia lesions can produce depression. Among CVA subjects it was lesions in the left

anterior region (cortical as well as subcortical) which were involved (Starkstein et al. 1987). Furthermore as with depression associated with cortical lesions, (e.g., Robinson & Szetela, 1981) they found a significant correlation between proximity to the left frontal pole and severity of depression. In their study of depression (1990), PD subjects were found to be most depressed at Hoehn & Yahrs Stages, I, IV and V, but less so in Stages II and III. Jankovic et al. (1990) reported greater depression at Stage II compared to Stage I. A further interesting finding with depressed PD subjects was hypometabolism in the caudate nucleus and inferior orbital areas of the frontal lobes (Mayberg et al., 1990). Other studies to simply confirm this finding of depression were by Huber, Freidenberg, Shuttleworth and Christy (1990) and Mohr et al. (1990), (both using PD subjects). In a major review of evidence linking depression and Parkinson's Disease, Cummings (1992) reported 'Neurobiological investigations suggest that depression in Parkinson's disease may be mediated by dysfunction in mesocortical/prefrontal reward, motivational, and stress-response systems. Neuropsychological, metabolic, clinical, pharmacological, and anatomical studies support the involvement of frontal dopaminergic projections in patients with Parkinson's disease and depression' (p. 443).

Further studies investigated interactions between between depression and other variables. Lipe, Longstreth, Bird and Linde (1990) found depression among PD subjects to be negatively correlated with sexual satisfaction. An association with impairment in activities of daily living among PD subjects was reported by Kostic, Filipovic, Lecic, Momcilovic and Sternic (1994). Menza and Mark (1994) found disability and 'harm avoidance' (a trait related to central serotonergic systems) both related to depression among PD subjects. Starkstein, Preziosi, Bolduc et al. (1990) found a positive correlation between depression and L-Dopa usage. Mayeux, Stern, Williams, Cote Frantz and Dryenfurth (1986) found level of CSF 5-hydroxyindoleacetic acid was lowest in PD patients with major depression and was related to psychomotor retardation. A similiar finding was reported by Wolfe et al. (1990).

Taylor et al. (1986), in a study of PD patients, found no relationship between WAIS, Wechsler Memory Scale scores and depression, although a study by Troster, Paolo, Lyons, Glatt, Hubble and Koller (1995) did report a link between depression in PD and memory deficits. Mayeux et al. (1981) and Starkstein et al. (1990) reported PD subjects with lower scores on a dementia screening test (Mini-Mental-State) showing significantly less depression. Starkstein et al.'s (1989) study was their most serious attempt to investigate possible links between depression and neuropsychological deficits. They reported that more depressed PD sufferers scored significantly worse on all aspects of neuropsychological functioning, particularly 'frontal lobe tasks'. The link between depression and neuropsychological function is far from conclusive however. Starkstein et al.'s (1989) finding is somewhat isolated. Another very similiar study by Bieliauskas and Glantz (1989) reported the opposite conclusion. There were no apparent differences between the studies which could account for the results. In another study by this group (Starkstein & Robinson, 1989), aphasia (including subcortical aphasia) was not related to depression.

It has been reported that depressed people tend to achieve lower scores on neuropsychological tests even in the absence of known brain lesions (Richards & Ruff, 1989). Tsourtos and Stough (1996) reported that major depression, among neurologically intact subjects, was associated with reduced speed of information processing. While antidepressant medication tended to reduce this effect, it did not eliminate it. Therefore whatever the link between the two in the presence of basal ganglia lesions, any survey of neuropsychological test performance in any sample needs to take account of possible depression.

2.6.6.2 Other Behavioural Changes

The main other behaviour studied in relation to the basal ganglia is obsessive compulsive disorder (OCD). Significant associations have been reported between OCD symptoms and basal ganglia pathology. For example, Tomer, Levin and Weiner, 1993, found severity of left sided (but not right sided) motor signs of people with Parkinsons Disease (PD) to be positively correlated with OCD severity. Hollander, Cohen,

Richards, Mullen, DeCaria and Stern (1993) reported similiar neuropsychological deficits (visuospatial fuction) among patients diagnosed with OCD and people with PD. Several reviewers (e.g., Otto, 1992, Saint-Cyr, Taylor & Nicholson, 1995; Alarcon, Libb & Boll, 1994) have argued that OCD is a result of disruption to one of the cortico-basal-thalamo-cortical circuits. The available data is complex, and some inconsistencies have been reported. Wurthmann (1995) has strongly questioned the circuit disruption explanation. Baxter (1992), after a very extensive review of neuroimaging studies of OCD argued it resulted from a disruption to the balance of excitatory and inhibitory influences operating within a cortical basal circuit made up of, the orbital prefrontal cortex, the caudate nucleus, globus pallidus and the thalamus (which is connected back to the orbital prefrontal cortex).

Another set of studies has assessed the presence of behaviours classically considered part of the 'frontal lobe syndrome' among groups of people with basal ganglia pathology. A group of HD patients studied by Burns, Folstein, Brandt and Folstein (1990) were significantly aggressive (Yudofsky Aggression Scale), apathetic and irritable (assessed with special rating scales). The three personality traits were not significantly correlated. Dubois, Defontaines, Deweer, Malapani and Pillon (1995) concluded after an extensive review that there was an association between basal ganglia conditions, (e.g. HD and PD) and the behaviours of inertia and flattened affect.

To conclude this review of personality changes associated with basal ganglia lesions, all circuits have been potentially associated with the full set of behavioural changes. Those include, most strongly, depression (particularly with left hemisphere circuits), and obsessive compulsive disorder (particularly with right hemisphere circuits). A possible association has been found also with aggression, apathy, inertia, flattened affect and irritability. However, although these have been reported as independent phenomena, they may just be some of the more specific manifestations of depression.

2.6.7. Functions Associated with the Basal Ganglia: A summary

2.6.7.1. Caudate nucleus

2.6.7.1.1. Movement Programming

Reaction time (HD & PD –Willingham, Treadwell, Koroshetz & Bennett, 1995).
Slowed reaction time to random sequences.
Sequential finger tapping (Taylor et al. 1987; Benecke et al. 1987; Robertson & Flowers, 1990; Godefroy et al. 1992; Jones, Phillips, Bradshaw, Bradshaw & Iansek, 1992).
Impaired learning of repeated motor sequences, (HD Willingham & Koroshetz, 1993).
new motor skills, learning to use a joystick (PET of intact normals, Brooks, 1995).
Drawing between numbers (Taylor et al. 1987; Katz, Alexander, Seliger & Bellas, 1989, etc).

2.6.7.1.2 Executive Functions

Orienting of attention to a visuo-spatial target (Sharpe, 1986).
Deliberate orienting to object of attention (Crosson, 1992).
Counting backwards by 7s from 100 & WAIS-R Digit Span (Jacobs & Huber, 1992).
Simultaneous monitoring of different input channels in a divided attention task, response flexibility (HD, Sprengelmeyer et al., 1995).
Attentional shift between goal directed physical activities (Connolly & Burns, 1995).
Shift between two goal directed motor acts (Jackson & Houghton, 1995).
Pattern & spatial recognition, simultaneous matching to sample, visuospatial paired associates, Tower of London, spatial working memory, a visual discrimination learning & reversal paradigm and perception of of position or movement in relation to the observer (HD, Brandt, 1991; Jacobs & Huber, 1992; Lange et al. 1995).
Slowed processing of more complex visual stimuli –"Simon task" effect (Cope et al. 1996).

2.6.7.1.3. Memory

Both Hemispheres

Estimation of how many times, or how long ago something occurred.

Reduced long term memory capacity, weaker memory traces, faulty registration in the long term memory store (HD Crosson, 1992).

Defective strategies for search long term memory, causing faulty retrieval (HD Crosson, 1992).

Left Only

Counting backwards by 7s, recall of digit sequences.

Deep encoding of verbal material.

Verbal comprehension (review of CVA studies Crosson, 1992).

Lesions resulting in nonfluent aphasia (review of CVA studies Crosson, 1992).

Word-list generation (HD, Crosson, 1992).

Right Only

Visual Neglect (R caudate nucleus, CVA, Damasio, Damasio & Chang Chui, 1980, R putamen CVA, Hier et al., 1977, R CVA in the basal ganglia, Ferro, Kertesz & Black, 1987, Levine et al. 1988) (Left sided PD sufferers, Villardita, Smirni & Zappala, 1983)

Visual tracking tasks

Resolution of competing action alternatives

Generation of multiple response alternatives

Maintainance of set and goal directedness

Modification of behaviour in response to feedback

Integration of multimodal sensory output

Lesions result in perseveration & inflexibility, stereotyped, limited responses

Pattern & spatial recognition

Visual discrimination learning

Tower of London problems

Perception of egocentric space, facial identity and affect

Effortful, meaning based retrieval of verbal and visual material

2.6.7.1.4. Language

Verbal comprehension (review of CVA studies Crosson, 1992)

Lesions resulting in nonfluent aphasia (review of CVA studies Crosson, 1992)

Word-list generation (HD, Crosson, 1992)

Shorter utterances, a smaller proportion of grammatical utterances, a larger proportion of simple sentences, and fewer embeddings per utterance (HD subjects produced utterances that were shorter and syntactically simpler, compared to PD subjects.) (HD, Murray, 2000)

2.6.7.2. Globus Pallidus and the Substantia Nigra

While data on the role of this very specific structure is in very short supply, more data is available on the role of larger brain structures that include this one (i.e., the full set of structures affected by Parkinson's disease). Data from this source suggests that this larger set of structures that includes the much smaller one-in-question, (the Lateral Dorsomedial, internal segment of the Globus Pallidus and the rostrolateral Substantia Nigra) are involved in:

2.6.7.2.1. Motor Functions

Dystonia (globus pallidus, Lee & Marsden, 1994)

Motor deficits (especially with focal lesions to the putamen & globus pallidus (Bhatia & Marsden, 1994)

Sequential finger tapping (PD Taylor et al. 1987, Benecke, Rothwell, Dick, Day & Marsden, 1987, etc)

Sequential left/right clenching (PD Horstink et al. 1990)

Stereotypical behaviour (PD Ridley, 1994, PD Ebersbach, Hattig, Schelosky, Wissel & Poewe, 1994)

Reaction time (PD Rafal, Posner, Walker & Friedrich, 1984)

Suppression of unwanted movements during motor tasks

Adapting to novel circumstances or facilitating rewarded actions

Movement preparation and execution to achieve a goal

2.6.7.2.2. Memory

Inability to generate responses based on an internal data base leading to faulty retrieval (PD Crosson, 1992)

Deficits of procedural and working memory

2.6.7.2.3. Language

(All left hemisphere only)

Responding to the irrelevant channel in a dichotic listening task

Verbal repetition (Crosson, 1992)

Verbal comprehension (review of CVA studies, Crosson, 1992)

Colour association

Lesions resulting in nonfluent aphasia (review of CVA studies, Crosson, 1992)

Naming (PD, Crosson, 1992)

Semantic paraphasia (Crosson, 1992)

Smaller proportion of grammatical sentences (PD, Murray, 2000)

Use of complex syntax (PD, Crosson, 1992)

2.6.7.2.4. Visual Processing

Both Hemispheres

Orienting to a visuo-spatial target (Sharpe, 1986)

Construction of block patterns (Terman & Merrill, 1973, Hollander, Cohen, Richards, Mullen, DeCaria & Stern, 1993).

Writing & drawing (PD Lie-Ganchia & Kinsbourne 1987 etc)

Small number of categories achieved on the WCST (PD Giles, 1988, Perlmutter & Raichle,1985)

Driving simulator (PD Madeley, Hulley, Wildgust & Mindham 1990)

Tower of London problems (Saint-Cyr et al.1992)

Right Hemisphere

Visual neglect (left side motor signs in PD, Villardita et al., 1983)

Tower of London Problems

Copying block patterns

Computerized maze performance

Category Learning on the WCST

Perseveration on the WCST

Impaired comprehension of emotional tone of language

2.7. Functions Associated with the Thalamus

2.7.1. Attention

In terms of Posner's framework, at the most basic level, the thalamus has been found to play a role in phasic arousal (Part IA of Posner's framework, see Table 3 above). It is involved in reducing and increasing, in tune with the overall sleep and wakefullness cycle, the general level of sensory information relayed on to the cortex (McCormick & Bal, 1994). Tasker and Kiss (1995) reported, from their own literature review, that one thalamic nucleus played a role in directing attention to sensory stimuli (Stage IIA & IIB from Posner's framework); that nucleus being the anterior nuclei principalis. This seems compatible with the act of directing resources for actively processing incoming information', attributed to the thalamic intralaminar nuclei by Crosson (1992). Another, and related, possible role for the thalamus proposed by Crosson involved the thalamic intralaminar nuclei and the ventral lateral nucleus helping to prepare an aroused organism to respond to a meaningful event. They suggested, further, that this preparation 'could involve directing resources for actively processing incoming information' (p.188). This resource allocation assisted storage of information into a long term store.

2.7.1.1. Visual Neglect

In a comprehensive review of outcome studies following thalamic infarcts, Bogousslavsky, Regli and Uske (1988) reported that infarcts in the territory of the paramedian artery were most likely to result in hemi neglect and possibly visual memory deficits. This artery supplies the intralaminar group of thalamic nuclei and the dorsomedial nucleus. Three other artery territories are involved in the thalamus. Bogousslavsky, et al.'s review of outcome studies for infarcts in the other three did not reveal any noteworthy incidence of hemi neglect. The other main overall review of evidence for the role of the thalamus by Tasker and Kiss (1995) did not list any major additional visual processing linked to the thalamus.

2.7.2. Motor Function

The role of the thalamus in motor function has been long recognized. Indeed, surgical removal of the ventrolateral thalamic nucleus is recognized as the treatment of choice for various movement disorders, especially tremor control (Burchiel, 1995). Evidence for the contribution of the thalamus to motor function has been comprehensively reviewed by Lee and Marsden (1994). They reported that dystonia has been reported most commonly after thalamic lesions, particularly when the posterior or midline nuclei are involved, but not when the ventrolateral or ventroanterior thalmic region nuclei are involved. As a point of qualification, they note that lesions in the globus pallidus can also result in dystonia. They go on to suggest that 'Subtle effects of the relative balance of subthalamic excitation via the indirect striato-pallidal pathways and inhibition via the direct striato-pallidal system on the globus pallidus may underlie the expression of dystonia. Dystonia also may involve a contribution from disordered descending pallidal output to brainstem regions, in addition to disordered thalamo-cortical control.' (p. 505). Chorea or Ballism is commonly caused by lesions in the subthalamic nucleus or subthalamic region, but not convincingly so after isolated thalamic lesions.

2.7.3. Visual Processing

Schwartz (1994), McCormick and Bal (1994) have eloquently described the role played by the thalamus, as its being just one link, in a long chain of brain areas that connect the

initial reception of sensory data to the cerebral cortex. In fact the thalamus is the final link, before such information passes to cortical areas. As such the thalamus plays an important role in the control of sensory gating and analysis.

In a comprehensive review of outcome studies following thalamic infarcts, Bogousslavsky, Regli and Uske (1988) reported that infarcts in the territory of the paramedian artery were most likely to result in hemi neglect and possibly visual memory deficits. This artery supplies the intralaminar group of thalamic nuclei and the dorsomedial nucleus. Three other artery territories are involved in the thalamus. Bogousslavsky et al's review of outcome studies for infarcts in these other three did not reveal any noteworthy incidence of hemi neglect. The other main overall review of evidence for the role of the thalamus, by Tasker and Kiss (1995), did not list any major additional visual processing linked to the thalamus.

2.7.4. Memory

The most thorough review of the thalamus and memory was published by Crosson (1992). He concluded that 'A number of recent studies suggest that severe memory problems are produced after thalamic lesions only if either the dorsal medial nucleus or the ventral amygdalofugal pathway *and* either the anterior nuclei or the mammillothalamic tract are both involved.' (p.188). According to Tranel and Damasio (1995), the left sided thalamic nuclei are specialized for verbal information and the right sided ones for visuo-spatial information. However a recent PET study by Shallice, Fletcher and Dolan (1998) reported that both the left and right thalamus were significantly activated in both verbal semantic and verbal episodic memory retrieval tasks. Anterior parts of the thalamus make an important contribution to the ordering of memories into their correct time sequence. Another and related role for the thalamus proposed by Crosson was an 'attentional' one; that the thalamic intralaminar nuclei and the ventral lateral nucleus may help prepare an aroused organism to respond to a meaningful event. He suggested further that this preparation 'could involve directing resources for actively processing incoming information' (p.188). The function of this resource allocation was to assist storage of information into a long term store. However,

memory deficits linked to these 'attentional' problems are considered to take a milder form than the former type (those where the dorsal medial nucleus or the ventral amygdalofugal pathway *and* either the anterior nuclei or the mammillothalamic tract are both involved.). Both main reviewers of this literature (Crosson, 1992, and Tranel & Damasio,1995) concluded that much is still unknown about the thalamus and memory.

2.7.5. Language

Certainly, the role of the thalamus in language is probably its best recognized function. There is even an aphasic syndrome called 'thalamic aphasia' (see Table 4.). This literature has been thoroughly reviewed by Crosson (1992). 'When aphasia does occur with thalamic lesions, it occurs almost exclusively with lesions in the dominant thalamus. The syndrome of semantic paraphasias sometimes deteriorating into jargon, less severely affected auditory verbal comprehension, and relatively preserved repetition fits cases of dominant hemorrhage well, but not in cases of dominant thalamic infarction. Yet, relatively preserved repetition does exist in a vast majority of aphasias due to thalamic lesion, both for hemorrhage and infarction.' (p. 110). However, significant uncertainty about the thalamus and language continues.

Table 4

Criteria of Cambier et al. (1982)* and Crosson, (1984) for Thalamic Aphasia

Cambier et al. (1982)	Crosson (1984)
Paraphasia in naming (primarily semantic)	Frequent paraphasia (primarily semantic)
Incoherence in narrative discourse	Jargon
Absence of significant comprehension deficits	Less severe deficits in auditory comprehension
Normal repetition	Intact or minimally impaired repetition
Reduced vocal volume (increasing across the course of a verbalization)	
Aspontaneity in oral expression	
Pauses in oral expression	
Word finding deficit (with frequent perseveration)	

* Cited by Demonet (1987)

(From Crosson, 1992, p. 90)

2.7.6. Functions Associated with the Thalamus: A Summary

2.7.6.1. *Thalamic Nuclei*

(Ventralis anterior pars parvocellularis & medialis dorsalis pars parvocellularis)
While data on the role of this very specific structure is in very short supply, more data is available on the role of the larger brain structure that includes this one (i.e., the complete thalamus). Data from this source suggests that this larger structure that

includes the much smaller one-in-question, (the thalamic nuclei described above) is involved in:

2.7.6.1.1. Attention

Directing attention to sensory stimuli (anterior nuclei principalis, Tasker & Kiss, 1995)

2.7.6.1.2. Processing-Resources Allocation

General level of sensory information relayed to the cortex (general thalamus, McCormick & Bal, 1994).

Directing resources for actively processing incoming information, preparing an aroused organism to respond to a meaningful event (thalamic intralaminar nuclei & ventral lateral nucleus –Crosson, 1992)

2.7.6.1.3. Memory

Both Hemispheres

Ordering of memories into their correct time sequence (anterior parts of the thalamus – Shallice, Fletcher & Dolman, 1998)

Visual memory (territory of the paramedian artery –Bogousslavsky et al.1988)

Right Hemisphere

Visual Memory (Tranel & Damasio, 1995)

2.7.6.1.4. Motor Function

Dystonia, tremor (Lee & Marsden, 1994)

2.7.6.1.5. Visual Processing (right hemisphere only)

Hemi neglect (territory of the paramedian artery –Bogousslavsky et al.1988)

2.7.6.1.6. Language (left hemisphere only)

Verbal memory (Tranel & Damasio, 1995)

Thalamic aphasia involving semantic paraphasia, and some audio-verbal incomprehension (Crosson, 1992)

2.8 The Role of the Basal Ganglia Cortical Circuits: integration of diverse research findings.

Essentially because of their greater size, it has been easier to research the role played by the cortical sections of these circuits. Other sections of the circuits are considerably smaller, and they don't tend to be impaired as discreetly. For example, conditions for which there are sufficiently large numbers of impaired subjects for group studies (e.g. PD, HD and CVA), tend to affect groups of other structures all at the same time. Therefore the functions associated with the cortical sections of the circuits provide a starting point for defining function of a circuit. However a variety of functions have been linked to other structures (e.g. the thalamus) that contain (but are not limited to) noncortical elements of the circuits (e.g. the ventralis anterior pars parvocellularis & medialis dorsalis pars parvocellularis within the thalamus). This suggests that functions associated with the cortical areas do not reveal the complete picture. The first challenge to interpretation of the data available is its diversity. For example people with PD have been found to be impaired in their capacity for sequential left/right clenching (PD, Horstink, Berger, van Spaendonck, van den Bercken & Cools, 1990) and the ability to complete the Tower of London problems (Saint-Cyr, Taylor, Trepanier & Lang, 1992). The creativity required to identify a unifying cognitive process across these two tasks would be very great indeed. We know that the structures impaired among subjects yielding these results (those affected by PD), are more than a single circuit. Therefore, it could be argued that some of the functions linked to these larger, subcortical structures are not associated with one or more of the circuits. The next challenge is differentiating between functions involved with a circuit and functions that are not.

In the absence of any better basis, the most plausible hypothesis of circuit functions is the cortical ones plus functions linked to other structures (containing circuit-elements, e.g. thalamus) which are conceivably complementary to the cortical ones. For example, resolution of competing action alternatives has been associated with the dorsolateral prefrontal cortex (Roberts & Pennington, 1996). Another element of that circuit is the dorsolateral head of the caudate nucleus. However little is known about the function of this very narrow section of that nucleus, but a great deal is known about the effects of Huntington's Disease (HD). That disease primarily involves the degeneration of the caudate, but subjects yielding those results will not

all have the same parts, or the same proportion, of that structure affected. It has been found that simultaneous monitoring of different input channels in a divided attention task, and response flexibility, is impaired among people with HD (Sprengelmeyer, Lange & Homberg, 1995). This is conceivably similar, or related to, resolution of competing action alternatives. Both involve dynamic allocation of attention between two competing objects of attention, and making associated responses. Therefore these similarities across functions may provide some preliminary indications of the role of that circuit.

As discussed in section "2.5. Cognitive Deficits Associated with Lesions of the Basal Cortical Circuitry: Preliminary Issues", this approach to the identification of the role of a circuit as a whole is not new. An example of the application of this approach is from Gabrieli (1995). See Table 2 in section 2.5. One initial criticism of Gabrieli's interpretation of this approach is that he has included data relating to the frontal lobes, as a whole, rather just than the subsection involved in a particular circuit alone. This is necessary if we are to be precise about circuit roles. The first step is summarizing data available on each cortical section of the circuits. Then, data from the other three stages of the circuits (striatum, pallidum/substantia nigra and the thalamus) will be scrutinized for complementary aspects. It will be argued that each circuit performs some overall, "key" functions, with each component link possibly making it's own distinctive contribution to performance of that key function.

2.8.1. Dorsolateral Prefrontal Circuit

2.8.1.1. *Review of Functions associated with the cortical part of the Circuit*

2.8.1.1.1. Attention

Knight (1991) has argued that attentional capacity is invariably impaired once disorders affecting the dorsolateral prefrontal cortex have reached an advanced stage or become bilateral. On the basis of a review of evoked potential studies he argued that the dorsolateral prefrontal cortex of the right hemisphere is more important than the left to focussed sustained attention and the capacity to ignore irrelevant stimuli ('gating'). Sasaki, Tsujimoto, Nambu, Matsuzaki,

and Kyuhou (1994) reported a consistent finding. They found counting backwards by 3s from 100 was associated with evoked potential measures of the prefrontal and premotor sections of the frontal lobes. The control of saccadic eye movements, an important part of a subject's responding to any attentional task, has also been linked to this area by work with monkeys and humans (Morrow & Sharpe, 1995). Mennemeier et al. (1994) reported a study of stroke patients with dorsolateral prefrontal lesions. They did not report any decline in their awareness of stimuli within their peripheral vision (a phenomenon referred to as 'Troxler fading'), unlike patients with parietal lesions. These findings are not necessarily contradictory. They may go some way toward clarifying the very specific nature of attentional difficulties associated with this part of the brain. Posner and Dehaene (1994) reported that lateral areas of the prefrontal cortex were important to holding a representation of past events in conscious awareness.

2.8.1.1.2. Motor Function

Motor functions linked to this area of the brain include hand strength (Leonard, Jones & Milner, 1988), movement programming (Kolb & Milner, 1981) and corollary discharge (Teuber, 1964). Goldman-Rakic (1995) argues on the basis of nonhuman primate research that prefrontal neurons are responsible for coding the preparation and organization of movements required for an action plan, and also for keeping the action plan focussed on, and consistent with, attainment of a goal. Goldman-Rakic analyses the possible neurophysiology involved in some depth. This has been elaborated further by Arbib and Dominey (1995) in relation to saccadic eye movements. In fact, they proposed a rather elaborate information processing model to account for data in relation to this task.

2.8.1.1.2.1. Motor Function and General Frontal Lobes

The Motor cortex of the frontal lobes (Brodmann's area 4) is associated with the control of fine motor movement. (Kuypers, 1981). Large lesions can result in flaccid hemilegia on the contralateral side of the body, less severe ones just in weakness and incoordination (Malloy & Richardson, 1994). Likewise, the Premotor cortex (Brodmann's area 6) is important to sensorimotor integration and complex volitional movement or praxis. Lesions to this area can result in inability to make use of sensory feedback to modify movements smoothly, and in apraxia (Malloy & Richardson, 1994). Broca's area, in which lesions lead to nonfluent, highly

effortful and paraphasic speech, is also within the frontal lobes. Ridley (1994) has reported support for Luria's (1973) report that 'lesions in the more posterior areas of the frontal lobes result in simple motor perseverations, e.g., repeating rather than terminating an action whereas more anterior lesions resulted in more subtle perseverations, e.g., intrusion errors' (p 224). Other motor behaviours, e.g., the motions of using an object when such use was inappropriate, have also been linked to the frontal lobes (Ridley 1994).

2.8.1.1.3. Executive Functioning

This section of the frontal lobes is responsible for executive functions. These have been defined as the combination of planning, decision making, judgement and self perception. Given the importance of these functions it is hardly surprising that they represent the most extensively studied aspect of the frontal lobes (Fuster, 1989; Tranel, Anderson & Benton, 1994; Malloy & Richardson, 1994). These include, integration of multimodal sensory input, generation of multiple response alternatives, maintenance of set and goal directedness, modification of behaviour as conditions change, and self evaluation. Lesions result in perseveration and inflexibility, a stereotyped or limited response repertoire, easy loss of task set, difficulties integrating diverse sensory elements into a coherent whole, and poor self monitoring of errors. Roberts and Pennington (1996) argued that the prefrontal cortex resolves competing action alternatives (including performance of motor performance alternatives) by the interaction of working memory activations and inhibitory suppressions. Visual aspects of executive functions have typically been associated with the right hemisphere. For example, the verbal fluency task has often been associated with the left frontal lobe and a visual counterpart of the same task has been associated with the right frontal lobe. That visual task involved someone producing as many drawings as possible in 5 minutes (Jones-Gotham & Milner, 1977). Fuster (1989) conducted a very extensive review of research into prefrontal function. He concluded that the dorsolateral prefrontal cortex makes a distinct contribution to executive functioning. This is a retrospective function of provisional short term memory, and a prospective function of preparatory set.

Frith (2000) proposed that top down regulation of responses was a function of the left dorsolateral prefronal cortex. Shallice (2001), in his most recent review of investigations of

executive functions and the left dorsolateral prefrontal cortex, argued that Frith's proposed function corresponded to the Norman-Shallice position of top-down modulation of the supervisory system of the schema in contention scheduling (see section 2.8.1.2.2.1., "Models of Executive Functioning").

2.8.1.1.3.1. Executive Processing and the General Frontal Lobes

Norman and Shallice's model of frontal function clearly includes the processing of visual information (see Figure 8). However, as yet there seems to be no specific linkage of elements of the system to smaller neurological structures within the frontal lobes (e.g., dorsolateral prefrontal cortex). Goldberg and Podell (1995) have cogently argued that the right hemisphere generally, including the right frontal lobes, is critical for coping with novelty (?novel 'schema control units' referred to in Figure 8). Conversely, the left hemisphere deals with more routine, practiced knowledge (?well practiced 'schema control units'). Again, clearly a lot of visual processing is involved, but despite some vague allusions to smaller neurological structures within the frontal lobes, no specific linkages are proposed.

Another significant research tradition has focussed very strongly on the Wisconsin Card Sorting Test (WCST). Various researchers have compared frontal and basal ganglia subjects in terms of WCST performance (see section "2.6.3. Visual Processing"). Both groups have shown deficits, but with important qualitative differences. Generally, in all studies, the impairment displayed by the frontal groups was more severe in some respects. However, it is not clear just how much the same circuits were affected in each group. Robbins and Rogers (2000) have argued that the WCST tests the central cognitive functions of Alexander et al.'s (1986) basal-cortical circuits. This test has become widely accepted as a conclusive indicator of frontal lobe disturbance within clinical neuropsychology practice. However recent reviews have seriously questioned the validity of this assumption (Anderson, Damasio, Jones & Tranel, 1991; Reitan & Wolfson, 1994). For example, lesions in nonfrontal areas have been also been associated with poor WCST performance (Strauss & Hunter, 1993).

There are also, of course, the data gathered during previous generations of research into 'the frontal lobes'. The crudity of investigative, especially imaging, technology in earlier years

seems to have prevented those researchers from differentiating functions of areas within the frontal lobes. However, they created most of the more simple cognitive assessment tasks which have since been so useful in conjunction with MRIs and PET scans. Kevin Walsh (1987) has provided a very readable and succinct description of this work. Visual tasks so linked to general frontal dysfunctions include maze learning, the Complex Figure of Rey, Koh's Block Design and The Tower of London problems. However, later researchers re-examining the data find much reason for clinicians to be cautious about these 'rules of thumb' (e.g., in relation to maze learning and the frontal lobes, Bowden & Smith, 1994).

2.8.1.1.4. Memory

In a major review of deficits associated with the dorsolateral prefrontal cortex, Grafman (1994) listed five types of memory deficits. Those are in temporal coding (i.e., sequencing and frequency of items to be remembered), retrieving lesser known quantitative information, working memory (see definition in 2.5.4.1.2, above), maintenance of information over time, retaining information associated with specific items (eg knowing the names of all players in a team; knowing all the positions in that game, but not being able to recall which player occupies which position). Grafman went on to propose a theoretical framework for integrating this diverse set of findings. He argued that the prefrontal cortex is responsible for forming a series of 'structured event complexes' (SECs). See section "2.8.1.2.3.1. The Psychology of Memory" above, declarative memory specifically, for a description of these.

Various neuropsychological tasks with a major memory component have been associated with the prefrontal cortex (Daigneault, Braun & Whitaker, 1992). These authors listed eleven indices. Four out of those eleven had a distinct memory emphasis. Those were:

1. The number of correct words on the Controlled Oral Word Association Test .
2. The number of different and unnamable drawings on the first condition of the Design Fluency Test.
3. The proportion of recency judgement errors out of the items explicitly recognized on the Recency Test.

4. The number of words from List A reported on recall of List B, divided by the number of correctly recalled words, plus, the number of words from List B reported on recall of List A, divided by the number of correctly recalled words on the last step of the Rey-Auditory Verbal Learning Test.

(Daigneault, Braun, & Whitaker, 1992a, p. 54).

In an important paper on this subject, D'Esposito and Postle (2000) performed a meta-analytic review of prefrontal cortex lesion studies using working memory tasks and compared early-stage Parkinson's disease subjects and traumatic brain injury subjects on working memory tasks. They concluded that the prefrontal-striatal regions, interacting with dopamine, contribute to rehearsal and control processes.

The abilities to estimate the number of times that a particular event has occurred, or how long ago something took place, have been linked to this part of the prefrontal lobes (Tranel & Damasio, 1995). They also concluded that the left side is dominant for verbally encoded information of this type and the right for nonverbal, visuospatial information. Another important memory function that Tranel and Damasio argue is associated with this part of the brain (largely on the basis of work with nonhuman primates) is working memory (see section "2.8.1.2.3.1.3. Activated Memory", for definition). Presumably the exercise of working memory is integral to the performance of the executive functions so strongly linked to this part of the brain (see section "2.8.1.2.2.1 Models of Executive Functioning"). A PET study of verbal memory with human subjects conducted by Petrides, Alivisatos, Meyer and Evans (1993), and another involving evoked potentials and visual object information conducted by Seeck et al. (1995), both reported further supporting evidence. Roberts and Pennington (1996) also supported this view after reviewing more recent studies. They went on to argue that the prefrontal cortex resolves competing action alternatives by the interaction of working memory activations and inhibitory suppressions.

Our knowledge of the role of this section of the cortex in memory has been considerably advanced by a recent wave of PET studies (reviewed by Shallice, Fletcher & Dolan, 1998). Complementing findings of earlier lesion studies, significant new detail and further

clarification of left/right differentiation have been reported. Kapur, Craik, Tulving, Wilson, Houle and Brown (1994) found the left dorsolateral prefrontal region to be critically involved in deep encoding (see section "2.8.1.2.3.1.4.1. Important Process in Long term Memory") of episodic memories. Fletcher, Shallice and Dolan (1998) found it was also involved in another facet of encoding, the organization of word lists to facilitate recall. Stuss, Eskes and Foster (1994) and Fletcher, Frith, Grasby, Shallice, Frackowiak and Dolan (1995) presented evidence that the right dorsolateral prefrontal lobe plays an important role in retrieval, particularly in the monitoring and checking that is part of this process. (Visually presented word lists were used.) In fact evidence has been mounting for mediation by the right prefrontal cortex in a range of retrieval functions. Functions reported have included sentence recognition (e.g., Tulving, Kapur, Markowitsch, Craik, Habib, & Houle 1994), other forms of cued recall (e.g., Cabeza, Kapur, Craik, McIntosh, Houle & Tulving, 1995), word item completion (e.g., Squire, Ojemann, Miezin, Petersen, Videen & Raichle,1992) and a variety of nonverbal tasks (Nyberg, Cabeza & Tulving, 1996). Shallice, Fletcher and Dolman (1998) have further explored this issue using the subtractive-control PET methodology. Using word pairs, two factors were investigated, imagability of the word pairs (how well the combination lent itself to generation of a visual image combining the two words) and semantic distance between word pairs (e.g., king and queen are semantically close while puppy and hurricane are distant). Imagability was not related but semantic distance was. Retrieval of the second member of a word pair was associated with increased activation of the right dorsolateral prefrontal lobe when it was semantically close, or semantically most distant, but less so when it was only moderately distant. The authors suggested that each end of the semantic distance continuum required extra verification. In the close condition, verification that the response choice was not an automatic word association, and in the distant condition, responding to a retrieval task that was simply more difficult.

Finally, in his most recent review of the investigations of memory and the dorsolateral prefrontal cortex, Shallice (2001) concluded that the right dorsolateral prefrontal cortex is actively involved in retrieval from verbal episodic memory and possibly involved in monitoring or checking. On the other hand he challenged the widely held view of the importance of the left dorsolateral prefrontal cortex in working memory, arguing instead, that

this area is only activated when information held in working memory is operated upon. For example, Rowe, Toni, Josephs, Frackowiak and Passingham (2000), using event-related functional magnetic resonance imaging, found that selection of a spatial item from memory, rather than maintenance of it in working memory, was associated with the dorsolateral prefrontal cortex.

2.8.1.1.4.1. Memory and the General Frontal Lobes

While various distinctive memory problems have been described among people with frontal lesions, they have frequently been interpreted as secondary consequences of other types of dysfunction, particularly in the categorization and organization of information, critical to retrieval (Luria, Sokolov & Klimkowski, 1967; Tranel & Damasio, 1995). A difficulty with interpretation of the data is the uncertainty about why some people with frontal lesions have memory difficulties and others do not (Grattan & Eslinger, 1991). Various forms of erratic and inefficient performance in the anterograde compartment of memory, secondary to executive control and self regulatory impairments, have been linked to frontal lesions. These are specifically, 'forgetting to remember', difficulty following instructions, limited effort, heightened susceptibility to interference, impaired registration of incoming stimuli, perseveration, disorganization and poor monitoring of material to be remembered, inability to use aids or mnemonic strategies to assist in memorizing, and cognitive inflexibility (Grattan & Eslinger, 1991).

Sections of the frontal lobes linked to distinctive kinds of memory impairments are discussed below. This account largely follows the conclusions of literature reviews by Tranel and Damasio, (1995) and Grattan and Eslinger (1991).

2.8.1.1.4.2. Other Memory Regions: Ventromedial Frontal Region

This area includes Brodman's areas 11, 12, and parts of 32 and 10, closely related to nearby areas 25 and 24. Rolls, Hornak, Wade and McGrath (1994), and Tranel and Damasio (1995) have argued that this area is responsible for linking emotions and feelings with particular sets of factual knowledge, for instance the association of the painful feeling of being burned with the sight of a red hot flame.

2.8.1.1.4.3. Other Memory Regions: The Basal Forebrain

This region also plays a role in contextual memory, by 'binding together different modal components of a particular memory' (Tranel & Damasio, 1995, p 44), for example, linking memory for a face with a name, an accent and various facts about the person. While not technically part of the frontal lobes, it is often involved in injury to the ventromedial frontal cortices.

2.8.1.1.5. Language

Generation of multiple response alternatives (including verbal) has been linked to this area. The Controlled Oral Word Fluency Test is the most widely used verbal measure of this function (Malloy & Richardson, 1994). Poor performance on this task has been linked to lesions of this region in the left hemisphere. The task involves someone being asked to say as many words as possible, all beginning with the same set letter, in one minute. Considerable research has been done with this task. However, data linking the task with this part of the frontal cortex (along with other research on behavioural consequences of frontal lesions) have their limitations. Reitan and Wolfson (1994) have expressed this view most strongly in an article which was very critical of frontal lobe/behaviour research in general. A model of information processing specific to this brain area has been proposed by Parks et al. (1992). They argued that the neuropsychological processing involved in the word fluency task was the same as the one they proposed for another linked to this area, the Wisconsin Card Sorting Test. However, they admitted that their model was speculative, and yet to be subjected to conclusive testing.

A new perspective on the connection between verbal fluency and the left prefrontal lobes has been provided by PET studies. Boivin et al. (1992), in a study of neurologically intact adults, reported that "verbal fluency was found to correlate positively with left temporal cortical region metabolic activity but to correlate negatively with right and left frontal activity.... An explanation for the disparate relationships that were observed between frontal and temporal brain areas and verbal fluency might be found in the mediation of different task demands by these separate locations, i.e. task planning and/or initiation by frontal regions and verbal memory by the left temporal area." (p. 238). The debate is far from concluded however,

because of the limitations of the PET methodology. Some studies have revealed significant ambiguity in patterns of PET results during cognitive task performance (e.g., Haxby et al., 1986). Another important verbal function served by the prefrontal lobes has been described as 'verbal self regulation of behaviour'. This takes the form of internal 'self talk' which directs behaviour. There is some controversy over exactly how this occurs (Daigneault, Braun & Whitaker, 1992).

On the other hand, the right dorsolateral frontal lobe has been associated with modulation of the affective part of language, for instance tone, emotional gesturing (Ross & Rush, 1981).

2.8.1.2. *Review of Functions associated with the Dorsolateral Prefrontal Circuit: A Summary*

In conclusion, the areas of cognition most strongly associated with the cortical level of this circuit are threefold, motor programming, executive functions and memory. Possible, more specific hypotheses will be explored by examination of current accepted theoretical models for an area of processing (e.g., motor functions). These models will then provide a structure for consideration of research findings for all levels of this circuit. These are summarized in the tables below (Tables 5, 6 and 7). Research findings cited for the lower levels sometimes come from studies performed on subjects with additional brain structures affected (e.g., under pallidum and substantia nigra, findings obtained with PD subjects will be listed even though structures affected by this disease are not always limited to the pallidum and substantia nigra). Furthermore the number of studies for some relevant conditions, such as PD, are far too numerous to cite all of them in this table. Therefore, where available, conclusions of recent overviews of such research will be cited instead.

2.8.1.2.1. Theoretical Models of Motor Function

An influential, early contribution to theory of motor function has come from Marsden and colleagues (Marsden, 1982, 1984a, 1984b; Marsden & Obeso, 1994; Benecke, Rothwell, Dick, Day & Marsden, 1986). Marsden (1984a) concluded that the basal ganglia automatically and subconsciously run the sequence of motor programmes that

comprise a motor plan. The programs themselves may be learnt and stored elsewhere in the brain, and perhaps are assembled into the coherent plan in the premotor (and other frontal) areas. But the initiation and automatic execution of the sequence of motor programmes required to complete the motor plan of a complex motor act may depend on the basal ganglia.

Attempts to characterise motor function as a 'serial or hierarchical' process (e.g., Marsden's model above) have a long history. However they have been strongly criticised. Since Marsden and colleagues contributions, significant new strides have been achieved in our understanding of the basal ganglia and motor control (Groves, 1983; Alexander, 1994; Baev, 1995; Mink & Thach, 1991). Alexander, DeLong and Crutcher (1992) have drawn attention to the lack of correspondence between those models (particularly the concept of 'motor program') and what is known about neuronal functioning in those brain areas where lesions have been associated with motor deficits. They advocated a 'connectionist' style of model,. "The essence of most connectionist models is that they are layered, self organizing networks of highly interconnected processing units with properties in some ways analogous to those of biological neurons. In connectionist networks, information is not stored in discrete locations (as in conventional computers), but rather in the overall pattern of variable strength connections among neurons." (p. 662). Important, and similiar, new models of motor function in relation to the basal ganglia have been proposed by Penney and Young (1983, 1986) and Ballard, Hayhoe and Pelz (1995). While they have the 'connectionist' form advocated by Alexander and colleagues, they still give a central place to the concept so strongly criticized by them, the 'motor plan'.

Other researchers have proposed new 'micromodels' of specific motor functions, e.g. saccadic eye movements (Arbib & Dominey, 1995) and obstacle avoiding limb movements (Connolly & Burns, 1995). A new model which applies to general motor function, and which takes account of new knowledge about motor control, has been developed by Neilson, Neilson and O'Dwyer (1997).

Their model ('Adaptive Model Theory' [AMT]), is based on computational modeling of adaptive signal processing and adaptive control of dynamic systems. The central nervous system is characterized as an adaptive, optimizing controller. Motor responses are planned intermittently. These plans are the basis for a set of commands to be sent to relevant muscle groups. However the commands are modified, or 'fine tuned' by another process occurring between their being issued and the performance of the motor act. This intermediate process involves a check of how well the planned motor act will achieve the person's intended purpose, and the identification of any revisions that would make the motor act more effective. The planned action is fine tuned and then executed. Neilson et al. expanded their explanation of the system at several levels. See Figure 7 below.

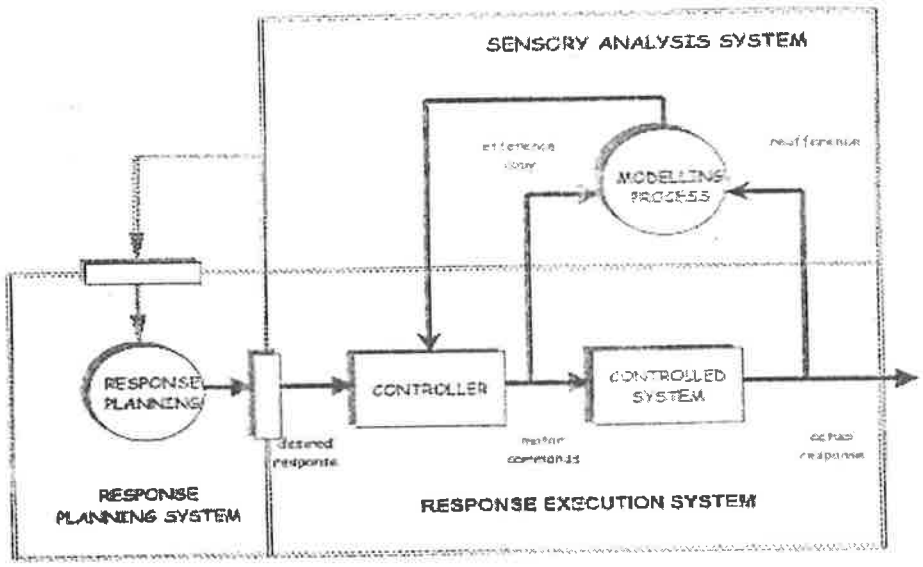

Figure 7
Schematic diagram illustrating the three processing systems.
These are the Sensory Analysis (SA) System, the Response Planning (RP) System, and the Response Execution (RE) system, which are hypothesized to operate independently and in parrallel. The rectangular blocks on the border of the RP system represent working memory buffers. Only modelling of the controlled system and adaptive tuning of the controller are illustrated. Other sensory inputs to the RP system are represented by the dashed line and open arrow. (Adapted from Neilson et al. 1997, p 348)

Neilson et al.'s model is complex, reflecting the larger amount of neurophysiological data that has been taken account of, in comparison to earlier models. Many of the concepts that form the basic building blocks of the model are themselves novel and complex, and the full description is presented within Neilson et al's paper. They concluded that dopaminergic striatal terminals modulate the through traffic of the matrix compartment. This is supported by the observations (Delong, Crutcher & Georgopolous, 1983; Grace & Bunney, 1985) that neurons in the substantia nigra pars compacta fire at very low frequencies and are not closely related to ongoing movements but are involved in the acquisition of learned movement (Kimura, Aosaki & Graybiel 1993) and respond to rewards such as food and drink (Schultz, Ljungberg, Apicella, Romo, Mirenowicz & Hollerman, 1993). Anatomical and physiological findings imply that distinct input/output subsystems in the striatum are modulated by different sets of dopaminergic neurons and participate in neural processing related to movement control. Evidence suggests that the modulatory loops are crucial in controlling the motor functions of the basal ganglia (Graybiel, 1990).

Neilson et al. do not acknowledge any inspiration from Marsden's earlier work. However, in some ways the detailed descriptions of how motor plans are refined, and the identification of likely neural substrates to these processes, could be described as an elaboration of Marsden's model. Marsden's conclusion that the basal ganglia are responsible for the initiation and automatic execution of the sequence of motor programmes, which have possibly been assembled in the frontal areas, is very compatible with the model of motor circuit operation proposed here (Section 2.8.1.2.1.). Likewise, Neilson et al.'s proposal, that output from structures connected to the basal ganglia (i.e. "modulatory loops") exercise critical control over the acquisition of learned movement, is directly compatible with the role proposed here for the cortico-basal-thalamic circuits.

A critical implication of the circuit concept is that lesions at any point along it should disrupt the overall function of the circuit. One overall function proposed here is control over complex programmes of motor activity.

The theoretical framework proposed by Neilson, Neilson and O'Dwyer (1997), more specifically the three broad divisions of sensory analysis, response planning and response

execution have been used to provide a structure for Table 5 (below). This is a sequential conceptualization of the process. Analysis of sensory data provides the basis for planning of a motor response, prior to its execution.

Table 5

Motor Related Activity and the Dorsolateral Prefrontal Circuit

Form of Motor Related Activity	**Level of Circuit**			
	Dorsolateral Prefrontal Cortex	***Caudate Nucleus***	***Pallidum/Substantia Nigra***	***Thalamus***
Sensory Analysis				
Attentional shift between goal directed physical activities		Connolly & Burns, 1995, Jackson & Houghton, 1995		
General level of sensory information relayed to the cortex				General thalamus, McCormick & Bal, 1994
Perception of position or movement in relation to the observer		HD -Brandt, 1991 Jacobs & Huber, 1992, Lange et al., 1995		
Response Planning				
Coding the preparation & organization of movements required for an action plan & keeping it goal focussed	Goldman-Rakic, 1995			
Movement programming,	Kolb & Milner, 1981			
Directing resources for actively processing incoming information, preparing an aroused organism to respond to a meaningful event				Thalamic intralaminar nuclei & ventral lateral nucleus – Crosson, 1992

Table 5 (Cont.)
Motor Related Activity and the Dorsolateral Prefrontal Circuit

Form of Motor Related Activity	Level of Circuit			
	Dorsolateral Prefrontal Cortex	*Caudate Nucleus*	*Pallidum/Substantia Nigra*	*Thalamus*
Response Execution				
Performance of Motor Sequences				
Sequential finger tapping		Taylor et al., 1987, Beneke et al., 1987, Robertson et al., 1990, Godefroy et al., 1992, Jones et al., 1992	PD Taylor et al., 1987, Beneke et al., 1987, etc	
Sequential left/right clenching			PD Horstinck et al., 1990	
Impaired learning of repeated motor sequences		HD, Willingham & Koroshetz, 1993		
Drawing between numbers		Taylor et al., 1987, Katz et al., 1989 etc		

Table 5 (Cont.)
Motor Related Activity and the Dorsolateral Prefrontal Circuit

Form of Motor Related Activity	Level of Circuit			
	Dorsolateral Prefrontal Cortex	*Caudate Nucleus*	*Pallidum/Substantia Nigra*	*Thalamus*
Response Execution				
Reaction time		HD Willingham et al., 1995 To random sequences, Kanazawa, 1986	PD, Rafal et al., 1984, Willingham et al., 1995	
Hand strength,	Leonard et al., 1988			
Saccadic eye movements	Morrow & Sharpe, 1995, Arbib & Dominey, 1995			
Simultaneous performance of two motor acts			PD -Kanazawa, 1986, Bennett et al., 1995	
Impairment of voluntary movements		Kanazawa, 1986		
New motor skills, learning to use a joystick		PET of intact normals, Brooks, 1995		
Construction of block patterns			Terman & Merrill, 1973, Hollander et al., 1993	
Writing & drawing			PD Lie-Ganchia et al., 1987 etc	
Driving simulator			PD Madeley et al., 1990	
Lesions result in Dystonia			Lee & Marsden, 1994	Lee & Marsden, 1994
Lesions result in Stereotypical behaviour			PD Ridley, 1994, Ebersbach et al., 1994	

Several observations can be made of the data compilation in Table 5. Only the caudate nucleus and the thalamus were associated with the sensory analysis stage. However, the lack of data among results set out in Table 5 probably does not eliminate the complete circuit having a role in sensory analysis. All four levels of the circuit were associated with both of the subsequent stages. Speculation about the dynamic interplay of component structures within basal cortical circuits, to produce overt motor activity, is beyond the scope of this thesis. The sheer extent and complexity of relevant data is considerable. Neilson et al.'s attempt is probably the best available to date (see below).

2.8.1.2.2. Executive Processing

2.8.1.2.2.1. Models of Executive Functioning

Fuster (1989) provided an impressive synthesis of considerable research data on the prefrontal cortex and executive functioning. The central tenet of his thesis is that the prefrontal cortex plays a critical role in the temporal structuring of behaviour. Essentially this consists of the integration of sensory information and motor acts into complex, novel and purposive behavioural sequences. The prefrontal cortex presumably achieves that synthetic function by coordinating three subordinate cognitive functions under its control: (1) a retrospective function of provisional short term memory, (2) a prospective function of preparatory set, and (3) the suppression of external and internal influences, including disruptive memories that interfere with the formation of behavioural structures. However Fuster argues that it is only the first two that are associated with the dorsolateral part of the prefrontal cortex.

Our most widely accepted model of executive processing comes from Norman and Shallice (Shallice & Burgess, 1991, 1996), see Figure 8. The system they described has been loosely linked to the frontal lobes.

Parks, et al. (1992) have developed a micro theory that falls within the broader category of executive functions. It attempts to explain neuropsychological findings related to Wisconsin Card Sorting Test (WCST) performance. In fact, the WCST has generated by far the most studies concerned with visual processing and the basal ganglia. Robbins and Rogers (2000) have argued that the WCST includes key functions of the basal-cortical circuits described by Alexander et al. (1986). The WCST involves sorting cards according to regularly changing criteria (categories), which must be learned by deduction. Parks, et al. (1992) proposed a single parallel distributed processing model to account for both WCST and verbal fluency task performance. The first stage was attention (either to card features –WCST, or to stored memories of previous memories of previous stimuli –verbal fluency task). The second stage was a special kind of instrumental learning ("the reinforcement-bias pathway"). The examiner's tolerance, praise, for certain types of words, and rejections of others on the verbal fluency task, being analagous to reinforcement of correct card placements and rejection of incorrect ones, as occurs on the WCST.

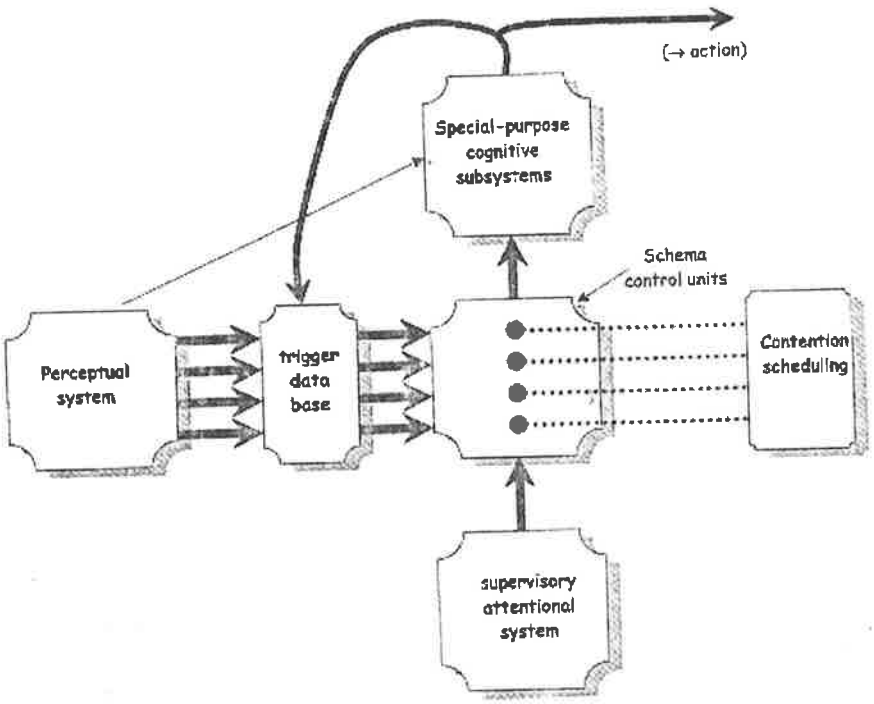

Figure 8
Norman & Shallice's Model of Executive Functions
(Adapted from Shallice & Burgess, 1991, p 127)

Shallice's model (above) is used to organize research findings linked to each level of the circuit. See Table 6.

Table 6
Executive Function Related Activity and the Dorsolateral Prefrontal Circuit

Executive Function Related Activity	Level of Circuit Involved			
	Dorsolateral Prefrontal Cortex	*Caudate Nucleus*	*Pallidum/Substantia Nigra*	*Thalamus*
Allocation of Processing Resources				
General level of sensory information relayed to the cortex				General thalamus, McCormick & Bal, 1994
Directing resources for actively processing incoming information, preparing an aroused organism to respond to a meaningful event				Thalamic intralaminar nuclei & ventral lateral nucleus – Crosson, 1992
Complex Attention				
Focussing on relevant channel only during a dichotic listening task			PD,-Sharpe, 1986, Yamada et al., 1990	
Simultaneous monitoring of different input channels in a divided attention task, response flexibility		HD Sprengelmeyer et al., 1995		

Table 6 (Cont.)
Executive Function Related Activity and the Dorsolateral Prefrontal Circuit

Executive Function Related Activity	Level of Circuit Involved			
	Dorsolateral Prefrontal Cortex	***Caudate Nucleus***	***Pallidum/Substantia Nigra***	***Thalamus***
Complex Attention (Cont.)				
Resolution of competing action alternatives	Roberts & Pennington, 1996			
Attentional shift between goal directed physical activities		Connolly & Burns, 1995		
Simultaneous performance of two motor acts			PD Kanazawa, 1986, Bennett et al., 1995	
Shift between two goal directed motor acts		Jackson & Houghton, 1995		
Directing attention toward sensory stimuli				Anterior nuclei principalis, Tasker & Kiss, 1995
Counting backwards by 3s from 100	Sasaki et al., 1994			
Counting backwards by 7s from 100 & WAIS-R Digit Span		Jacobs & Huber, 1992		

Table 6 (Cont.)
Executive Function Related Activity and the Dorsolateral Prefrontal Circuit

Executive Function Related Activity	Level of Circuit Involved			
	Dorsolateral Prefrontal Cortex	***Caudate Nucleus***	***Pallidum/Substantia Nigra***	***Thalamus***
Problem Solving				
Executive functions *	Tranel et al., 1994, Malloy & Richardson, 1994			
Top-down regulation of responses	Left hemisphere, Frith (2000)			
Tower of London problems		HD, Brandt, 1991, Jacobs & Huber, 1992, Lange et al., 1995	Saint-Cyr et al., 1992	
Small number of categories achieved & perseveration on the WCST			PD Giles, 1988, Perlmutter et al., 1985	
Construction of block patterns			Terman & Merrill, 1973, Hollander et al., 1993	
Writing & drawing			PD Lie-Ganchia et al., 1987 etc	
Driving simulator			PD Madeley et al., 1990	

**These have been defined as the combination of planning, decision making, judgement and self perception. Given the importance of these functions it is hardly surprising that they are the most extensively studied aspect of the frontal lobes (Tranel, Anderson & Benton, 1994; Malloy & Richardson, 1994). These include, integration of multimodal sensory input, generation of multiple response alternatives, maintainance of set and goal directedness, modification of behaviour as conditions change, and self evaluation.*

The compilation of data in Table 6 has highlighted important patterns across a diverse set of data. The data available do not indicate any differentiation in the contribution of dorsolateral prefrontal cortex, caudate, pallidum and substantia nigra to executive function. All three were involved in the broad categories identified across executive functioning tasks (complex attention and problem solving).

Figure 3 shows that the cortex (i.e. dorsolateral prefrontal area) sends excitatory input to the striatum (i.e., caudate nucleus). This responds by passing on inhibitory input to the pallidum and substantia nigra. Then in turn, this inhibitory input is relayed on to the respective thalamic nuclei (different nuclei for different basal cortical circuits). The input to the thalamic nuclei subsequently serves to moderate the mutual excitatory inputs exchanged directly between the thalamic nuclei and the dorsolateral prefrontal cortex.

Neither complex attention or problem solving were associated with the thalamus however, which challenges the circuit explanation of executive function. The thalamus provides the link between the pallidum/substantia nigra and the cortex. The role of the thalamus in executive functioning may be more distinctive, and more limited, compared to other links within this circuit (dorsolateral prefrontal). The thalamus is involved in allocation of processing resources. This is arguably associated with executive functions. With executive functions being a more complex form of cognition they probably require a higher volume of processing resources, and more intricate orchestration, in their allocation to a range of subsystems.

It is argued that the thalamus is possibly the first stage in performance of executive functions, allocating processing resources and priming the dorsolateral prefrontal cortex for more complex and intricate problem solving. As the latter mental processing proceeds, stimulation is fed back to its original source (thalamic nuclei) to allocate more resources, in what direction, identified by the cortex as necessary for the mental operation to be completed. (Like the university administrator [thalamus] funding a

research project, and the researcher [the dorsolateral prefrontal lobe], halfway into a project telling the university administrator that more funding is required if the project is to be completed, and what specific, unforeseen tasks are involved.) The dorsolateral prefrontal lobe stimulates the caudate nucleus into further subprocessing necessary for completing of a particular executive processing event. The data available do not allow us to differentiate between what the prefrontal dorsolateral cortex and the caudate nucleus contribute to executive processing. Then, the caudate nucleus, sends inhibitory input to the pallidum. To continue our university administration analogy, this is like the subcontractor (the caudate nucleus) submitting an account to the university finance department (the pallidum), who then relays on this inhibition to the thalamic nuclei, [don't over spend our finances!], which as a consequence moderates it's stimulation of the dorsolateral frontal lobe.

On this basis it is argued that executive functions are linked to the dorsolateral prefrontal circuit.

2.8.1.2.3. Memory Functions

2.8.1.2.3.1. The Psychology of Memory

The field has produced a particularly large volume of research data and efforts directed at theory construction. Comprehensive reviews of this literature have appeared (e.g., Wilson, 1987, Moscovitch, 1992, Baddeley, 1990, 1995). Crosson (1992) has strongly argued that Cowan's model (e.g., Cowan, 1988, 1996) is most successful in accounting for basal ganglia related memory phenomena. Cowan proposed that short term memory was just a subset of items from long term memory that were in a heightened state of activation. If such a subset of items are the subject of effortful processing, they are referred to as the focus of attention. All items entering short term memory were later available to "procedural memory", but only those that are effortfully processed were available to explicit memory. Brief sensory memory is distinct from short term memory, having a greater capacity, but feeds information into short term memory. The central executive is also distinct from long term memory but controls effortful processing.

2.8.1.2.3.1.1. Brief Sensory Storage

This system contains very brief sensory-memory stores which perform immediate processing of information received by sensory organs (e.g., iconic -visual, echoic -verbal). Baddeley (1984) has commented that a breakdown in such a system would however almost certainly manifest as a perceptual difficulty rather than a memory problem. The time-period over which information can be held in this store is so short (no more than seconds) that virtually all conventional memory tasks require additional aspects of memory.

2.8.1.2.3.1.2. Activated Memory

This (also called Short term, Working or Primary Memory) is a limited capacity, temporary store which holds information for a few seconds. It consists of a set of allied temporary storage systems, coordinated by a "central executive". Also involved is a series of slave systems consisting of the "articulatory loop" and the "visuo-spatial scratch pad". The former involves use of subvocal speech. Some features of visual neglect may reflect a deficit in the latter. Type of coding used tends to be acoustic or articulatory. This short term store, in its verbal form, is arguably very important to receptive language processing. Deficits in this process could conceivably present as language deficits. This issue has been treated at length by Cowan (1996).

Atkinson and Shiffrin (1968), in their very influential model of memory processes, argued that short term memory (STM) is quite distinct from long term memory, and that it is a prerequisite, earlier stage of mental processing, before information can be entered into long term memory. In Cowan's (1988) model on the other hand, short term memory is construed to be no more than that subset of long term memory items which are in a heightened state of activation at any one time. Incoming information typically activating related items from the long term store, thereby bringing them into short term memory. Another description, which further clarifies this cognitive function is by Tranel and Damasio (1995), 'a transient type of memory processing, of the order of seconds, in which we hold 'on-line' the relevant stimuli, rules and mental representations that are needed to execute a particular task' (p. 43). Exploration of the relationship between working

memory and other cognitive processes has been a most dynamic area of recent memory research (Logie & Gilhooly, 1998).

2.8.1.2.3.1.3. Long term or Secondary Memory

This store is far more durable, holding information for periods of minutes to decades. Capacity is very large and information is coded more by meaning than by speech characteristics. Greater 'depth of processing' ensures storage in long term memory. Various important subcategories of long term memory have been identified. In fact this has been among the more dynamic research areas in the memory field over the past decade (Baddeley, Wilson & Watts, 1995). It is most succinctly summed up in Squire's categories (1992):

In Squire's categories (see below), long term memory is categorized and subcategorized. The first distinction is between declarative (or explicit) memory and nondeclarative (or implicit) memory.

Memory
Declarative (Explicit)
- Facts (Semantic)
- Events (Episodic)

Nondeclarative (Implicit)
- Skills and habits
- Priming
- Simple Classical conditioning
- Nonassociative learning

Declarative memory can involve specific knowledge about the world, e.g. how many centimeters in a metre. This is the first subcategory of declarative memory called '***semantic memory***'. The other subcategory of declarative memory is '***episodic memory***'. The latter involves acquisition of a different type of facts, eg particular experiences or episodes. Grafman (1994) has proposed what appears to be a special type of this phenomenon. He has described it as a 'structured event complex' (SEC), which is a complex set of information about a single situation or environment, of significance to the person (eg having a shower). The long term memory of a normal functioning human includes multiple SECs, ranging from simple to complex. At the top of a person's

hierarchy of related SECs (e.g., all the recurring situations one might experience in a workplace) is a pre-eminent one, called a'Managerial Knowledge Unit' (MKU). This one is specifically involved with planning, social behaviour and the management of knowledge. Thus a person would possess multiple MKUs, also ranging from episodic and context dependent to more abstract and context free.

Nondeclarative memory, on the other hand involves four subcategories, independent of declarative memory. ***Priming*** reflects the phenomenon whereby someone who has heard or seen a fragment of something, for instance the first syllable of a word, or a piece of bark from a tree, can automatically call the complete item to mind. ***Procedural learning*** involves the acquisition of skills, like riding a bycycle or driving a car. ***Associative conditioning*** is another well known form of this type of memory, as in the case of salivation in response to hearing a bell that has been regularly associated with meal times. Finally there is the subcategory of ***evaluative conditioning***. People attach an affective value to specific stimuli, (e.g., a sense of how pleasant a piece of music is) on the basis of their experience of it.

2.8.1.2.3.1.3.1. Important Processes involved in Long Term Memory

Encoding: research has shown that greater 'depth of processing' of the material to be remembered enhances retention. For example, having a subject remember PET by asking 'Does the word PET fit in with the following sentence "Many people keep cats as a -----", involves much less time and effort than repeating "PET" over and over.

Storage: difficulties in devising the right types of research tasks have confounded attempts to find out why some people seem to lose information over time (Baddeley. 1995). One unresolved controversy involves whether forgetting reflects spontaneous decay of the memory trace or interference effects. The latter have been established as reliable and experimentally robust phenomena. At the very least these findings support the importance of 'storage' as an important part of the overall process of memory.

Retrieval: dissimilarity between the recall context and the original learning context has been found to impair retrieval but not recognition. Again, 'retrieval' is not fully understood, but current data suggest it is a distinct and important aspect of memory function.

Memory Failure: the 'human amnesic syndrome' has been associated with a range of neuropathology. This syndrome includes a variety of superficially similar memory impairments. However they fit two basic types, anteriorgrade amnesia and retrograde amnesia. Wilson (1987) has reviewed the seven different cognitive psychological explanations for the syndrome. They involved theories of how memory failure occurs, namely, encoding deficit theories, failure of effortful processing, failure of automatic processing, storage deficit theories, more rapid rate of forgetting, failure of consolidation and retrieval deficit hypotheses. However after examining studies performed on people suffering any of a wide range of neurological disorders, she concluded they did not satisfactorily account for all features of this syndrome.

Research findings for each level of the dorsolateral prefrontal circuit and the types of memory described above are summarized in Table 7.

Table 7

Memory Related Activity and the Dorsolateral Prefrontal Circuit

Form of Memory Related Activity	**Level of Circuit**			
	Dorsolateral Prefrontal Cortex	***Caudate Nucleus***	***Pallidum/Substantia Nigra***	***Thalamus***
Allocation of Processing Resources/Attention				
Directing attention toward sensory stimuli				Anterior nuclei principalis, Tasker & Kiss, 1995
General level of sensory information relayed to the cortex				General thalamus, McCormick & Bal, 1994
Directing resources for actively processing incoming information, preparing an aroused organism to respond to a meaningful event				Thalamic intralaminar nuclei & ventral lateral nucleus – Crosson, 1992
Activated Memory				
Word Lists etc				
Recall of digit sequences		HD, left hemisphere Crosson, 1992		
Monitoring and checking during retrieval of visual word lists	RH Fletcher et al., 1995			
Organization of word lists to facilitate recall	LH Fletcher, Shallice & Dolan, 1998			
Working Memory	LH Shallice (2001)		PD Gabrielli, 1995	

Table 7 (Cont.)
Memory Related Activity and the Dorsolateral Prefrontal Circuit

Form of Memory Related Activity	Level of Circuit			
	Dorsolateral Prefrontal Cortex	***Caudate Nucleus***	***Pallidum/Substantia Nigra***	***Thalamus***
Long Term Memory				
Declarative Memory: Semantic				
Verbal semantic retrieval				L&R Thalamus –Tranel & Damasio, 1995
Producing as many drawings as possible within a time limit	RH Jones-Gotman & Milner, 1977			
Generation of responses based on an internal data base, critical to retrieval			PD, Crosson, 1992	
Recalling as many words as possible within a time limit	LH Malloy & Richardson, 1994			
Word list generation		HD, Left hemisphere Crosson, 1992		
Effortful, meaning based retrieval of verbal and visual material	RH Shallice et al., 1998	HD, Right Only Crosson, 1992		
Deep encoding of verbal material	LH Kapur et al., 1994	HD, left hemisphere Crosson, 1992		
Retrieving lesser known quantitative information, working memory, maintenance of information over time, retaining information associated with specific items	Bilateral, Grafman, 1994			

Table 7 (Cont.)
Memory Related Activity and the Dorsolateral Prefrontal Circuit

Form of Memory Related Activity	Level of Circuit			
	Dorsolateral Prefrontal Cortex	***Caudate Nucleus***	***Pallidum/Substantia Nigra***	***Thalamus***
Long Term Memory (Cont.)				
Declarative Memory: Episodic				
Verbal episodic retrieval	RH, Shallice (2001)			L&R Thalamus –Tranel & Damasio, 1995
Holding representation of past events in awareness	Bilateral, Posner & Dehaene, 1994			
Estimation of how many times, or how long ago something occurred bilateral (temporal coding)	en this is encoded visuo-atially, Right Hemisphere anel & Damasio, 1995 When this is encoded verbally LH Tranel & Damasio, 1995 Bilateral Grafman, 1994	Crosson, 1992		Anterior parts of the thalamus – Bilateral, Shallice et al. 1998
Declarative Memory: Encoding, Storage & Retrieval				
Reduced long term memory capacity, weaker memory traces, faulty registration in the long term memory store		HD Crosson, 1992		
Strategies for searching long term memory, critical to retrieval		HD bilateral Crosson, 1992		

Table 7 (Cont.)
Memory Related Activity and the Dorsolateral Prefrontal Circuit

Form of Memory Related Activity	Level of Circuit			
	Dorsolateral Prefrontal Cortex	*Caudate Nucleus*	*Pallidum/Substantia Nigra*	*Thalamus*
Long Term Memory (Cont.)				
Nondeclarative Memory: Priming				
Cued recall	RH Cabeza et al. 1995			
Sentence recognition	RH Tulving et al. 1994			
Nondeclarative Memory: Procedural Memory				
Procedural Memory			PD Crosson, 1992; Tranel & Damasio, 1995	
General				
Verbal Memory				Left hemisphere, Tranel & Damasio, 1995
Visual Memory				Right hemisphere, Tranel & Damasio, 1995 Territory of the paramedian artery, bilateral, Bogousslavsky et al. 1988

The relative contribution of each level of the dorsolateral prefrontal circuit to memory function, is set out in Table 7. However, as outlined in 2.8.1.2.3.1 'The Psychology of Memory,' memory is a multi-facetted entity and various brain areas beyond this circuit are also associated with memory (Tranel & Damasio, 1995). Some with connections to circuit structures. It has already been argued that this same circuit is involved with executive processing (see section "2.8.1.2.2. Executive Processing"). Fuster (1989) has argued that some memory functions are integral to executive processing (see section "2.8.1.2.2.1. Models of Executive Functioning"). Thus it is plausible that the memory functions linked to this circuit are those most directly involved in executive processing. The only type of memory associated with all four levels of this circuit has been declarative, semantic, long term memory (cortex, caudate, pallidum/substantia nigra and thalamus, see Table 7). Other researchers have already attempted to speculate on how basal cortical circuits are involved in memory processing (Golman-Rakic,1995; Arbib & Dominey, 1995). These have been described earlier (see section "2.6.4.1. Micro Models of Memory Function and the Basal Ganglia.")

Figure 3 shows that the cortex (i.e. dorsolateral prefrontal area) sends excitatory input to the striatum (i.e., caudate nucleus). This responds by passing on inhibitory input to the pallidum and substantia nigra. Then in turn, this inhibitory input is relayed on to the respective thalamic nuclei (different nuclei for different basal cortical circuits). The input to the thalamic nuclei subsequently serves to moderate the mutual excitatory inputs exchanged directly between the thalamic nuclei and the dorsolateral prefrontal cortex.

The types of memory associated with the thalamus lack precision, suggesting that these are really indirect effects on other memory systems of thalamic lesions. The thalamus is involved in allocation of processing resources. Thus, like with executive functions, the thalamus is possibly the first stage in memory processing linked to this circuit, allocating processing resources and priming the dorsolateral prefrontal cortex for more complex and intricate remembering (e.g., Grafman's, 1994, "structured event

complexes"). The dorsolateral prefrontal lobe has been linked to a wide range of memory phenomena, including activated (primary or working) memory, long term memory (semantic, episodic and procedural). As the latter mental processing proceeds, stimulation is fed back to its original source (thalamic nuclei) to allocate more resources, in what direction, identified by the cortex as necessary for the mental operation to be completed.

The caudate nucleus was uniquely associated with storage and retrieval. It is plausible that this would be activated by excitatory input from the dorsolateral prefrontal lobe. Then, the caudate nucleus sends inhibitory input to the pallidum. A possible stimulus of inhibitory input from the caudate nucleus could conceivably be successful storage and retrieval support for cortical memory activity. The operation is successful, the mental event can be concluded. This inhibition is relayed on to the thalamus via the pallidum, for the apparent purpose of maintaining an equilibrium between excitatory and inhibitory input to the thalamus. It is difficult to speculate about the pallidum's role in this kind of process.

2.8.2 Lateral Orbital Frontal Circuit

2.8.2.1 *Functions Associated with the Cortical part of the Circuit (Lateral Orbital Frontal cortex)*

2.8.2.1.1. Attention

Distractibility has been linked to lesions in the lateral orbital frontal cortex (Grattan & Eslinger, 1991). However, Knight (1991) reported the opposite finding, so the picture is still unclear.

2.8.2.1.2. Motor

The lateral orbital frontal cortex has not been strongly linked in the literature to motor functions (Malloy & Richardson, 1994).

2.8.2.1.3. Visual Processing

One strong conclusion in relation to the lateral orbital frontal cortex is that it has a specialized role in activating the somatic states necessary for applying knowledge in the social domain (Damasio, Tranel & Damasio, 1990). Social knowledge is quite possibly represented visually in the minds of many people, and effective exercise of this specialized role probably involves the complex integration of external and internal events.

2.8.2.1.4. Memory

The lateral orbital frontal cortex is the only one of the areas of the frontal lobes linked to the basal-ganglia-cortical circuits of Alexander et al. (1986), that has not been clearly and specifically linked to distinctive memory difficulties.

2.8.2.1.5. Language

Fisher, Alexander, Esposito and Otto (1995) reported an association between orbital frontal lesions and transient or provoked confabulatory responses. ('Confabulation' being the report of fallacious memories, not simply due to error or lying, and usually in connection with amnesia.) This echoes an earlier conclusion by Kaczmarek (1984) to the effect that the left orbital region may be crucial for the development and maintenance of a verbal narrative.

2.8.2.1.6. Review of Functions associated with the Lateral Orbital Frontal Cortex: A summary

Application of social knowledge and coherent, socially appropriate verbal expression standout as the function associated with the lateral orbital frontal cortex. This is consistent with Cummings' (1998) conclusion about the role of this circuit. In summary, this research review has not revealed a strong and distinctive role for this circuit in cognition. Therefore, no cognitive skills are proposed as associated with this circuit.

2.8.3. The Anterior Cingulate Circuit

2.8.3.1. Functions Associated with Cortical part of the Circuit (Anterior Cingulate Cortex)

2.8.3.1.1. Attention

Grattan and Esslinger (1991) and Knight (1991) have argued that the anterior cingulate cortex is crucial for initiating and driving various systems, including attention. Posner and Dehaene (1994) reviewed PET studies of attention. They concluded that the anterior cingulate, in combination with the basal ganglia, was involved in the 'attentional recruitment and control of brain areas to perform complex cognitive tasks' (p. 76). PET studies requiring selection of targets from competing inputs resulted in the prominent activation of the anterior cingulate and left lateral areas. The intensity of the cingulate activation tended to increase with the number of targets in a set of stimuli, and to decrease with practice on a stimulus set. Lesions to the anterior cingulate gyrus can lead to akinetic mutism, in which the person fails to respond to environmental stimuli and remains inert. (Malloy & Richardson, 1994). The anterior cingulate cortex is now widely believed to be involved in the regulation of attention (Posner & DiGirolamo, 1998). However recently a controversy has developed about the specific nature of this regulation. Two rival theories have been proposed. One is the selection of environmental objects as triggers of or targets for actions. The other is detection and signalling of the occurrenc e of conflicts in information processing. (Botvinck, Nystrom, Fissell, Carter& Cohen, 1999).

2.8.3.1.2. Motor Function

Anterior Cingulate Cortex: Grattan and Eslinger (1991) have argued that this area of the frontal lobes may play a very strong activation role that is crucial for initiating and driving motor (as well as other) systems. Lesions to the anterior cingulate gyrus can also lead to akinetic mutism (Malloy & Richardson, 1994).

2.8.3.1.3. Visual Processing

Anterior Cingulate Cortex: Grattan and Eslinger (1991) have argued that this area of the frontal lobes may play a very strong activation role that is crucial for initiating and driving cognitive and attentional (as well as other) systems. Systems from both areas operate across all modalities, including of course, the visual one. Posner and Dehaene (1994) reviewed PET studies of attention. They concluded that the anterior cingulate, in combination with the basal ganglia, was involved in the 'attentional recruitment and control of brain areas to perform complex cognitive tasks' (p 76). PET studies requiring selection of targets from competing inputs resulted in the prominent activation of the anterior cingulate and left lateral areas. The intensity of the cingulate activation tended to increase with the number of targets in a set of stimuli and to decrease with practice on a stimulus set. Lesions to the anterior cingulate gyrus can lead to akinetic mutism, in which the person fails to respond to environmental stimuli and remains inert. (Malloy & Richardson, 1994).

2.8.3.1.4. Memory

Anterior Cingulate Cortex: Lesions within this region have been associated with apathy, akinesia, mutism and impaired complex attention (Damasio & Van Hoesen, 1983; Leimkuhler & Mesalam, 1985; Ross, Damasio & Eslinger, 1986). Grattan and Eslinger (1991) argued that these could potentially interfere with memory processing, 'particularly the motivation and effort needed for encoding of new information and experiences' (p. 308). A recent PET study reported that the left anterior cingulate cortex was significantly more activated during verbal semantic and verbal episodic memory retrieval tasks (Fletcher et al. 1995).

2.8.3.1.5. Language

Anterior Cingulate Cortex: Lesions to this region (left more than right) have been linked to mutism (Damasio & Van Hoesen, 1983; Gelmers, 1983; Jurgens & von Cramon, 1982; Ross, Damasio & Eslinger, 1986); the only form of language expression impaired being spontaneous speech production (not comprehension, writing or reading). Crosson (1992) proposed that the anterior cingulate cortex is involved in

holding language segments in a buffer for reference by subsequent segments of language. This is necessary for an individual to maintain coherent, continuity of verbal communication and thought. Wallesch and Papagno (1988) proposed that the anterior cingulate cortex, in concert with the anterior and posterior language cortex relayed information on to the striatum, then on to the globus pallidus, and further again to the ventral lateral and ventral anterior thalamus. This allows a selection to be made of the best lexical alternative among multiply generated choices. More specifically the anterior cingulate (and supplementary motor area) act to convey information about motivations internal to the organism.

2.8.3.1.5.1. Language and the General Frontal Lobes

Broca's area (sometimes referred to as the anterior language cortex) is within the frontal lobes. It forms the left lateral and inferior frontal region, or Brodmann's areas 44 and 45 in the lower tier of the premotor region. Its contribution to language is well known. Broca's aphasia results from lesions to that region, and is characterized by sparse, dysarthric and highly effortful speech, with generally preserved comprehension. Left lateral frontal lesions that are anterior and dorsal to Broca's area will result in transcortical motor aphasia. This is characterised by nonfluent or semifluent speech, with preserved repetition and echolalia (Grattan & Eslinger, 1991). Lesions to these sections of the right hemisphere have not been found to result in verbal deficits. An early review by Walsh (1987) of the frontal literature reported additional difficulties associated with left frontal lesions. They included a tendency towards perseveration or, even echolalia, and difficulties with repetition of word sequences and sentences. Another problem reported was a difficulty in reading certain words, specifically prepositions and terms of relationship, which are syntactically important.

2.8.3.2. Review of Functions Associated with the Anterior Cingulate Circuit: a summary

2.8.3.2.1. Attention

2.8.3.2.1.1. An Information Processing Model of Attention

Theories of attention are extensive (Parasuraman, 1998). The currently, most highly regarded theory of attentional function among neuropsychological researchers comes from the work of Posner and associates (e.g., Posner & Rafal, 1987; Posner & Dehaene, 1994). A significant body of research into attentional mechanisms associated with the basal ganglia has been specifically inspired by their model (e.g., Wright, Burns, Geffen & Geffen 1990; Sprengelmeyer, Lange & Homberg, 1995; Bennett, Waterman, Scarpa & Castiello, 1995). One of the more lucid renditions of the model comes from Posner and Rafal. Another, possibly complementary, model of attentional control has been advocated by Norman and Shallice (Norman & Shallice, 1980; Shallice, 1988). See Figure 8 in section 2.8.1.2.2.1. 'Models of Executive Processing'. This model includes two basic 'control mechanisms' involved in self monitoring of activities. They are the *contention scheduler,* operated by automatic and direct priming of stored knowledge by thinking or environmental stimuli (eg stopping at a red traffic light). Then there is the *supervisory attention system*, analagous to deliberate choice making, which can override the automatic (almost relexive) contention scheduler, eg choosing not to answer the phone in another person's office. This could be argued to correspond to the Preconscious and Conscious forms of selective attention in Posner's model, above.

2.8.3.2.1.1.1. The Psychology of Visual Neglect

Another visual processing disorder identified following basal ganglia lesions has generated quite a separate theoretical literature. That disorder is visual neglect, otherwise characterised as a set of related deficits, all of which demonstrate a predominantly lateralized problem of attention when using and working in space (Robertson & Halligan, 1999). Data and the five main theories of this phenomenon have been reviewed by various authors (e.g., Bradshaw & Mattingley, 1996, Halligan & Marshall, 1994, Heilman Watson & Valenstein, 1993). Bradshaw and Mattingley

concluded that the rival models of unilateral neglect could be classified according to the level where the deficit is believed to occur within cognitive processing. One set of models posits that the critical deficit is disruption of attentional mechanisms. The other set posits that the mechanisms disrupted involve the cognitive representation of space. This controversy is not yet resolved. Therefore selection of a model for interpretation of neuropsychological findings will be based on the fact that one (Heilman's) seems to give more prominence than the others to the role of basal cortical circuitry. Heilman, Watson and Valenstein (1993) proposed that sensory neglect is an attentional arousal disorder induced by dysfunction in a cortico-limbic reticular formation loop. They also raised the interesting possibility that bilateral neglect may give rise to akinesia, or 'akinetic mutism' (Akinesia [or disorder of voluntary movement] being the first disorder associated with basal ganglia disorders.).

Findings relating to attention for each level of the anterior cingulate circuit are set out according to Posner's theory of attention in Table 3 (in section '2.6.1. Attention').

Table 8
Attention Related Functions and the Anterior Cingulate Circuit.

Form of Attention Related Activity	Level of Circuit			
	Anterior Cingulate Cortex	*Ventral Striatum*	*Pallidum/Substantia Nigra*	*Thalamus*
I Alertness				
A. Tonic Arousal				
General level of sensory information relayed to the cortex				General thalamus, McCormick & Bal, 1994
B. Phasic Arousal				
Reaction time			PD Rafal et al. 1984	
Directing attention to sensory stimuli				Anterior nuclei principalis, Tasker & Kiss, 1995
Directing resources for actively processing incoming information, preparing an aroused organism to respond to a meaningful event				Thalamic intralaminar nuclei & ventral lateral nucleus – Crosson, 1992

Table 8 (Cont.)
Attention Related Functions and the Anterior Cingulate Circuit.

Form of Attention Related Activity	Level of Circuit			
	Anterior Cingulate Cortex	*Ventral Striatum*	*Pallidum/Substantia Nigra*	*Thalamus*
II Selective Attention				
A Preconscious				
Attentional recruitment and control of brain areas to perform complex cognitive tasks, Initiating and driving systems	Posner & Dehaene, 1994 Grattan & Eslinger, 1994, Knight, 1991			
Attending despite distractions	Grattan & Eslinger, 1994			
Attention to objects within lateralized divisions of the visual field (Lesions associated with Visual Neglect)		CVA in the R basal ganglia, Ferro et al. 1987, Levine et al. 1988	PD sufferers with right side motor signs, Villardita et al. 1983	Hemi neglect, territory of the paramedian artery, Bogousslavsky et al. 1988
B Conscious				
Deliberate orienting to object of attention			Visuo-spatial target PD, Sharpe, 1986	
Resonding to emotion provoking or novel stimuli		Rolls & Johnstone, 1992		
Lesions associated with: apathy, akinesia, mutism and impaired complex attention.	Posner & DiGirolamo, 1999 Left Hemisphere, Damasio et al. 1983, Leimkuhler et al. 1985, Ross et al. 1986, Malloy & Richardson, 1994			

Interpretation of findings in relation to Posner's theory of attentional functions is facilitated by Table 8. Essentially only the thalamus has been implicated in the first stage, alertness. The picture is different for selective attention, which forms the second stage. All levels of the circuit have been associated with the preconscious phase of selective attention, assuming the phenomenon of visual neglect can be interpreted as a disorder of preconscious attention.

All levels of the circuit other than the thalamus have also been associated with the conscious phase of selective attention. This is similar to the relationship between the dorsolateral prefrontal circuit and executive functions. The data available do not indicate any differentiation in the contribution of Anterior Cingulate cortex, ventral striatum, and the third level (pallidum and substantia nigra) to attention. All three were involved in conscious selective attention. Conscious selective attention was not associated with the thalamus however, which challenges the circuit explanation of attention. The thalamus provides the link between the pallidum/substantia nigra and the cortex. The role of the thalamus in attention may be more distinctive, and limited to allocation of the processing resources required for attention. It is on this basis that the anterior cingulate circuit is considered important to conscious and preconscious selective attention.

However, this is not to say that other systems are not as important to attentional processes. For instance, two pairs of researchers (Jackson & Houghton, 1995; Heilman & Valenstein, 1993) have proposed other models of cortical/subcortical networks to account for the type of visuo-spatial attention involved in visual neglect (see section 2.8.3.2.1.1.1 below). Systems outside of the anterior cingulate circuit have been implicated. One of these is the striatum (caudate nucleus and putamen). Attentional deficits have been associated with early stage Huntington's disease, for example (Brandt & Butters, 1996). Enlargement of the caudate nucleus among children and adolescents, both right and left, has been found in association with attention deficit disorder with hyperactivity (Mataro, Garcia-Sanchez, Junque, Estevez-Gonzalez & Pujol, 1997). This has been interpreted as a evidence for that disorder being a result of

caudate nucleus dysfunction, particularly of the right side. Furthermore several recent authors have argued on the basis of neuropsychological findings that attention deficit disorder with hyperactivity reflects a disruption of frontal striatal circuits (e.g., Williams, Stott, Goodyer & Sahakian, 2000). Then there is the long standing association of the right parietal lobe with visual neglect (Heilman & Valenstein, 1993). Exploration of the full set of structures associated with attention is beyond this thesis. It is argued on the basis of evidence considered, that the anterior cingulate circuit is one structure associated with attention, so it will be the one investigated.

2.8.3.2.2. Language and the Anterior Cingulate Circuit

Presentation of models of language processing is included in relation to another set of circuitry (see '2.8.4. Other Language Related Circuitry').

Table 9

Language Related Functions and the Anterior Cingulate Circuit.

Form of Language Related Activity	**Level of Circuit**			
	Anterior Cingulate Cortex	***Ventral Striatum***	***Pallidum/Substantia Nigra***	***Thalamus***
Comprehension				
Impaired comprehension of emotional tone of language			LH Crosson, 1992	
Processing of sentences with metaphoric, ambiguous or implied information, or with complex grammar			PD, Murray, 2000	
Verbal comprehension			Left Hemisphere, CVA studies, Crosson, 1992	Audio-verbal incomprehension as part of thalamic aphasia, Crosson, 1992
Expression				
Inability to generate responses based on an internal data base leading to faulty retrieval			PD, Crosson, 1992	
Naming			PD Crosson, 1992	
Semantic paraphasia,			Left Hemisphere, Crosson, 1992	As part of thalamic aphasia, Crosson, 1992
Use of complex syntax			Left Hemisphere, PD Crosson, 1992. PD, Murray, 2000	
Lesions resulting in nonfluent aphasia			Left Hemisphere, Review of CVA studies, Crosson, 1992	
Ability to hold language segments in a buffer for reference by subsequent segments, to maintain continuity of thought and communication.	Crosson (1992)	Nucleus Accumbens, Crosson, 1992.		

All levels of the circuit have been implicated in aspects of verbal expression, albeit different aspects. Circuit disruption therefore would be expected to disrupt verbal expression.

2.8.4. Other Language Related, Cortical Basal Circuitry

2.8.4.1. Models of Language Processing

The cortical basal circuitry considered so far has been limited to three of the five identified by Alexander et al. (1986). These three were the dorsolateral prefrontal circuit, the lateral orbital frontal circuit and the anterior cingulate circuit. The cortical sections of all three involve a part of the frontal/prefrontal lobes. However other authors have argued that other cortical basal circuitry also serve as the substrate for important aspects of cognition. These include, attention (Houghton & Jackson, 1995, see above), language (Crosson, 1992, see below; Bradshaw & Mattingley, 1995) and memory (also Crosson, 1992, see below). Areas of the cortex outside of the frontal lobes, linked in functional systems with basal ganglia structures, include Broca's and Wernicke's areas for language, the right parietal lobe for visual neglect, (hence attention) and the temporal lobes for memory. Hardly surprising given that those brain areas were once considered the main ones serving those respective functions (Heilman & Valenstein, 1993). The data gathered for this thesis allow one other of these sets of circuits to be examined, the one related to language.

Attempts to map the underlying processes in the comprehension and production of language have a long history (Caplan, 1994). Caplan's own models of linguistic processing are an excellent example of the more recent style of language processing models. Theory of the role of the basal ganglia in language is more advanced than theory development in any other area of mental processing and the basal ganglia. In fact there is not one but three rival theories. Alexander, Naeser and Palumbo (1987) have proposed the *Subcortical Pathways Model.* This holds that certain neural pathways connecting cortical areas involved with language travel through the

subcortical region of the brain. Hence, damage to those pathways can disrupt functioning of those cortical language involved regions, but the striatum itself is not involved in language in any significant way.

Then Wallesch and Papagno (1988) have proposed a second model, the *Lexical Decision Making model.* They argued that the striatum (among other subcortical structures) is involved in lexical decision making between alternatives generated within cortical areas. Following a very balanced and detailed evaluation of these alternatives, Crosson (1992) still felt the need to advance a third model (*'The Response-Release/Semantic-Feedback Model of Language'*). This model is developed across several publications (Crosson, 1985; Crosson & Early, 1990; Crosson, 1992). Crosson's synthesis is probably by far the most important single contribution to this literature.

Crosson's view (which he describes as *'The Response-Release/Semantic-Feedback Model of Language'*) is that cortico-striato-pallido-thalamo-cortical loops are involved in regulating the release of cortically formulated segments, that the thalamus is involved in tonic arousal of anterior language cortex, and that the cortico-thalamo-cortical pathways serve to transfer information from anterior to posterior language cortex (Broca's and Wernicke's areas respectively) and vice versa. (Crósson & Early, 1990).

2.8.4.2. Research Findings

A noteworthy representation of the comparative contributions of different brain areas to important aphasic syndromes was provided by Metter (1992). Broca's aphasia showed the greatest hypometabolism in the head of the caudate nucleus. The frontal regions are the most markedly depressed in Broca's aphasia as compared to Wernicke's and conduction aphasias. Wernicke's aphasia occupies a middle ground between Broca's and conduction aphasia with some left prefrontal metabolism that tends to be mild to moderate in severity. Metter concluded from these studies that the temporo-parietal cortex is primarily responsible for the language abnormalities associated with these types of aphasia, and the subcortical frontal system seems to be

associated with the modulation and modification of the underlying language problems.

2.8.4.2.1. Anterior Language Cortex

The frontal opercular region in the dominant frontal lobe, or the anterior language cortex, has classically been identified as Broca's area (Benson, 1993). Lesions in this area have been associated with nonfluent aphasic output and disordered repetition.

2.8.4.2.2. Posterior Language Cortex

This corresponds to an area of the left temporal lobe, particularly the auditory association cortex of the posterior-superior portion of the first temporal gyrus (commonly referred to as Wernicke's area, Benson, 1993). The language impairments associated with lesions in this area have been well known for many years. They include quite marked disorders of comprehension, repetition and naming, that are not helped by any kind of prompting.

2.8.4.2.3. Language and the Basal Ganglia

Crosson's (1992) review included an extensive discussion of research up to that date. His conclusions from CVA studies were that lesions to the head of the caudate nucleus and the globus pallidus tended to result in nonfluent aphasia and severe reduction in verbal comprehension. Lesions to the globus pallidus tended to produce the additional result of impaired repetition and semantic paraphasia. Results of PET studies are less clear. While there is some confirmation of the importance of the head of the caudate nucleus to language production, it is unclear just what type of language function is involved. Nor have PET studies provided unequivocal indications of the role played by other subcortical structures in language. Other important work has been performed with Parkinsons and Huntington's Disease subjects. Both groups have shown difficulties with naming tasks, and decreased use of complex syntactic structures. Crosson made a call for 'Future studies to explore the use of complex syntax in nonthalamic subcortical aphasias' (Crosson, 1992, p.78). HD subjects have shown the additional deficit of below normal performance

at word list generation. A final comment by Crosson on the data, with interesting implications for the circuit concept, was that 'it would appear that small lesions limited to one structure of the basal ganglia do not cause severe or lasting aphasia... One pertinent question to be addressed is whether the nervous system compensates easily for small lesions in the cortex, white matter, or basal ganglia, or whether some other process explains these phenomena.' (p.78-79). A possible explanation is that connections between one circuit and another may allow a damaged circuit to continue to function through bypassing its defective elements by means of longer, alternative chains of linked structures.

Starkstein, Federoff, Price, Leiguard and Robinson (1994) investigated a different aspect of the basal ganglia and language. They found right hemisphere basal ganglia lesions associated with impaired comprehension of the emotional tone of spoken language.

Finally, Crosson's conclusions are by no means universally accepted. For instance Alexander, Naeser and Palumbo (1987), Alexander and Naeser (1988) dispute the basal ganglia having any role in language processing. One of the most eminent contemporary aphasiologists in recent times, Harold Goodglass (1993) concluded that 'they (the basal ganglia) play little or no role in the symptomatology of aphasia' (p. 46).

2.8.4.2.5. Review of Language Functions & Other Language Related Circuitry: A Summary

Presentation of models of language processing is included in relation to another set of circuitry (see '2.8.4. Other Language Related Circuitry'). A summary of studies specifically related to the other language related circuitry proposed by Crosson (1992) in Table 10.

Table 10
Language Related Functions

Form of Language Related Activity	Level of Circuit				
	Anterior Language Cortex	Posterior Language Cortex	Striatum	Pallidum/Substantia Nigra	Thalamus
Memory Processes closely related to Language usage					
Deep encoding of verbal material			Left hemisphere, head of Caudate Nucleus (review of CVA studies, Crosson, 1992)		
Inability to generate responses based on an internal data base leading to faulty retrieval				PD, Crosson, 1992	
Verbal Comprehension					
Impaired comprehension of emotional tone of language				LH Crosson, 1992	
Processing of sentences with metaphoric, ambiguous or implied information, or with complex grammar			HD, Murray, 2000	PD, Murray, 2000	
Verbal comprehension		Left hemisphere as in Wernicke's aphasia (Benson, 1993)	Left hemisphere, head of Caudate Nucleus (review of CVA studies, Crosson, 1992)	Left Hemisphere, CVA studies, Crosson, 1992	Audio-verbal incomprehension as part of thalamic aphasia, Crosson, 1992

Table 10 (Cont.)

Language Related Functions

Form of Language Related Activity	Level of Circuit				
	Anterior Language Cortex	**Posterior Language Cortex**	**Striatum**	**Pallidum/Substantia Nigra**	**Thalamus**
Verbal Expression: formulation prior to Articulation					
Monitoring of semantic & phonological aspects of verbal expression, before articulation		Wernicke's area, Bradshaw & Mattingley, 1995			Thalamic pathways (Bradshaw & Mattingley, 1995)
Monitoring of phonological aspects of verbal expression before articulation		Wernicke's area and connection with Broca's area (arcuate fasciculus) Bradshaw & Mattingley, 1995			
Formulation of phonological aspect to verbal expression	Broca's area, Bradshaw & Mattingley , 1995				

Table 10 (Cont.)
Language Related Functions

Form of Language Related Activity	Level of Circuit				
	Anterior Language Cortex	Posterior Language Cortex	Striatum	Pallidum/Substantia Nigra	Thalamus
Verbal Expression: articulation					
Verbal repetition				Left hemisphere, Crosson, 1992	
Naming			HD, Crosson, 1992	PD Crosson, 1992	
Word list generation			HD, Crosson, 1992		
Use of complex syntax			Left Hemisphere, HD Crosson, 1992 HD, Murray, 2000	Left Hemisphere, PD Crosson, 1992	Semantic paraphasia occurring as part of thalamic aphasia, Crosson, 1992
Length of utterance			HD, Murray, 2000	PD, Murray, 2000	
Lesions resulting in nonfluent aphasia	Broca's aphasia		Left hemisphere, head of Caudate Nucleus (review of CVA studies, Crosson, 1992)	Left Hemisphere, Review of CVA studies, Crosson, 1992	

While areas involved with verbal comprehension do not include the anterior language cortex, it is noteworthy that all other areas included in this circuitry are, and they represent all levels of this circuit. Therefore, it is arguable that this complete circuit (excluding the anterior language cortex) is important to verbal comprehension.

All levels of this circuitry are involved with verbal expression, in some form. Thus it is also arguable that the complete set of circuitry is important to verbal expression.

3. LITERATURE REVIEW: CONCLUDING COMMENTS

The literature relevant to this thesis is extensive and complex. Neuropsychological research is a difficult undertaking. A vast number of studies over the last 30 years have produced a vast set of findings, which all but defy any attempt at integration. Clearly each of our current neuro-investigative techniques (e.g., PET, MRI and CT) have distinctive and critical limitations. Results from different studies of particular structures are frequently inconsistent. Neuropsychological assessment tasks rarely involve just one or two cognitive processes. Deciding which process is impaired, in the presence of a lesion, to reduce someone's overall score is often subjective. These shortcomings in our methodologies will compound each other. They may account for the diversity of functions linked to particular structures, and suggest one should be very cautious in accepting such diverse research conclusions. This phenomenon has seriously impeded our quest to understand brain functions. The fundamental importance of brain function to understanding of human behaviour however, means that we cannot throw up our hands and walk away from the endeavour.

First of all we have documentation of the set of interconnections between these neurological structures, that correspond to circuit configurations. This has been established by extensive neurological investigation, e.g. dissection and animal studies. Then we know that cognitive functions have been linked to the basal ganglia and to the cortex and certain neuropsychological functions can be associated with several (if not

all) structures making up individual basal cortical circuits. We know about the dynamic balance of excitatory and inhibitory input among circuit structures, and the direction and type of this input between any pair of those structures. This provides a starting point for speculation about corresponding information processing models.

The literature review has attempted to comprehensively list, and integrate our conception of these functions linked to the basal cortical circuits. The position is held by the author of this thesis that it is plausible to argue some degree of consistency across functions linked to elements within particular circuits, thereby suggesting that those circuits, rather than individual components, are critical to those functions. These hypothesized 'areas of consistency' have been able to be tested against test results gained from subjects with lesions at various points across those circuits. They are summarized in section 4.1.6. Testing results were considered systematically, over a series of studies.

4. PROJECT OBJECTIVES

Previously it was believed that functional systems including the basal ganglia were largely involved with motor functions only. Now there is some acceptance that the function of systems/circuits that include them may extend to mental activities of a 'higher' cognitive nature. The central goal of this thesis is to identify cognitive skills associated with these. The circuits of interest to this project were:

Left Dorsolateral circuit
Right Dorsolateral circuit
Left Anterior Cingulate circuit
Right Anterior Cingulate circuit
Left Lateral Orbitofrontal circuit
Right Lateral Orbitofrontal circuit
Other Language Related circuitry

From comprehensive examination of research into cognitive functions and elements of these circuits, it has been concluded that specific types of cognition are mediated by specific circuits. In summary, the types of cognition and associated circuits are:

Type Cognition	**Circuit**
Attention: Selective, Preconscious	Anterior cingulate circuit
Attention: Selective Conscious	Anterior cingulate circuit
Complex Programmes of Motor Activity	Dorsolateral prefrontal circuit
Declarative Semantic Memory	Dorsolateral prefrontal circuit
Executive Functions	Dorsolateral prefrontal circuit
Verbal Comprehension	Other left hemisphere, language-related circuitry
Verbal Expression	Anterior cingulate circuit Other left hemisphere, language-related circuitry

There is a considerable number of published assessment procedures relevant to the types of cognition listed above. Selection of instruments to be used in this project was based on certain key principles. Those were:

- Some cognitive impairment is very subtle. Consequently it is valuable if sensitivity of the potential testing task has already been established in previous research.

- Use of tests that are already the subject of an extensive research literature allows comparison with known consequences of a range of brain impairment (e.g., in terms of "cut-offs" on performance indices or qualitative descriptions of test performance).

- To facilitate interpretation of results, it is desirable that tasks chosen include comprehensive coverage of processing stages for a relevant area of cognition (e.g., executive processing).

However, it is widely recognized that there are very few 'pure' measures of a cognitive domain. Usually there will be other types of cognitive impairment that could result in poor performance of a given task. For example, one time honoured executive assessment task is the Rey-Osterrieth Figure. Apart from impaired executive functioning, the types of impairment that could result in poor performance include reaction time, attention, complex programmes of motor activity, visual perceptual and possibly even aphasic problems. The fact that a particular test is affected by a lesion location in previous research does not mean that the test is specifically affected by that lesion location per se. The variety of processing requirements typically involved means that a variety of lesion locations could affect test performance. The precise cognitive impairments of the lesion subjects have been explored through close comparison of tests (associated with a particular lesion), with other tests from the same category of cognition, not associated. Impairments so identified have been further scrutinized for any correspondence to elements of models of cognitive processing, in an attempt to establish the role of a circuit in that form of processing. The types of cognitive processing of interest to this study were sevenfold. They included selective attention (preconscious & conscious), complex programmes of motor activity, declarative semantic memory, executive functions, verbal comprehension and expression. How the tests selected reflect each particular type of cognition will be demonstrated for each one in turn.

4.1. TESTS

4.1.1. Neuropsychological Tests of Attention

When this study was planned and commenced, we did not have an available, developed, test battery which systematically evaluated the attentional processes identified by Posner and associates or Jackson and Houghton (1995). Since this project

first commenced, a series of studies have appeared using Posner's covert orientation of attention task (e.g., Wright et al., 1990; Bennett et al., 1995). However, these research findings and this equipment were not available when the project was first planned and commenced. Hence it has not been used. What was available was a collection of established testing tasks, with major attentional requirements, that many researchers and clinicians had repeatedly demonstrated were sensitive to brain impairment. Given the subtle nature of some brain impairment, established sensitivity is important. Use of tests which are already the subject of an extensive research literature allows comparison with known consequences of a range of brain impairments.

Selective attention has two levels, preconscious and conscious. It is argued that visual neglect is a manifestation of impaired preconscious selective attention. Thus assessment of this phenomenon would be one way to investigate this hypothesized circuit function. However many of the research findings leading to this conclusion only became available long after data gathering was largely complete, when it was no longer possible to include extra assessments in the project battery.

Measures chosen for the project battery with significant selective attention requirements were:
Computer task
Trail Making Test, Part A & Part B
WAIS-R Digit Symbol

The relevant processing requirements of these tasks are presented in Table 11.

Table 11
Attention Processes and Tests Chosen to Assess Them

Attention Related Process	**Tests**		
	Computer Task	***Trail Making Test, Part A & B***	***WAIS-R Digit Symbol SubTest***
I Alertness (Tonic & Phasic Arousal) All three tasks require basic alertness in both forms (tonic & phasic arousal).			
II Selective Attention **A. Preconscious**			
Attentional recruitment and control of brain areas to perform complex cognitive tasks, Initiating and driving systems	Basic initiation and driving of concentration was intrinsically involved.	Basic initiation and driving of concentration was intrinsically involved.	Basic initiation and driving of concentration was intrinsically involved.
Attending despite distractions	No specific distractions were built into task. This was not involved.	The automatic impulse to follow one series was a distraction. Hence this was involved.	While not distracting in the usual sense, the other arbitrary correspondences between number and symbol made it a complicated, hence 'distracting' task. This was a related, if slightly different requirement.
Attention to objects within lateralized divisions of the visual field (Lesions associated with Visual Neglect)	As subject had to respond to visual stimuli scattered across a computer screen both halves of the visual field are involved.	As subject had to respond to visual stimuli scattered across an A4 page, both halves of the visual field are involved.	As subject had to respond to visual stimuli set out in rows across a portrait orientation A4 page, both halves of the visual field are involved.

Table 11 (Cont.)
Attention Processes and Tests Chosen to Assess Them

Attention Related Process	Tests		
	Computer Task	***Trail Making Test, Part A & B***	***WAIS-R Digit Symbol SubTest***
B Conscious			
Deliberate orienting to object of attention	Deliberate orientation to stimuli critical, hence this was involved.	Deliberate orientation to stimuli critical, hence this was involved.	Deliberate orientation to stimuli critical, hence this was involved.
Resonding to emotion provoking or novel stimuli	Emotion-provoking stimuli were not involved. Hence this was not a feature of the task.	Emotion-provoking stimuli were not involved. Hence this was not a feature of the task.	Emotion-provoking stimuli were not involved. Hence this was not a feature of the task.
Lesions associated with: apathy, akinesia, mutism and impaired complex attention.	Complex attention (dynamic oscillation of attention between more than one object) was clearly involved (moving circle and square being moved with the joystick).	Subject had to alternate attention between two series, i.e., exercise complex attention. This was involved.	Subject had to switch between several arbitrary correspondences, to write symbols next to numbers at speed. Hence this was involved.

Table 11shows the essential elements of attentional processing were well covered. It is only emotion-provoking stimuli which were are not adequately represented among the tasks. However, none of the three measures in Table 11 are 'pure' measures of selective attention. Other types of impairment could result in poor performance on those tasks, e.g., reaction time, performance of complex motor programmes, executive processing, visual perceptual and possibly even aphasic problems. Likewise, several other tests in the project battery also involve selective attention, if not primarily. Impairment of that function could interfere with performance of those tasks also. Tests in the latter category include:

HLLST Auditory/Visual Comprehension
HLLST Reading Comprehension
HLLST Association Naming subtest
Rey-Osterrieth Figure, Copy & Recall
Story Recall, Immediate & Delayed
Wisconsin Card Sorting Test -Revised
Picture Recognition Task
Porteus Mazes

4.1.2. Neuropsychological Tests of Ability to Perform Complex Programmes of Motor Activity

At the present time we do not have an available, developed, motor skills test battery which systematically evaluates the components of motor function identified by Neilson et al. From a strict, research methodology point of view, developing such a battery would be the next step in pursuing this general line of research. Such a project is beyond the scope of this thesis. The resulting test battery would in all likelihood be time consuming for subjects. What we do have is a collection of established motor skills testing tasks, which many researchers and clinicians have repeatedly demonstrated to be sensitive to brain impairment.

Measures chosen for the project battery that involved complex programmes of motor activity were:

Computer task
Trail Making Test, Part A & Part B
Rey-Osterrieth Figure, Copy & Recall
WAIS-R Digit Symbol

Table 12 provides a qualitative examination of how each of these motor tasks assesses complex programmes of motor-related activity. Sampling of relevant motor-related activity was extensive, and these tasks were therefore considered a reasonable assessment of this type of processing. However, none of the measures listed above are 'pure' measures of this ability. Other types of impairment could result in poor performance on those tasks, e.g., delayed reaction time, attention, executive processing, visual perceptual and possibly even aphasic problems. Likewise, another test in the project battery also involved complex programmes of motor activity, if not primarily. Impairment of that function could interfere with performance of this task also (Porteus Mazes).

Table 12
Motor Related Processes and Tests Chosen to Assess Them

Form of Motor Related Activity	Tests & Motor-Related Activities Involved			
	Computer Task	**Rey-Osterrieth Figure, Copy & Recall**	**WAIS-R Digit Symbol**	**Trail Making Test, rt A & B**
Sensory Analysis				
Attentional shift between goal directed physical activities	Not clearly involved	Not clearly involved	Possibly involved when subject has to find symbol corresponding to different numbers	Probably involved when subjects shifts between letter & number series (Part B only)
General level of sensory information relayed to the cortex	As subject visually tracks target on screen and manipulates joystick from visual knowledge, clearly a feature	As subject must analyze visual figure, and draw it, this was clearly involved	Subject must learn correspondences between symbols that they write This is clearly involved	Subject must follow visuo-spatial trail by drawing connecting lines on paper, - clearly involved
Perception of position or movement in relation to the observer	Subject must deduce how joystick movement corresponds to movement on screen, hence this is involved	Subject must manipulate pencil to replicate stimulus figure, hence this is involved	Subject must write specific visual symbols, hence must perceive correct figure orientation	Subject is connecting small circles scattered over an A4 page, orientation of lines, hence this skill not strongly involved

Table 12 (Cont.)
Motor Related Processes and Tests Chosen to Assess Them

Form of Motor Related Activity	Tests & Motor-Related Activities Involved			
	Computer Task	**Rey-Osterrieth Figure, Copy & Recall**	**WAIS-R Digit Symbol**	**Trail Making Test, rt A & B**
Response Planning				
Coding the preparation & organization of movements required for an action plan & keeping it goal focussed (i.e., "Movement Programming")	Controlling joystick requires organized movement, staying on target is the goal This is clearly involved	Drawing detailed stimulus figure, accurately, requires an organized approach. This is clearly involved.	Writing the appropriate symbol requires quick organization of less complex movement	Following the sequence of numbered circles requires quick organization of less complex movements
Directing resources for actively processing incoming information, preparing an aroused organism to respond to a meaningful event	Following the moving target with the joystick demands high level of attentional resources. This is clearly involved	Correct replication of stimulus figure with detail requires concentration. This is involved to some extent.	This speed & accuracy task requires close concentration. This is clearly involved.	This speed & accuracy task requires close concentration. This is clearly involved.
Response Execution Performance of Motor Sequences Drawing between numbers	Not involved	Not involved	Not involved	This is the essential nature of this task
Other sequences	Not involved	Not involved	Not involved	Not involved

Table 12 (Cont.)
Motor Related Processes and Tests Chosen to Assess Them

Form of Motor Related Activity	Tests & Motor-Related Activities Involved			
	Computer Task	**Rey-Osterrieth Figure, Copy & Recall**	**WAIS-R Digit Symbol**	**Trail Making Test, rt A & B**
Response Execution				
Reaction time	This is involved indirectly. The target is darting around the screen and the subject must react quickly to follow it closely	This is not involved	This is a speed & accuracy task, so quicker reactions will be reflected in quicker performance. Hence only indirectly involved	This is a speed & accuracy task, so quicker reactions will be reflected in quicker performance. Hence only indirectly involved
New motor skills, learning to use a joystick	This describes the essential activity in this task	This is not involved	This is not involved	This is not involved
Writing & drawing	This is not involved	The subject is drawing a complex figure, this is a central feature of this task	The subject is writing symbols, this is an essential feature of this task	The subject is drawing lines between circles scattered across an A4 page, this is an essential feature of this task

4.1.3. Neuropsychological Tests of Declarative Semantic Memory

Declarative semantic memory was the only type of memory which was considered to be associated with one of the circuits, on the basis of the literature review (see section 2.8.1.2.3.1.). This is a narrow band of memory functioning, and tests relevant to this type of memory, with established sensitivity, were chosen for the thesis test battery. They were:

Rey-Osterrieth Figure recall

Story Recall, Immediate and delayed (from the Rivermead Behavioural Memory Test)

Features of these tasks associated with declarative semantic memory are set out in Table 13. Clearly the essential features of this type of memory are well represented among the two tasks. However, other types of impairment could also result in poor performance. For example, for the recall version of the Rey-Osterrieth Figure, attention, executive processing, motor coordination and visual perception. In the case of the story recall tasks, other abilities involved include attention, language comprehension and expression. Likewise, several other tests in the project battery also involve declarative semantic memory, if not primarily. Impairment of that function could interfere with performance of those tasks also. Tests in the latter category include:

HLLST Antonyms

HLLST Synonyms

HLLST Give Definitions

HLLST Provide a Word

HLLST Differences

HLLST Categories

HLLST Sentence Formulation

HLLST Analogies

HLLST Homonyms

HLLST Absurdities

HLLST Association Naming

HLLST Sequencing

WAIS-R Similarities

Table 13
Long Term Memory (Declarative Semantic Type), and Associated Tests

Form of Memory Related Activity	**Tests Involving Memory**	
	Rivermead Behavioural Memory Test, Paragraph Recall (Immediate & Delayed)	Rey Osterrieth Figure, Recall
Capacity for retention over minutes or decades	The delay version involves recall of a paragraph, approximately 10 minutes after hearing it.	The presentation/recall interval is typically a few minutes only.
Specific knowledge or facts about the world	The content of the story corresponds to 'specific facts about the world'.	The visuo-spatial configuration is analogous to 'facts about the world'.
Storage	The orally presented story has to be stored to allow later retrieval.	The complex figure has to be stored to allow later retrieval.
Encoding by meaning	The story stimulus material involves meaning. Thus meaning is clearly a likely basis for encoding with this task.	Features of the figure probably resemble known images, e.g., Union Jack, smiley face, TV arial etc. Thus meaning-based encoding is a possibility.
Retrieval	As verbal description is the type of response, retrieval is involved.	As the figure has to be produced from memory, it has to be retrieved.
Verbal Modality	The presentation and response are both verbal, hence this is the verbal modality.	Unless the subject chooses to translate the figure into verbal description, rather than the visual image, this is probably not involved.
Visual Modality	Probably not involved, unless the subject chose to generate a visual image of the story.	This task , recall of a visual figure, is clearly involved.
Motor Modality	This is not involved.	As the subject had just copied the figure, prior to retrieval, motor movements entailed in drawing were possibly part of the memory.

4.1.4. Neuropsychological Tests of Executive Functions

Although knowledge of executive functions, and associated theoretical models, is developing, test instruments capable of evaluating a subject's performance in the context of such models are not yet available. The 'Behavioural Assessment of the Dysexecutive Syndrome' developed by Wilson, Alderman, Burgess, Emslie and Evans (1996) is an important step forward, but still lacks a comprehensive theoretical foundation and research data showing how various types of brain impairment are manifest in test performance. From a strict research methodology point of view, developing such a battery would be the next step in pursuing this general line of research. Such a project is beyond the scope of this thesis.

What we do have is a collection of established executive function tasks, which many researchers and clinicians have repeatedly demonstrated to be sensitive to brain impairment. Measures chosen for the project battery to represent this area were:

Wisconsin Card Sorting Test –Revised

Perseverative Responses,

Category score

Conceptualization Index

Porteus Mazes

Trail Making Test, Parts A&B

Rey-Osterrieth Figure, Copy & Recall

Verbal Fluency (HLLST, Association Naming)

The extent to which these tests include the key elements of executive processing is set out in Table 14. Generally the relevant features of executive processing are reasonably well represented. However, some features were not as well represented. For example, the form of complex attention involving performance of two motor activities simultaneously. Then there are the particular types of problem solving that have been a

focus of much past research into executive functions, that is, the tower of London problems, block patterns and driving simulation.

Furthermore, none of the tests listed above is a 'pure' measure of executive function. Other types of impairment could result in poor performance on those tasks, e.g., in reaction time, attention, complex programmes of motor activity, visual perceptual tasks and possibly even aphasic problems. Likewise, several other tests in the project battery also involve executive processing, if not primarily. Impairment of that function could interfere with performance of those tasks also. Tests in the latter category include:
HLLST Sequencing subtest
WAIS-R Similarities subtest

As with other areas of cognition under investigation, the precise cognitive impairments of the lesion subjects needed to be explored through close comparison of tests (associated with a particular lesion) with other tests from the same category of cognition, not associated (Phase 7). Impairments so-identified were to be further scrutinized for any correspondence to elements of models of executive function, in an attempt to establish the role of the circuit in executive functioning.

Table 14
Executive Function Related Activity and Associated Tests

Executive Function Related Activity	**Tests of Executive Functions**				
	Wisconsin Card Sorting Test –Revised **Perseverative Responses**	**Porteus Mazes**	**Trail Making Test, Part B**	**Rey Osterrieth Figure**	**Verbal Fluency (HILLST Association Naming)**
Allocation of Processing Resources As responses on all tests involve cortical processing, allocation of processing resources is arguably a part of the process for them all.					
Complex Attention					
Simultaneous monitoring of different input channels in a divided attention task, response flexibility. Resolution of competing action alternatives	The subject has to monitor four separate, growing stacks of cards to deduce the sorting principle. This possibly involves a related process.	This does not seem to be involved.	The two different series that the subject has to alternate between, are analogous to rival input channels. This is probably involved.	This does not seem to be involved.	This does not seem to be involved.
Non-automatic counting tasks requiring mental control	This is not involved.	This is not involved.	The act of alternating between two series (numbers & letters) is analogous to this.	This is not involved.	Having to retrieve words satisfying specific criteria, under time pressure has some similarities, although not identical.
Performance of two motor activities, simultaneously, or in competition	This is not involved.	This is not involved.	This is not involved.	This is not involved.	This is not involved.

Table 14 (Cont.)
Executive Function Related Activity and Associated Tests

Executive Function Related Activity	Tests of Executive Functions				
	Wisconsin Card Sorting Test –Revised **Perseverative Responses**	**Porteus Mazes**	**Trail Making Test, Part B**	**Rey Osterrieth Figure**	**Verbal Fluency (HLLST Association Naming)**
Problem Solving					
Top-down regulation of responses	Card sorting had to conform to a deduced sorting principle, which constitutes the 'top' that regulates the 'down', which were the individual card sorts.	Subject's drawing had to be in accord with a derived mental plan of how to get through the maze. Hence this is arguably involved.	As control of automatic responses was a key process, this is arguably involved.	Subject's drawing had to be in accord with a derived mental plan of how to construct the complex figure. Hence this is arguably involved.	As word retrieval had to conform to specific criteria, such regulation of responding was arguably involved.
Tower of London problems	This was not involved.	Visuo-spatial problem solving is involved in both tasks, hence they are probably related.	This was not involved.	This was not involved.	This was not involved.
Small number of categories achieved & perseveration on the WCST	This test and this task are one and the same.	This is not involved.	This is not involved.	This is not involved.	This is not involved.

Table 14 (Cont.)
Executive Function Related Activity and Associated Tests

Executive Function Related Activity	Tests of Executive Functions				
	Wisconsin Card Sorting Test –Revised Perseverative Responses	**Porteus Mazes**	**Trail Making Test, Part B**	**Rey Osterrieth Figure**	**Verbal Fluency (HLLST Association Naming)**
Problem Solving (Cont.)					
Construction of block patterns	This was not involved.	Two-dimensional, visuo-spatial problem solving is involved in both tasks, hence they are probably related.	This was not involved.	This was not involved.	This was not involved.
Writing & drawing	This was not involved.	This is a drawing task, so it is related.	Although pencil manipulation was involved, it was not to draw or write.	This is a drawing task, so it is related.	This was not involved.
Driving simulator	This was not involved.	This was not involved.	This was not involved.	This was not involved.	This was not involved.

**These have been defined as the combination of planning, decision making, judgement and self perception. Given the importance of these functions it is hardly surprising that they are the most extensively studied aspect of the frontal lobes (Tranel, Anderson & Benton, 1994; Malloy & Richardson, 1994). These include, integration of multimodal sensory input, generation of multiple response alternatives, maintainance of set and goal directedness, modification of behaviour as conditions change, and self evaluation.*

4.1.5. Neuropsychological Assessment Procedures Appropriate for Functions of Language-Related Circuits

The review of language functions and other language-related circuitry (2.8.4.1.5.) concluded that both language-related circuits were involved in language comprehension and expression. While various levels of each circuit were associated with more specific functions (e.g., deep encoding of verbal material with the striatum, see Table 10), none of these more specific functions has been associated, by research reported so far, with more than one level of the circuitry. Therefore the data only allow the more general function to be associated with the complete circuits, (i.e., comprehension or expression).

It was observed by Dodd (1988) that language difficulties associated with these circuits tend to be subtle. Therefore assessment procedures sensitive to subtle language comprehension and expression difficulties were required. Traditional aphasia batteries (e.g., the Boston or Schuell Aphasia batteries) do not tend to detect these. In fact it was this very observation that prompted Clarke, Dodd, Lowe and Densley (1987) to embark on the demanding task of developing the Higher-Level Language Screening Test (H-LLST). This comprehensive test of higher level language includes tasks for auditory comprehension, auditory/visual comprehension, reading comprehension and verbal expression. Therefore it was considered a suitable instrument for assessing relevant language functions. It is described in section 5.4.5.1.

One additional task is well established as sensitive to brain lesions, especially at the level of the frontal lobe. This is the Similarities subtest of the WAIS-R (Lezak, 1995). It requires the subject to explain how pairs of words are related. Thus it too involves more sophisticated forms of verbal processing, verbal abstraction and verbal description, and hence seemed potentially sensitive to circuit-related deficits.

4.1.6. Project Objectives: Conclusions

The central goal of this thesis is to identify cognitive skills associated with the seven basal-cortical circuits listed above. An investigation, divided into a series of phases, has been conducted in pursuit of this central goal.

The data gathered were complex, and addressing issues in relation to that data required a special and somewhat elaborate analysis in its own right before the central analysis of this project could proceed with confidence. These data related issues were the focus of the first phase (4.1 Phase 1: Resolution of Data Issues). Two distinct data-related issues were involved.

Subsequent phases (Phases 4.2 to 4.4) addressed the central issues of the thesis. Twenty five brain injured subjects were verified by expert scrutiny of neuroimaging to have involvement of any one of the seven basal cortical circuits.

All measures listed in sections 4.1 to 4.5 above, considered likely to reveal deficits associated with these five circuits, are listed in Table 15. Some of the literature also reports that such deficits are more likely to be found with lesions in one hemisphere rather than the other. This particularly applies to verbal deficits and the dominant hemisphere. However even in relation to verbal deficits, reports of exceptions abound (Goodglass, 1993; Joanette, 1990). Therefore, all deficits potentially linked to a circuit have been considered in relation to both left and right brain injured subjects.

No previous study has grouped subjects in this way as a means of investigating the functions of these circuits. Nor has the role of these circuits ever been investigated with such a comprehensive battery, based on an exhaustive literature review. The inevitably small numbers of rather heterogeneous subjects, with suitable lesions available, meant that multivariate analyses were not viable. A rather creative adaptation of Godefroy et al.'s (1998) classification tree analysis was devised. This method is described in detail in the results section in the description of Phase 2.

Table 15

Circuits, Functions and Tests

Circuit	Functions	Tests Primarily Relevant to this Function	Tests Secondarily relevant to this Function
Dorsolateral Prefrontal Circuit	Ability to Perform Complex Programmes of Motor Activity	Computer task Trail Making Test, Part B Rey-Osterrieth Figure, Copy Rey-Osterrieth Figure, Recall WAIS-R Digit Symbol	Porteus Mazes
Dorsolateral Prefrontal Circuit	Executive Functions	Wisconsin Card Sorting Test –Revised *Perseverative Responses* *Category Score* *Conceptualization Index* Porteus Mazes Trail Making Test, Part B Rey-Osterrieth Figure, Copy Rey-Osterrieth Figure, Recall Verbal Fluency (HLLST, Association Naming)	HLLST Sequencing. WAIS-R Similarities

Table 15 (Cont.)

Circuits, Functions and Tests

Circuit	Functions	Tests Primarily Relevant to this Function	Tests Secondarily relevant to this Function
Dorsolateral Prefrontal Circuit	Declarative Semantic Memory	Rey-Osterrieth Figure, Recall Story Recall, Immediate and delayed (from the Rivermead Behavioural Memory Test)	HLLST Antonyms HLLST Synonyms HLLST Give Definitions HLLST Provide a Word HLLST Differences HLLST Categories HLLST Sentence Formulation HLLST Analogies HLLST Homonyms HLLST Absurdities HLLST Association Naming HLLST Sequencing WAIS-R Similarities
Anterior Cingulate Circuit	Selective attention A. Preconscious:		

Table 15 (Cont.)

Circuits, Functions and Tests

Circuit	Functions	Tests Primarily Relevant to this Function	Tests Secondarily relevant to this Function
Anterior Cingulate Circuit	Selective attention, B Conscious:	Computer Tracking Task Trail Making Test, Part A Trail Making Test, Part B Wisconsin Card Sorting Test –Revised *Perseverative Responses* *Category Score* *Conceptualization Index* WAIS-R Digit Symbol	Porteus Mazes Rey-Osterith Figure, Copy Rey-Osterith Figure, Recall HLLST Auditory/Visual Comprehension HLLST Reading Comprehension HLLST, Association Naming Story Recall, immediate & delayed Picture Recognition task

Table 15 (Cont.)

Circuits, Functions and Tests

Circuit	Functions	Tests Primarily Relevant to this Function	Tests Secondarily relevant to this Function
Anterior Cingulate Circuit	Verbal Expression	HLLST Antonyms HLLST Synonyms HLLST Give Definitions HLLST Provide a Word HLLST Differences HLLST Categories HLLST Sentence Formulation HLLST Analogies HLLST Homonyms HLLST Absurdities HLLST Association Naming HLLST Sequencing WAIS-R Similarities	

Table 15 (Cont.)

Circuits, Functions and Tests

Circuit	Functions	Tests Primarily Relevant to this Function	Tests Secondarily relevant to this Function
Other language related cortical basal circuitry	Verbal comprehension Verbal expression	HLLST Yes/No Questions HLLST Vocabulary HLLST Grammar HLLST Auditory/Visual Comprehension HLLST Reading Comprehension HLLST Antonyms HLLST Synonyms HLLST Give Definitions HLLST Provide a Word HLLST Differences HLLST Categories HLLST Sentence Formulation HLLST Analogies HLLST Homonyms HLLST Absurdities HLLST Association Naming HLLST Sequencing WAIS-R Similarities	

Finally, if another group with presumed basal ganglia impairments could be shown to have the same deficits as the 25 brain injured subjects, this would give strong support to these conclusions. People suffering from early stage Parkinson's Disease (PD) would be such a group (i.e., <Stage III of the Hoehn & Yahr scale). A group of these subjects were given the same battery and results presented in Phase 5.

4.2. Phase 1: Resolution of Data Issues

Objective 1: Comparison of individual brain injured subjects' test scores with spinal-injury control group data was the basic test of deficit performance. Whether this control group was representative of the general population, except for a small number of predictable deviations (associated with the psychological reaction to trauma and debilitation), required verification. The first objective of Phase 1 is verification of the adequacy of these data. (See 6.2.1 Comparison of Control Subjects and General Population.)

Objective 2: The methodology used to address the central goals of this thesis (Phase 2) depended on the accuracy of neuroimaging (CT and MRI). However, previous studies have questioned its accuracy. (See 6.2.2 Testing the Accuracy of Neuroimaging (CT & MRI) available to all lesion subjects.) The second objective of Phase 1 is to verify the accuracy of neuroimaging available, and to identify any limitations on this accuracy. (See 6.2.2 Testing the Accuracy of Neuroimaging (CT & MRI) available for all lesion subjects.)

4.3. Phase 2: Neuropsychological Deficits among Brain Injured Subjects with Verified Lesions of the Dorsolateral Prefrontal Circuit.

Objective: A set of tests that are potentially sensitive to lesions of various basal cortical circuits (including the dorsolateral prefrontal circuit) had been identified from the literature (see Table 15). It was the objective of this phase to identify the ones from that pool which are sensitive to lesions of this circuit.

4.4. Phase 3: Neuropsychological Deficits among Brain Injured Subjects with Verified Lesions of the Anterior Cingulate Circuit.

Objective: A set of tests that are potentially sensitive to lesions of various basal cortical circuits (including the anterior cingulate circuit) had been identified from the literature (see Table 15). It was the objective of this phase to identify the ones from that pool which are sensitive to lesions of this circuit.

4.5. Phase 4: Neuropsychological Deficits among Brain Injured Subjects with Verified Lesions of other Language Related Circuitry.

A language related basal cortical circuit has been proposed by Crosson, 1992 (see Table 10). However, unlike the circuits examined in Phase 2 and 3, cortical areas outside the frontal areas were involved (Broca's and Wernicke's areas). A set of tests that are potentially sensitive to lesions of various basal cortical circuits (including Crosson's language related circuit) had been identified from the literature (see Table 10). It was the objective of this phase to identify the ones from that pool which are sensitive to lesions of this circuit.

4.6. Phase 5: Broad Areas of Cognition Associated with Basal Cortical Circuitry: An Integration of Findings from Phases 2 to 4.

A subset of the tests from the phase battery were associated with individual basal cortical circuits in Phases 2, 3 and 4. Individual circuits were associated with more than one type of cognitive processing and different circuits were involved with the same forms of cognition. Considering lesion profiles of tests for each area of cognition should therefore further clarify neuropsychological processing associated with these circuits. However, as further data analysis would be involved, involving results yielded by all three previous phases, this effectively became another phase. This analysis is presented for each area of cognition involved. Those were complex programs of motor activity, executive functions, verbal comprehension and expression.

4.7. Phase 6: Neuropsychological Deficits of Parkinson's Disease Subjects

Our investigation of subjects with circuit disruption due to brain injury (Phases 2, 3 and 4) identified deficits associated with that disruption (see section 6.6.). However group numbers were relatively small, and this set of findings has not been reported before. Therefore these findings are less than strongly conclusive. If another group with presumed basal ganglia impairments could be shown to have the same deficits, this would give strong support to these conclusions. People suffering from early stage Parkinson's Disease (PD) would be such a group (i.e., <Stage III of the Hoehn & Yahr scale).

Objective: To find out the degree of correspondence between the circuit lesion subjects' and the PD subjects' deficits.

5. METHOD

5.1. General Subject Inclusion Criteria

Testing the project hypotheses essentially involved comparing subjects with impairments at any point in the seven basal cortical circuits (dorsolateral prefrontal, lateral orbital, anterior cingulate of either hemisphere, and Crosson's language-related circuitry) with an otherwise comparable group of control subjects. Types of subjects available in Adelaide (in significant numbers) with significant, relatively discrete, impairments of those circuits included traumatic basal ganglia haematoma (TBGH), Parkinson's Disease (PD), tumours and Cerebrovascular Accidents (CVAs). The project sought to include subjects with impairment of those circuits at the cortical level (i.e., frontal lobe) as well as at the level of the basal ganglia.

Subjects with a history of significant other impairments (e.g. epilepsy) were excluded. Subjects not of an English-language based educational background and those with a debilitating psychiatric illness were also excluded. All these factors could have produced poor test performance in the absence of the brain pathology which was of interest to this project. Subjects unable to meet the basic requirements of the testing situation were also excluded (e.g., in terms of simple attention, visual acuity, verbal communication and the ability to engage in pencil manipulation).

As lateralisation of brain functions was being examined by this project, subjects with less predictable brain lateralization (i.e. subjects who did not use their right hand for writing) were excluded. Satz, Achenbach and Fennell (1967) and Volpe, Sidtis and Gazzaniga (1981) reported consistent left hemisphere dominance for speech function among right-handers, unlike left handers.

Gathering a sufficiently large sample of PD and CVA subjects required the inclusion of significant numbers of older subjects. To minimize the possible affects of age-related

cognitive decline within the sample, no subjects over the age of 75 years were included. The incidence of dementia is also well known to be higher in older populations. To avoid the inclusion of subjects so affected, the Mini-Mental-State Exam (Folstein & Folstein, 1975) was administered the all subjects over the age of 70 years. When their total score was 20 or below they were not included in the project. This measure, and cut-off level, are widely accepted as a simple screen for dementia (Measso et al.1993).

People who had suffered spinal injuries were chosen for the control group. The reason for this was that this group can be argued to be characterised by the same 'extrinsic', or 'nonneurological' factors that are known to affect neuropsychological test performance. Those are hospitalization, fatiguability, depression, anxiety or severe general conditions (Godefroy, Duhamel, Leclerc, Saint Michel, Henon & Leys, 1998). As closed head injuries and spinal injuries most commonly occur in motor vehicle accidents, it is arguable that people with spinal injuries will display the same demographic profile that has been so strongly associated with people with closed head injuries (aged 17-35 years, 3 to 1 in favour of males, and tending to have a background of lower socio-economic status (Rimel, Jane & Bond, 1990)). Both groups will have experienced traumatic, if not also catastrophic injuries.

For example, Binks, Radnitz, Moran and Vinciguerra (1997) found that a significant proportion of people with Spinal Cord Injuries tended to also have Post Traumatic Stress Disorder (PTSD). This debilitating mental disorder has been associated with verbal memory impairments and significantly slowed reaction times on tasks involving the detection of target stimuli (Wolfe & Schlesinger, 1997). In fact, Gilbertson, Gurvitts, Lasko and Pitman (1997), reported that Vietnam veterans with PTSD performed less well on a wide range of neuropsychological tasks than a veteran control group without PTSD. They attributed this to a possible attention disorder associated with PTSD. PTSD has been associated with a reduction of hippocampal volume and a greater incidence of focal white matter lesions on MRI (Canive et al. 1997). Also of relevance is the established association between PTSD, substance abuse and depression, both associated with disrupted brain function in their own right. Of course,

a similar proportion of the non-control subjects had conditions with quite different demographic profiles, e.g. Parkinson's disease (PD, N=13) and Cerebrovascular accidents (CVA, N=7). People experiencing these tend to be much older, and less likely to have a background of social disadvantage. However the possible differences between the Spinal Injury controls and the non-CHI subjects, if anything, would have tended to minimize any impression of neuropsychological deficits among the latter. Consequently this was thought unlikely to result in any methodological problems for the project.

5.2. Method of Contacting Subjects

Subject recruitment occurred between 1/2/89 and 28/7/95.

5.2.1. Subjects with Traumatic Basal Ganglia Haematoma (TBGH), Cerebrovascular Accidents (CVAs) and Tumours

These subjects were contacted via three possible avenues. All subjects with TBGH were identified from Royal Adelaide Hospital (RAH) Neurosurgery Department records. Peter Oatey, Neurosurgeon, sponsored the project within the RAH. All others were made known to the researcher by Dr Chris Rowe, Chief of Nuclear Medicine Department at the Queen Elizabeth Hospital (QEH) and Dr Ravi Ravindran, Medical Director of the SA Head Injury Service, at the Julia Farr Centre (JFC). Those staff also sponsored the project in their respective agencies. Permission was first obtained from the Human Ethics Committee of each agency. Potential subjects were all invited to participate by letter. Those responding were contacted by the researcher. Testing was performed at a location of mutual convenience, either at the RAH Neurosurgery Department, QEH wards, JFC, Regency Park Centre for Young Disabled (the researcher's work place) or their own homes.

5.2.2. Parkinson's Disease (PD)

PD sufferers were contacted via the Parkinson's Syndrome of SA Incorporated. All new members of that society who had joined in the six months preceeding testing (who were not known to have impaired balance reactions, and therefore be at stage III or higher on

the Hoehn & Yahr scale, [1967]) were invited by letter to participate. Those responding were contacted by the researcher, and testing was always done at their homes. Subjects at Stage III or higher have been found much more likely to demonstrate 'frontal-lobe-like' impairments on neuropsychological testing (Giles, 1988; Perlmutter & Raichle, 1985). Therefore they were excluded from the project. These selection criteria were identical to those of another investigation of functions of the basal-cortical circuitry using PD subjects (D'Esposito & Postle, 2000).

5.2.3. Spinal Injuries (SI)

All subjects with Spinal Injuries were identified from Royal Adelaide Hospital (RAH) Spinal Injuries Unit records. Dr Ruth Marshall, Rehabilitation Medicine Specialist sponsored the project within the Spinal Injuries Unit. Potential subjects were all invited (by letter) to participate. Those responding were contacted by the researcher and testing was always done at their homes.

5.3. Basic Demographics of Total Sample

Table 16

General

	Spinal Injury Controls (N=11)	Parkinsons Disease Subjects (N=13)	All Brain injured Subjects (N=25)	Total Sample (N=49)
Age in years: Mean (SD)	31.83 (11.12)	63.08 (4.84)	34.80 (15.61)	41.64 (18.01)
Gender	Males: 10 Females: 1	Males: 5 Females: 8	Males: 19 Females: 6	Males: 34 Females: 15
NART-R IQ: Mean (SD)	106.27 (8.49)	115.15 (6.68)	101.76 (13.53)	106.33 (12.23)
Beck Depression Inventory (Short Form) Raw Score*	6.55 (4.03)	1.58 (2.35)	5.74 (5.93)	

* *Significantly different between groups at p<.05 (Oneway-ANOVA).*

Table 17

Occupations

	Spinal Injury Controls (N=11)	Parkinsons Disease Subjects (N=13)	All Brain Injured Subjects (N=25)	Total Sample (N=49)	National Australian data (from 1991 Census)
	No (%)	No (%)	No (%)	No (%)	(% of all employed persons)
Managers/ Admin.	2 (18%)	1 (8%)	4 (16%)	7 (14%)	(13%)
Professional	1 (9%)	2 (15%)	1 (4%)	4 (8%)	(13%)
Para-professional					(7%)
Trades-persons	2 (18%)	2 (15%)	2 (8%)	6 (12%)	(14%)
Clerks		4 (31%)	2 (8%)	6 (12%)	(16%)
Sales & Personal Services	2 (18%)	1 (8%)	4 (16%)	7 (14%)	(16%)
Plant, machine operators & drivers	3 (27%)	1 (8%)	4 (16%)	8 (16%)	(8%)
labourers etc		1 (8%)	4 (16%)	5 (10%)	(13%)
Not employed (also includes home duties and students)	1 (9%)	1 (8%)	4 (16%)	6 (12%)	The category not included in census data

Table 18

Vocational Qualifications

	Spinal Injury Controls (N=11)	Parkinsons Disease Subjects (N=13)	All Brain injured Subjects (N=25)	Total Sample (N=49)	National Australian data (from 1991 Census)
	No (%)	No (%)	No (%)	No (%)	(%)
Higher degree		1 (8%)		1 (2%)	(1%)
Post grad Diploma					(1%)
Bachelor's Degree	1 (9%)		1 (4%)	2 (4%)	(6%)
UnderGrad Diploma		1 (8%)	1 (4%)	2 (4%)	(4%)
Associate Diploma					(1%)
Skilled Vocational Qual-ification	2 (18%)	4 (31%)	1 (4%)	7 (14%)	(12%)
Basic Vocational Qual-ification	1 (9%)		4 (16%)	5 (10%)	(4%)
Not qualified	7 (64%)	7 (54%)	18 (72%)	32 (65%)	(70%)
Years of formal education: Mean (SD)	12.45 (2.42)	11.54 (2.99)	10.68 (1.97)	11.31 (2.43)	

Table 19

Basic Medical Information

Medical Diagnosis

	Spinal Injury Controls (N=11)	Parkinsons (N=13)	All Brain Injury (N=25)
Spinal Injury	11		
Parkinson's Disease	13		
Closed Head Injury: Traumatic Basal Ganglia Hematoma			7
Closed Head Injury: Frontal Lobes			7
Closed Head Injury: nonspecific			1
Cerebrovascular Accident (CVA)			7
Cerebral Abscess			1
Brain tumour			2
Years post injury or diagnosis: Mean (SD)	7.80 (9.73)	2.26 (2.41)	5.78 (5.16)
Years post neuro-imaging (i.e. that used to localize involvement): Mean (SD)	(no imaging done)	(no imaging done)	3.56 (5.96)
No of subjects scanned with the different scanning devices (ie CT or MRI)	(no imaging done)	(no imaging done)	CT: 18; MRI: 7

Note. Complete information, demographic background, areas of brain injury etc for each subject individually are shown in the Appendix B.

Table 20

Areas of Brain Involvement

(Note: total numbers in this table exceed the total of subjects in this group [25] as many subjects were counted in more than one cell. This was due to the diffuse nature of brain damage in a large proportion of the sample.)

	All Brain Injury (N=25)
Basal Ganglia: left unilateral	7
Basal Ganglia: right unilateral	9
Basal Ganglia: bilateral	
Other subcortical: left unilateral	8
Other subcortical: right unilateral	10
Other subcortical: bilateral	1
Frontal: left unilateral	1
Frontal: right unilateral	4
Frontal bilateral	4
Other cortical: left unilateral	2
Other cortical: right unilateral	3
Other cortical: bilateral	1

5.4. Tests Administered

5.4.1. Rationale for Test Inclusion

Tests of cognitive and language skills were chosen if there was a reasonable indication in the literature that they tested skills relevant to the seven basal cortical circuits of interest (dorsolateral prefrontal, lateral orbital and anterior cingulate, left and right hemispheres, and the other language-related circuitry of the dominant left hemisphere). See sections 4.1.1 to 4.1.5 for a detailed rationale for test selection. Considerable literature was reviewed to identify skills previously found relevant to lesions in all elements of the basal cortical circuits. However, since this project was first planned (1988), the literature has progressed considerably. When sufficient data had finally been gathered to perform the analysis, a major updating of the literature review was

necessary to check that the hypotheses remained novel, plausible and relevant. Fortunately the original battery was sufficiently comprehensive to include a substantial proportion of skills since linked to the basal cortical circuits. Inevitably some were not included (e.g. tests of visual neglect). This is why some skills linked to the circuits of interest were not included. For full listing of tests linked to these circuits see Table 15. As depression (Richards & Ruff, 1989) and premorbid intellectual ability are known to affect performance on neuropsychological tests, assessment of these two was included. Older subjects have a significantly greater risk of dementia. To exclude any so affected the Mini-Mental State Exam was used. Tests administered are described below.

5.4.2. Motor and Visuo-Motor Tests

5.4.2.1. Assessment of Motor Signs

Motor signs provide, an approximate, and very easily obtained measure of two things. Those are laterality of brain damage (the extent of motor signs on one side of the body reflecting the approximate extent of contralateral brain lesions) and overall severity of brain damage (Lezak, 1995). For this reason a simple questionnaire about these was administered to all experimental subjects. They were asked to rate the severity of any impaired coordination in each of a specified set of body parts. This was a modified section of an index of motor impairment devised for Parkinson's Disease sufferers by Yahr, Duvoisin, Schear, Barrett and Hoehn (1969), known as the Columbian Rating Scale (also described in Wade, 1992). Instead of separate indices for tremor, rigidity and bradykinesia, a single index of impaired coordination was used. This made it equally relevant to all the neurologically impaired subjects, and not just the ones with PD. Instead of just left and right arms and legs being rated, other lateralized body parts (hands, feet and trunk) were added to enhance sensitivity.

Following the style of the Columbian Rating Scale, impaired coordination in all body parts were rated as:

Absent (0)

Slight, and infrequently present (1)

Moderate in amplitude, but intermittently present (2)
Moderate and present most of the time (3)
Marked in amplitude and present most of the time (4)

Also following the style of the Columbian Rating Scale, ratings for all right sided body parts were totaled to give an index of right sided motor signs, and the same for the left. No other rating scale of motor impairments described in Wade's (1992) comprehensive review of these measures included the same critical features of established sensitivity to more subtle motor impairments in PD, relative brevity and separate, comprehensive indices of motor impairment for each side of the body.

5.4.2.2. Digit Symbol Subtest, Wechsler Adult Intelligence Scale -Revised (WAIS-R)

The WAIS-R Digit Symbol subtest (Wechsler, 1981) requires the subject to write in as many symbols next to numbers as they can within 90 seconds. An arbitrary correspondence between symbols and numbers is taught at the start of the test. (Time: 2 minutes.)
Skills Assessed (and Hypothetical Associated Circuits): Ability to perform complex programs of motor activity (dorsolateral prefrontal).

5.4.2.3. Trail Making Test

Two short tasks are involved in this (Reitan, 1958). The first (Part A) involves connecting (by drawing lines), a scattered array of small, numbered circles, in sequence. The second (Part B) only differs by virtue of some circles being identified with letters and the subject having to alternate between sequences when linking up the circles (i.e. 1 A 2 B 3 C etc). (Time: 5 minutes.)
Skills Assessed (and Hypothetical Associated Circuits): Ability to perform complex programs of motor activity (dorsolateral prefrontal).

5.4.2.4. Rey-Osterrieth Figure, Copy

This is a very well known, classic neuropsychological assessment task (Rey, 1941 in Lezak, 1995). The subject is required to copy a complex geometric figure, a rectangle divided according to a 'Union Jack' configuration, with various embellishments. The Taylor (1959) scoring system was used (as described in Lezak, 1995). (Time: 5 minutes.)

Skills Assessed (and Hypothetical Associated Circuits): Ability to perform complex programs of motor activity (dorsolateral prefrontal).

5.4.2.5. Visual Tracking and Reaction Time Assessment Task

This task was presented on an Apple IIe microcomputer using commercially produced software (Sbordone, 1983) and a joystick. The subject was required to use the joystick to keep a 5 mm diameter circle inside a 15 mm square, which shifted around the screen at random. The program allowed 2 minutes per trial and calculated the percentage of time the circle was kept within the square. That percentage, averaged over four trials, was used as the performance index for this task. (Time: 10 minutes)

Skills Assessed (and Hypothetical Associated Circuits): Ability to perform complex programs of motor activity (dorsolateral prefrontal), selective attention, conscious (anterior cingulate).

5.4.3. Visual Processing Tests

5.4.3.1. Wisconsin Card Sorting Test -Revised (WCST-R)

Subjects doing this task are presented with 128 cards, one at a time, and asked to match each to one of four others. The pattern on each card included up to four of one of four kinds of shapes, in one of four colours. However the subject was not informed of the basis for matching, but had to deduce it from feedback on the correctness/incorrectness of each placement (Healton, Chelune, Talley, Kay & Curtiss, 1993). After 10 consecutive correct placements, the matching criterion was changed. The criterion was

any one of shape, colour, number. Various indices of performance were included in the analysis. (Time: 20-40 minutes.)

Perseveration

Conceptualization Index

Skill Assessed (and Hypothetical Associated Circuit): executive functions (dorsolateral prefrontal).

No. of Categories

Skill Assessed (and Hypothetical Associated Circuit): selective attention, conscious (anterior cingulate).

5.4.3.2. Porteus Mazes

This is Porteus's (1965) time honoured maze drawing task. A series of pencil and paper mazes are presented to the subject, progressively more difficult. Unlike the WISC-III Mazes, they are not timed. (Time: 10 minutes.)

Skill Assessed (and Hypothetical Associated Circuit): executive functions (dorsolateral prefrontal).

5.4.4. Memory Tests

5.4.4.1. Rivermead Behavioural Memory Test (RBMT)

5.4.4.1.1. RBMT, Paragraph Recall

A short paragraph is read out to the subject, who is then asked to give as comprehensive a paraphrasal/repetition of it as possible (Wilson, Cockburn & Baddeley, 1985). They are asked again after 15 minutes without being given a second hearing of the paragraph in between. It provides a measure of immediate and delayed recall. (Time, [spread over 20 minutes]: 7 minutes.) This test includes four parallel forms. The paragraph used came from version A. The paragraph, divided into elements for scoring purposes was as follows:

Mr Brian/ Kelly/ a Security Express employee/ was shot dead/ on Monday/ during a bank raid/ in Brighton./ The four raiders/ all wore masks/ and one carried/ a sawn-off/ shotgun./ Police detectives/ were sifting through/ eye-witness accounts/ last night./ A police spokesman said/ 'He was a very brave man./ He went for/ the armed raider/ and put up a hell of a fight. (21 elements)

Skill Assessed (and Hypothetical Associated Circuit): declarative semantic memory (dorsolateral prefrontal).

5.4.4.1.2. RBMT, Picture Recognition

This was another subtest from the same test as the Paragraph recall task (Wilson et al. 1985, see 4.4.4.1.1 above). The subject is presented with 10 cards, one at a time for 5 seconds each. On each card is a simple line drawing of a common object. As well as looking at it for the 5 seconds, the subject is asked to name it and is told the name by the examiner if unable to do so (very rare). 15 minutes later the subject is presented with the same set again, intermingled with 10 additional 'distractor' pictures not included in the first presentation. For each card they are asked to say whether it had been part of the first presentation or not. This is essentially a delayed visual recognition task. (Time: 2 minutes)

Skill Assessed (and Hypothetical Associated Circuit): visual recall (right dorsolateral prefrontal).

5.4.4.2. Rey-Osterrieth Figure, Recall

This followed the copy administration of this figure (see 4.4.2.4 above). Immediately after the subject had completed their copy production, both it and the stimulus figure were withdrawn, and they were asked to do it again from memory. The Taylor (1959) scoring system was used (as described in Lezak, 1995). (Time: 3 minutes)

Skill Assessed (and Hypothetical Associated Circuit): declarative semantic memory (dorsolateral prefrontal).

5.4.5. Verbal Tests

The range of verbal and language difficulties linked to lesions in various elements of the basal cortical circuits is extensive. (See section 5.5.2.1. in the Introduction). However, as a general comment, they tend to be less severe. Consequently an assessment of Higher Level Language Functions primarily seemed more likely to identify the key verbal functions associated with the basal cortical circuits. A new instrument developed at the Repatriation General Hospital at Daw Park in SA (the 'Higher-Level Language Screening Test') was the only test of this aspect of language available.

5.4.5.1. Higher-Level Language Screening Test (H-LLST)

This is a new test of higher level language functions (Clark, Dodd, Lowe & Densley,1987, Dodd, Lowe, Densley & Clark, 1989, 1991a, 1991b) (Time for the whole test: 25 minutes) *For those subtests where no component skills are identified as hypothetically associated with particular circuits, none have been specifically identified.*

A. Auditory Comprehension

This section (A) yielded an individual score for each subtest.

1. Yes/No Questions

This was a comprehension task involving complex sentences. Each of the 4 items involved the examiner reading a question, to which the subject had to answer yes or no.

'If I'm speaking to my brother's sister, am I speaking to my cousin?'

'Is a tall midget taller than a short giant?'

'If 7 canine years equals one human year, is a 5 year old child older than a one year old dog?'

'The policeman was shot by the burglar. Was the burglar wounded?'

2. Vocabulary

A different set of four pictures was presented to the subject for each of the 4 items in this task. For each item the examiner spoke a word and the subject had to point to two of the four pictures best represented by the word. The words, and the four pictured items, with correct choices in italics, are given below.

Punt, petrol pump, suspension bridge, *punt kick, man having a punt (bet),*

Coast, toast, glass on coaster, *coastal scene, girl coasting on a push bike,*

Wire, coiled spring, *wire mesh, telephone wire*, tyre,

Mine, *woman holding baby*, mime mask, *mining operations by excavator*, couple watering plants.

3. Grammar

This subtest included 3 items. Each one included three sentences, and the subject was asked to identify which two of the three were closest in meaning.

Item 1: (a) I'm sick, (b) I'm not unwell, (c) I'm healthy.

Item 2: (a) The man's books stood on the shelf, (b) On the shelf were the man's books, (c) The man's books were on the shelves.

Item 3: (a) The doctor performed surgery on Friday, (b) The patient had an operation after the weekend, (c) The patient was taken to recovery on Monday.

Skills Assessed by whole of Section A (and Hypothetical Associated Circuit): verbal comprehension (anterior cingulate and other language related circuitry).

B. Auditory/Visual Comprehension

This section (B) involved only one subtest, yielding a single score. All 5 items of this subtest involved the subject following the examiner's instructions in relation to a picture. It represented a family engaged in various domestic activities in a garden setting. The items were as follows. Point to the combustion.

Point to the liquid refreshment.

Point to the smaller door.

Point to the paw off the ground

Point to the ball, the sprinkler, the door and the fire.
Skills Assessed (and Hypothetical Associated Circuit): verbal comprehension (anterior cingulate and other language related circuitry).

C. Reading Comprehension

Another section, like B, where only one subtest, yielding a single score, was involved. The same picture used for Section B was also used in this task, but this time the subject followed written rather than spoken directions in relation to the picture. The instructions were as follows.
Point to the ball in the flower bed and to the bottom rung of the chair.
If the man is not cooking the barbeque point to the rake.
Before you point to the left tyre point to the ladder.
If there is water in the air, then point to the hair pin.
Skills Assessed (and Hypothetical Associated Circuit): verbal comprehension (anterior cingulate and other language related circuitry).

D. Expression

This section (D) yielded an individual score for each subtest.

1. Antonyms

For each of the four items involved, the subject was told a word and asked to give a word which meant the opposite. The words were, ignorant, prosperity, mournful and courageously.

2. Synonyms

As for 'Antonyms' (above), except that for the four items of this subtest, the subject was asked to give a word that means the same. The words were, frequent, tranquil, entirely and scheme.

3. Give Definitions

For each of four words in turn the subject was required to explain what it means. The words were, rehearsal, consequences, persist and oppose.

4. Provide a Word

This was the reverse of the previous task. The examiner gave the meaning, and the subject had to say what the word was. The meanings were as follows.

An instrument measuring heat and cold.

A group of people gathered together to hear a concert.

The opening for coins in an automatic drink machine.

Slightly wet.

Lovely to look at.

5. Differences

Four items were included. For each the subject had to tell the most important difference between two words spoken by the examiner.

To run and to walk.

A servant and a slave.

A creek and a river.

To gargle and to drink.

6. Categories

The subject was required to name 5 items in nominated groups. A different group for each of the three items. The nominated groups were, 5 parts of a tree, 5 words beginning with "PR", 5 things that are illegal.

7. Sentence Formulation

A subtest with a single item. The subject was required to put 3 words into the one sentence (money, shop, although).

8. Analogies

Listening to an incomplete sentence and filling in the last word were what was required here. The subtest included 4 items. The items were,

Full is to empty as dirty is to…..

Gosling is to goose as cygnet is to....
Pyramid is to triangle as cube is to.....
Painting is to artist as book is to....

9. Homonyms

This was another subtest with four items. The subject was asked to give two different meanings for each word said by the examiner, one word per item. The stimulus words were, hide, fast, field and slip.

10. Absurdities

The subject was presented with three statements, one at a time. They were as to tell the examiner if there was something rediculous about each statement.

'An elderly man said, "I can no longer take a stroll right around the park every day. I can only go half way round and back again."'

'A man and his wife saw a sign in the window of a garden shop. It read "Passionfruit vines for sale, guaranteed to bear fruit in 10 months time". The man was excited and said to his wife, "Let's buy two vines so we can have our first passionfruit in five months."

'A large company was anxious to increase its sales. It decided to print and distribute catalogues to a large number of potential customers. On the bottom of each catalogue was printed "If you have not yet received a copy of this catalogue, please phone or write to us".'

11. Association Naming

This was a variation of the well known verbal fluency task, sometimes known as the Controlled Oral Word Association Test (Benton & Hamsher, 1989), or "FAS". There were two items. For the first, the subject had to name as many items of clothing as they

could within one minute. The second involved them giving as many words as they could commencing with the letter "L".

Skills Assessed (and Hypothetical Associated Circuit): executive functions (dorsolateral prefrontal)

12. Sequencing

This was a simple, one item subtest. The subject is asked to give the examiner six steps for planting a rose, in the order that they would do them.

Skills Assessed by whole of Section D (and Hypothetical Associated Circuit): Verbal Expression (anterior cingulate and other language related circuitry).

5.4.5.2. WAIS-R Similarities Subtest

This is the well known subtest of the WAIS-R (Wechsler, 1981). The subject is presented with a series of word pairs, one by one and asked to explain how the words are alike. (Time: 5 minutes)

Skills Assessed (and Hypothetical Associated Circuit): Verbal Expression (anterior cingulate and other language related circuitry).

5.4.6. Test of Pre-Morbid Ability

Comparison of experimental subjects' performance with the spinal injury control group is the primary method used for establishing the presence of neuropsychological desfits in this study. This is discussed in section 6.2.1. However for one of the experimental groups, subjects with PD, a more traditional method was considered appropriate, comparison with an estimate of the subject's own pre-morbid function. This is because the PD subjects were not characterized by the two things which made this approach invalid among the lesion subjects. Those things were probable impairment of skills used to estimate premorbid function (e.g., ability to read phonetically irregular words, NART-R) and the psychological and neuropsychological impacat of traumatic, disabling injury. Thus the PD subjects were administered the NART-R (described in section 5.4.6.1.).

5.4.6.1. National Adult Reading Test (2nd Edn) (NART-R)

It is well established that one skill less likely, than all other skills, to be affected by a brain injury (in the absence of any aphasic disturbances) is the ability to read phonetically irregular words (Lezak, 1995). This is the task involved in this test (Nelson & Willison, 1991). Thus this was included as a well validated, and reliable, measure of a non-affected skill for that section of the project sample without aphasic problems. (Time: 5 minutes)

5.4.7. Assessment of Depression

Richards and Ruff (1989) reported that depressed people tend to achieve lower scores on neuropsychological tests even in the absence of known brain lesions. Therefore, to avoid distortion of results from depression related effects, this was assessed to check for the presence of this distorting factor.

5.4.7.1. The Beck Depression Inventory

The Beck Depression Inventory Beck (1987) is a very widely recognized instrument for measuring presence and severity of depression. Normally it involves 21 multiple choice items, each one concerned with a particular aspect of the experience and symptomatology of depression. Response options for each item cover a range of severity levels for the individual symptom. However, as some researchers have pointed out (Kaszniak & Allender, 1985; Gordon & Kravetz, 1991) 7 of those 21 items refer to somatic symptoms (e.g. weight loss, fatiguability). As those researchers have demonstrated, the inclusion of the somatic items could give a misleading impression of the level of depression among the subjects with physical ailments. Gordon Kravetz's data indicated that the 7 somatic items could be excluded without compromising the instrument. The measure of depression used was the total score for the 14 nonsomatic items only. Subjects completed it by ticking their preferred response after a silent reading of it. (Time: 5 minutes)

5.4.8. Screening for Dementia

The risk of dementia increases with age. For this reason subjects over that age were screened for dementia. The Mini-Mental-State Exam is the most widely used and respected instrument for this purpose (McLean, 1987; Lezak, 1995).

5.4.8.1. Mini-Mental-State Exam

To avoid the inclusion of subjects so affected, the Mini-Mental-State Exam (Folstein & Folstein, 1975) was administered to all subjects over the age of 50 years. When their total score was 20 or below they were not included in the project. This measure and cut off level are widely accepted as a simple screen for dementia (Measso et al., 1993). Items included orientation questions, repetition of three items, counting backwards by sevens, verbal comprehension and design copying. It is also very short (Time: 5-10 minutes).

5.5. Lesion Verification

The most recent brain scans (Computerised Axial Tomography [CT Scans] or Magnetic Reasonance Imaging [MRI Scans]) were used to identify the brain lesions of each brain injured subject. All scans were rated at a special examination for this project by two raters, one: Dr Chris Rowe, Chief of Nuclear Medicine Department at the Queen Elizabeth Hospital (QEH) and two: Mr Peter Oatey Neurosurgeon, formerly staff neurosurgeon at the Royal Adelaide Hospital (RAH).This is in keeping with current widely accepted practice (Mitchener et al. 1998). The format used for ratings is included in Appendix C. Initial ratings were performed independently without the other rater present or the other rater's assessment being available. On 18 of the 25 scans so rated, agreement was above 80%. For this set the first rater's ratings were used. For the remaining seven scans where agreement fell below 80%, a special meeting of the two raters was convened. The scans were discussed until a consensus was reached. Subjects 4, 20, 24, 25, 27, 40 & 55 were involved. For this latter set the consensus ratings were used. The scan ratings for each subject are shown in Results Tables 24, 26, 28, 30 and 32.

This method of lesion verification posed several problems for this project. One was the considerable variation in quality of individual scans. Scanning technology has improved considerably in terms of resolution and availability between the first and last subject's neurological investigations (1/4/83 and 24/8/94). As well as improvement of CT-scans there has been the advent of MRI scans. See Metter (1987) for a detailed description of these technological developments. The greater sensitivity of MRI scans compared to CT-scans has been verified, (e.g., by Levinet al.1987). Lobato et al.(1986) reported that some people with severe closed head injuries even had normal CT scans. The slice taken of each subject's head for their scans was also dictated by treatment and management considerations, which didn't necessarily result in scanning the brain structures of interest to this project. Fortunately all these were able to be minimized to a large extent by the involvement of not one but two raters with qualifications in appropriate fields, Neurosurgery, Neurology and Nuclear Medicine. Furthermore, the raters were both very experienced, senior and well regarded members of their professional communities in South Australia.

For a significant proportion of subjects, there was an unusually long interval between scanning and testing. (See Table 21.) Serial scanning of subjects with brain lesions has found that lesions tend to reduce with time (Levin et al.1987; Mitchener et al.1998), although Mitchener et al. did report exceptions to this tendency. Levin et al. reported the additional finding that lesion reduction was paralleled by improvement in cognition and memory. Wilson, Wiedmann, Hadley, Condon, Teasdale and Brooks (1988) found that when more than one MRI was performed, it was the most recent one that correlated strongly with measures of neuropsychological outcome. The implication for this project is that, for subjects tested at longer intervals after scanning, lesions identified from their scans may well have resolved by the time of testing. Neuropsychological deficits might then not be found simply because they too had resolved, and not because such deficits are not associated with such lesions. This possibility will be considered for each grouping of brain injured subjects.

Another important issue is the chance of lesions going undetected. Of the 25 brain injured subjects, 18 were scanned with CT, 7 with MRI. That CT does not reveal as many pathologically significant lesions as MRI is well documented (e.g., Levin et al. 1987). Jones et al. (1998) found that no lesions of less than 5 mm in diameter (revealed by postmortem) were detected by CT, and for those larger lesions that were detected, size was underestimated by about 50%. The largest lesions missed by CT in their study were 10-15 mm in diameter. Autopsy (Jones et al. 1998) and single photon emission tomography -SPECT (Newton et al.1992) have shown that some pathologically significant lesions are not detected by MRI either. In Jones et al.'s study, MRI failed to detect areas of non-haemorrhagic axonal injury confirmed at postmortem. Another factor, other than simple resolution and detail, that may distinguish the different scanning technologies, could be inferred from Levin et al.'s (1987) results. They reported that MRI tended to reveal frontal and temporal lesions missed by CT. As this finding was not reported in other comparisons of CT and MRI (e.g., Jones et al.), could this possibly reflect variations in staff practices across units where this technology is applied; for example, in the position of the 'slice' of the brain taken in each scan. Or could it reflect some diversity in quality of the equipment? There is not enough information to answer these questions.

These limitations to the scanning technology raise the possibility of additional, undetected lesions being present for the whole group of 25 brain injured subjects. However, available scanning had already revealed that the pattern of brain injury was highly variable across the group. Conclusions were only drawn as to a likely association between a neuropsychological deficit and a type of lesion when a clear majority of the set of subjects with the same lesion had the same deficit, regardless of what additional lesions and deficits they had. Thus, such a conclusion would only be invalid if such a subgroup all had the same undetected lesions in other areas. Undetected lesions could occur anywhere across the entire brain. It seems quite unlikely that the complete set of 6-10 subjects in any one of the subgroups considered in this project, with brain injury of varying etiology, could all have the same undetected lesions. Consequently this was not considered to be a serious methodological problem.

Table 21

Scanning-Testing Interval for Brain injured Subjects (N=25)

Interval (Yrs.)	Cumulative % of Subjects
<.05	25
.18	50
.21	
.85	62.5
2.21	
3.85	
4.72	75
4.91	
7.60	
11.94	
12.22	
13.00	
23.16	100
Mean=3.56 SD=5.96	

Table 22

Areas of Brain Involvement

(Note: total numbers in a column could exceed the total of subjects in that respective subgroup as many subjects were counted in more than one cell. This was due to the diverse nature of brain damage in a large proportion of the sample.)

	Spinal Injury Controls (N=11)	All CVAs (N=7)	All Closed Head Injuries (N=15)	Other (N=3)
Basal Ganglia: left unilateral		4	2	1
Basal Ganglia: right unilateral		3	6	
Basal Ganglia: bilateral				
Other subcortical: left unilateral		4	2	2
Other subcortical: right unilateral		2	7	1
Other subcortical: bilateral			1	
Frontal: left unilateral				1
Frontal: right unilateral			4	
Frontal bilateral			4	
Other cortical: left unilateral		1	1	
Other cortical: right unilateral		2	1	
Other cortical: bilateral			1	

6. RESULTS

6.1. Structure of Results Presentation

The analysis required for this thesis was complex. Before the analysis required for the central analysis of the project could be performed, critical data issues had to be addressed. This occurred in Phase 1, 'Resolution of Data Issues'. Their resolution then made possible the further analysis required for achieving the main objective of this thesis (Phases 2 to 4). Further analysis of the combined results from these three phases was required to clarify the overall pattern of relationships between brain lesions and test performance. This effectively involved another phase (Phase 5). A subset of ten tests from the complete set of 31 making up the project battery were associated with individual basal-cortical circuits. These conclusions from Phase 5 were then tested with another set of (presumably) circuit-impaired subjects, people with early-stage Parkinson's Disease (Phase 6 Neuropsychological Deficits of Parkinson's Disease Subjects).

6.1.1. PHASE 1: Resolution of Data Issues

Comparison of individual test scores with control-group data was the basic test of deficit performance for the brain-injured subjects. This method was chosen in preference to the more popular comparison with a measure of premorbid function. The language impairments, which were found among this group (see section 6.6.), can also impair performance of the main task used to assess premorbid function in neurologically impaired populations. This task is reading phonetically irregular words (NART-R). However another experimental group was not characterized by aphasic disturbances, the PD subjects in Phase 6. It was possible to check for deficits among this group using the premorbid measure comparison method (see Table A.16 in Appendix A.).

Issues requiring resolution before the central analysis could proceed were twofold. How representative were the spinal injury control group, of the general population (except for psychological reaction to trauma, debilitation and rehabilitation)? This required verification. Comparison of individual brain-injured subjects' test scores with control-group data was the

basic test of significantly impaired performance after all. The other data-related issue involved the neuroimaging (CT and MRI) used to verify lesion location. Previous studies have revealed these imaging techniques to have significant limitations on how accurately they can reveal the full extent of any brain lesions. Both these issues were addressed under '6.2.1 Comparison of Controls Subjects and the General Population' and '6.2.2 Testing the accuracy of Neuroimaging (CT & MRI) available for all Lesion Subjects', respectively.

6.1.2. PHASE 2: Neuropsychological Deficits among Brain Injured Subjects with verified Lesions of the Dorsolateral Prefrontal Circuit.

A set of tests that are potentially sensitive to lesions of the basal-cortical circuitry (including the dorsolateral prefrontal circuit) has been identified from the literature (see Table 15). It is the objective of this phase to identify the ones from that pool that are sensitive to lesions of this circuit.

6.1.3. PHASE 3: Neuropsychological Deficits among Brain Injured Subjects with verified Lesions of the Anterior Cingulate Circuit.

A set of tests that are potentially sensitive to lesions of the basal-cortical circuitry (including the anterior cingulate circuit) has been identified from the literature (see Table 15). It is the objective of this phase to identify the ones from that pool that are sensitive to lesions of this circuit.

6.1.4. PHASE 4: Neuropsychological Deficits among Brain Injured Subjects with verified Lesions of other Language-Related Circuitry.

This phase is similar to Phase 2 and Phase 3, except that different circuitry was involved, language-related circuitry involving Broca's and Wernicke's areas. This is the language-related circuitry proposed by Crosson (1992). Unlike the circuits examined in those phases however, cortical areas outside the frontal areas were involved. A set of tests that are potentially sensitive

to lesions of the various basal-cortical circuits (including Crosson's language-related circuit) has been identified from the literature (see Table 15). It is the objective of this phase to identify the ones from that pool that are sensitive to lesions of this circuit.

6.1.5. PHASE 5: Broad Areas of Cognition associated with Basal-Cortical Circuitry: An integration of findings from Phases 2 to 4.

A subset of the tests making up the project battery were associated with individual basal-cortical circuits in Phases 2 to 4. Some different circuits were involved with the same forms of cognition and some individual circuits were associated with more than one type of cognitive processing. Considering lesion profiles associated with tests for each area of cognition should therefore further clarify neuropsychological processing associated with these circuits. Further data analysis was involved, involving results yielded by all four previous phases. This effectively became another phase. This analysis is presented for each area of cognition involved. Those areas were, complex programs of motor activity, executive functions, verbal comprehension and expression.

6.1.6. PHASE 6: Neuropsychological Deficits of Parkinson's Disease Subjects

Subjects with PD potentially have degenerative changes in all circuits. Phase 5 identified a set of ten measures (see Table 55), arguably sensitive to lesions in some of the circuits. Such findings needed support from further investigation to be considered conclusive. A survey of another group of subjects, with presumed basal ganglia impairments, (early-stage PD subjects), is an example of the type of investigation which would test the conclusions of Phase 5. Support required PD subjects to demonstrate comparable deficits. The objective of Phase 6 was establishing the correspondence between the PD subjects' and circuit-lesion subjects' deficits.

6.2. PHASE 1: Resolution of Data Issues

Objective 1: Comparison of individual brain-injured subjects' test scores with control-group data was the basic test of deficit performance. Whether this control group was representative of the general population, except for a small number of predictable deviations (associated with the psychological reaction to trauma and debilitation), required verification. It is the first objective of Phase 1 to verify the adequacy of these data. (See '6.2.1 Comparison of Control Subjects and the General Population.')

Objective 2: The methodology used to address the central goals of this thesis (Phases 2 to 4) depended on the accuracy of neuroimaging (CT and MRI). However, previous studies have questioned its accuracy. The second objective of Phase 1 is to verify the accuracy of neuroimaging available, and identify any limitations on this accuracy. (See '6.2.2 Testing the Accuracy of Neuro-imaging (CT & MRI) available for all lesion subjects')

6.2.1. Comparison of Control Subjects and the General Population

A traditional method for establishing the presence of a neuropsychological deficit is comparison of a subject's performance with an estimate of pre-morbid functioning. However, with the exception of the PD subjects, the subjects of this study were potentially impaired, by their brain lesions, on all skills normally assessed to measure pre-morbid functioning. For example, the most widely used such measure, National Adult Reading Test –Revised (NART-R), is affected by aphasic deficits (Lezak, 1995), which were clearly present among the lesion subjects. Furthermore, the lesion subjects would have arguably suffered additional neuropsychological impairment from other psychological aspects of their experience. The latter are discussed in detail in section 5.1. To control for this additional, confounding, non-lesion source of neuropsychological impairments, it has been argued that comparison of performance with that of another group with similar experience, for instance spinal injury subjects, is a more valid method of establishing the presence of deficits (Godefroy et al., 1998).

The adequacy of the spinal injury control group can be tested by data analysis. It was assumed that they were different from the normal population in predictable ways; ways that could be predicted from Post Traumatic Stress Disorder, depression, substance abuse and lower socio-economic status. Any kind of extensive normative testing with the thesis test battery was not possible. Normative data published by the constructors of each test was the only data available for checking this assumption. Comparisons of control group and published normative-sample means are shown in Table A.1 (See Appendix A.).

The controls and respective normative samples were significantly different on a small number of measures. The Spinal Injury controls scored significantly lower on five (WAIS-R Digit Symbol, Immediate Paragraph Recall, Delayed Paragraph Recall, HLLST Homonyms subtest, HLLST Association Naming subtest). They were significantly better than the normative samples on only one measure (Wisconsin Card Sorting Test, Perseverative Errors). Thus six out of the 29 of the t-tests revealed significant differences.

The danger of type 1 errors when this many t-tests are performed is well known. Bonferroni adjustments are usually advocated for guarding against this possibility. However, some (including the superviser of this project) have cogently argued that such corrections would have resulted in a loss of power disproportionate to the number of type 1 errors involved. 1.5 out of the 29 t-tests would be expected to be significant by chance alone. Careful scrutiny of any unexpected results was seen as a more appropriate method for guarding against type-one errors in this situation.

The poorer performance of the controls on Immediate and Delayed Paragraph recall and HLLST Association Naming are consistent with the verbal memory and attentional difficulties associated with post traumatic stress disorder (PTSD). Thus, for these three measures the control group mean was used for comparisons against the lesion groups, as these significantly lower average scores could be argued to reflect the effects of PTSD which are probably common to both groups. (The likelihood of closed head injury subjects having PTSD has been well argued by Bontke, 1996 and Brooks, 1996.) The lower WAIS-R Digit Symbol score probably reflects the effects of spinal injuries on fine pencil control. There was no obvious

explanation for the remaining two significant differences (HLLST Homonyms and the Wisconsin Card Sorting Test, Perseverative Errors). It should be noted that with this number of comparisons, a certain number of type-one errors would be anticipated. For this reason the normative data, rather than the spinal group data was used as a basis for z-score comparisons involving these two variables in subsequent analyses.

Proportions of the brain-injured sample at each main level of vocational qualifications were approximately consistent with the national percentages (from 1991 Australian Census). See Table 18, Method Section.

6.2.2. Testing the Accuracy of Neuro-Imaging (CT & MRI) available for all Lesion-Subjects

Low performance on some neuropsychological tests is well accepted as linked to certain lesions. This provided the basis for a test, albeit crude, of the accuracy of neuro-imaging. Accurate neuro-imaging implies that subjects should display the associated low scores on neuropsychological tests. It is acknowledged that there is some circularity in the logic of this approach, which runs, 'if Lesion A results in Deficit I, then the presence of Deficit I should indicate the presence of Lesion A.' However Deficit I can often result from other lesions, and Lesion A may not invariably result in Deficit I.

The methodological challenges facing this series of studies are substantial. A major one is possible inaccuracies of neuroimaging. This is discussed extensively in section 5.5. The error brought into our analysis from this source can be compounded by the inevitably imperfect test-retest reliability of neuropsychological tests. Thus a loose correspondence between neuroimaging and test performance (or between structural and functional data), in the direction predicted, would provide modest support for the validity of the two types of instrumentation critical to this study and thus increase confidence in study conclusions.

The sources of error in both neuroimaging and neuropsychological tests are potentially substantial, consequently reducing the correspondence between the two. These are discussed extensively elsewhere in this thesis, sections 5.5. and 4., respectively.

Possibly the most simple, established link in this regard has been the association between brain lesions of either hemisphere and contralateral motor impairments. Spearman Rank Order correlations were calculated between all four of, level of motor impairments on the left side, level of motor impairments on the right side, extent of left hemisphere brain lesions and extent of right hemisphere brain lesions. The index of motor signs is described in the method section ("5.4.2.1 Assessment of Motor Signs"). Number of major body parts displaying incoordination (hands, feet, arms, legs, trunk and face), and the severity of that incoordination are considered in the compilation of this index. For this phase, a simple index of brain hemisphere involvement was specially devised. For example, for our index of left-hemisphere involvement, one point was assigned for each left hemisphere brain region which the medical staff rating brain scans, so-judged to show any evidence of brain lesions. The division of the left hemisphere into regions for this purpose being, the frontal lobe, temporal lobe, parietal lobe, occipital lobe, and subcortex. The total of so-assigned points represented the left-hemisphere brain involvement index, likewise for the right hemisphere.

All correlations were significant, in the predicted directions. The extent of right hemisphere lesions was correlated with the level of motor signs on the left side ($r=.60$, $p<.01$), and conversely, the extent of left hemisphere lesions was correlated with the level of motor signs on the right side ($r=.56$, $p<.01$). Among these subjects, the reverse applied to associations between brain lesions and motor signs on the same side. The extent of right hemisphere lesions was negatively correlated with the level of motor signs on the right side ($r=-.46$, $p<.01$), and the extent of left hemisphere lesions was negatively correlated with the level of motor signs on the left side ($r=-.45$, $p<.05$).

With lesion lateralization being so strongly associated with side of motor signs, some lateralizing significance could be reasonably inferred from correlations between motor signs and test performance. The tests displaying significant correlations with level of motor signs on either side of the body are shown in Table 20 below. There was a marked contrast between the number of tests correlated with right-sided motor signs (12) and the number correlated with left sided ones (1). Significance of motor-signs is considered in more detail in Phase 2.

Table 23

Significant Correlations found between Tests and Lateralized Motor Signs within the Proje Battery

Test	Correlation with Left Motor signs	Correlation with Right Motor signs	Correlation with Total Motor Signs
Language Tasks			
HLLST Reading Comprehension subtest		-.73***	-.51*
HLLST Audio/Visual Comprehension subtest		-.70***	
WAIS-R Similarities subtest		-.48*	
HLLST Assoc. Naming subtest		-.47*	
HLLST Definitions subtest		-.45*	
HLLST Vocabulary subtest		-.44*	
HLLST Categories subtest		-.42*	
HLLST Sequencing subtest		-.42*	-.52*
HLLST Yes/No subtest		-.41*	
Visuo-Motor Tasks			
Trail Making Test, Part A	.56**		.66
Trail Making Test, Part B		.54**	
WAIS-R Digit Symbol subtest		-.44*	-.55**
Memory Task			
Story Recall, immediate		-.55*	-.48*

* p<.05 ** p<.01 *** *p<.001*

Further investigation of the accuracy of neuroimaging involved links between tests from the neuropsychological battery administered to all subjects and more localized brain areas. For

example, impaired expressive language has long been associated with Broca's and Wernicke's areas (Caplan, 1994). For each measure individually, the subgroup of lesion subjects obtaining significantly low scores on that measure was identified. Then the proportion of each of those subgroups with lesions in corresponding locations was also identified. If a majority of subgroups had a majority of subjects with lesions in the corresponding location, this would support the accuracy of the scans available. As revealed in Table A.2 (in Appendix A.), the data did not show this.

However, this may be explicable in terms other than as a reflection of widespread failure of neuro-imaging to detect lesions. For 37.5% of the lesion subjects, the interval between scanning and neuropsychological testing was more than two years (see Table 21). Studies of neuro-imaging (reviewed in the Method Section, under 'Lesion verification') have shown that correspondence, between neuropsychological deficits and lesions, reduces as the scanning-testing interval increases. To see if this same tendency was present in the data of this project, intervals for lesion subjects with predicted poor performance on neuropsychological tests, and intervals for those without these predicted difficulties, were compared. These comparisons are presented in Table A.3 (see Appendix A).

Two other intervals were examined in the same way. The length of the interval between brain injury and imaging was not associated with predicted deficits. However the interval between brain injury and testing was, albeit less strongly ($p<.05$, Sign test). This latter interval and the one between imaging and testing (that presented in Table A.3, in Appendix A.) were in fact highly correlated ($r=0.79$, $p<.001$). Thus this only reflects the same phenomenon.

As shown in Table A.3 (see Appendix A.), the number of tests where the average Imaging-Testing Interval was shorter for subjects with predicted deficits was 25 out of 29 ($p<.001$, Sign Test). Clearly a shorter Imaging-Testing interval is associated with greater likelihood of finding predicted areas of low performance on neuropsychological tests. That is, when the occasions of CT or MRI being performed are closer in time to the occasion when testing was performed, predicted deficits are more likely to be found. This appears to confirm the findings

reported in earlier studies (e.g., Wilson et al. 1988). These suggest some kind of brain-function recovery, and hence skill-recovery, occurring as time passes.

Therefore we might reasonably conclude that the pattern of results does in fact support the general accuracy of neuro-imaging data available for this project. For some subjects, however, some distortion may have been introduced by longer intervals between neuro-imaging and neuropsychological testing. Data from such subjects was scrutinized during analysis for Phases 2 to 4. In this way distortion from this source was minimized. Another important observation in this context is the fact that some subjects, tested five or more years after neuro-imaging, still showed considerable neuropsychological impairments (e.g. subject 20, Tables A.4. & A.5., subject 41, Tables A.6. & A.7., see Appendix A.).

In this context it is important to note that a lack of correspondence between neuropsychological deficit and neuroimaging deficit is quite common. In fact this is discussed extensively in other sections of this thesis. CT and MRI do not detect all the lesions revealed by post mortem, and the longer the interval between between injury and neuroimaging the weaker the correspondence (see section '5.5 Lesion Verification'). Furthermore, undetected brain disruption, remote from the main site of brain injury can be quite significant (see section '2.5. Cognitive Deficits associated with Lesions of the Basal Cortical Circuitry: Preliminary Issues.'). Therefore some lack of correspondence is predictable, and not a significant cause for concern.

6.3. PHASE 2: Neuropsychological Deficits among Brain Injured Subjects with Verified Lesions of the Dorsolateral Prefrontal Circuit.

Objective: All subjects in the project were administered a battery of tests. It is the objective of this phase to identify the ones from that battery which are sensitive to lesions of the dorsolateral prefrontal circuit.

6.3.1. Data Analysis and Rationale

The research methodology most suitable for establishing clear brain-behaviour relationships is controversial. While the traditional group comparison (lesion versus non-lesion, or lesion one versus lesion 2) has advanced our knowledge, it has well documented limitations. These result from the heterogeneity which is characteristic of almost any group of brain-injured people. Adams, Brown and Grant (1985) conducted statistical simulations of typical lesion-group comparisons. They concluded that "ANCOVA should not be used in neuropsychological research to equate groups unequal on variables such as age and education or to exert statistical control whose objective is to eliminate consideration of the co-variate as an explanation for results" (p. 445).

Another method that attempts to avoid the resultant methodological difficulties involves identifying the common lesion in a group of subjects who all perform poorly on the same neuropsychological measure (e.g., Blunk, De Bleser, Willmes & Zeumer, 1981). This approach has methodological difficulties of its own. Lesions in more than one location can produce the same deficit, e.g. lesions in the left infereoparietal, temporal lobes, thalamus, striatum or deep white matter can cause, for example, an impairment of naming (Alexander, Naeser & Palumbo, 1987; Mesulam, 1990; Kremin, 1994). Godefroy et al. (1998) have contributed a very comprehensive exploration of all these issues. On the basis of further research, they propose a new method, which they describe as 'Classification Tree Analysis'. It is the logic of this method that has provided the central methodology used in this project. It is, in fact, a development of the well established 'double dissociation' principle into a formalized research methodology, complete with it's own special type of statistical analysis. Bradshaw and

Mattingley (1995) have explained this principle. Dissociation is said to occur when one group of lesion subjects is impaired on task A, but normal on task B, and a group with different lesions is normal on task A and impaired in task B.

The set of measures identified in this way, Phases 2 to 4, are listed in Table 24. Godefroy et al.'s analysis includes a second stage. This involves closer scrutiny of individual subjects' complete set of brain lesions. Lesion profiles for subjects with deficits on all the final set of tests are compared with those of subjects without the deficits. This is essentially a qualitative style of analysis. It leads to stronger conclusions in regard to lesion-poor test performance relationships, and these relationships can be classified into four types. (See the beginning of section "6.6. Phase 5"). Phase 5 corresponds to the second stage of Godefroy et al.'s analysis.

6.3.1.1. Classification Tree Analysis

Godefroy et al. (1998) defined certain preconditions needing to be satisfied if a lesion is to be associated with poor performance on a particular test. Key elements of their approach are listed below.

1. It is hypothesized that *Lesion A* will lead to impaired performance of *Test 1*. Subjects with *Lesion A* performing poorly on *Test 1* will be called *Group P*. If a clear majority of other subjects, those who did not have *Lesion A*, did not perform poorly on *Test 1*, then poor performance is arguably associated with *Lesion A*.
2. If no other lesions (i.e., all lesions other than *Lesion A*) were found to be so associated with impaired performance *Test 1*, this corresponds to "unicity" (one lesion, *A* results in one deficit, on *Test 1*).
3. If any of the subjects who did not have *Lesion A* still performed poorly on *Test 1*, they were further categorized according to whether they had *Lesion B* or not, *Lesion B* having been hypothesized to be the second most likely lesion to result in impaired performance on *Test 1*.
4. If a majority of the remaining subjects, without *Lesion A* or *Lesion B*, did not perform poorly on *Test 1*, then it could be concluded that impaired performance on *Test 1* could be caused by either *Lesion A* or *Lesion B* ("Equivalence").
5. For *Test 2*, it is hypothesized that a combination of *Lesion A* and *Lesion C* will result in impaired performance. Firstly, it was checked whether a majority of subjects with *Lesion A*

& Lesion C, performed poorly on *Test 2*. If so, and a clear majority of other subjects, those who did not have the combination of *Lesions A & C*, did not perform poorly on *Test 2*, then poor performance is arguably associated with the combination of *Lesions A & C*. ("Association")

6. If there are further subjects, without the combination of Lesion A and Lesion C, who have performed poorly on Test 2, then step 3 (above) should be followed to see if additional lesions were associated with poor performance of Test 2.
7. This was complemented in Godefroy et al's approach by statistical analysis. Briefly, this consisted of linear regression with stepwise selection, to build the 'best' subset of predictive variables (i.e., possible lesion locations most associated with poor performance on a particular test). Then the independent variable with the largest correlation with the dependent variable was used as Lesion A in step 1 (above). This was followed by the Classification and Regression Tree Method (Brieman, Friedman, Olshen & Stone, 1984), which is based on a binary decision tree to predict a nominal or ordinal independent variable. However small numbers in the experimental groups of this phased investigation (6-10) are not sufficient to perform such analysis. Criteria which could be argued on a clinical basis, were used instead.

This approach does not have the flaws identified in the other widely used approaches to linking lesions and deficits discussed in 6.3.1. 'Data Analysis and Rationale'. The well-thought-through, sequential, logical process allows us to proceed with confidence and draw important conclusions from the data. This is despite the subject numbers being small and the heterogeneous brain involvement among those small numbers of subjects, preventing the kind of results analysis often considered a basic requirement of social science research (i.e., group comparisons of homogenous groups).

From the literature review it was argued that subjects with disruption to the dorsolateral prefrontal circuit (brain-injured subjects) would perform poorly on a set of associated neuropsychological tests. This required developing a definition of 'poor performance', which could be applied to each individual score. If fewer than one out of ten control subjects (i.e.

$p<0.1$) would have obtained a score above or below a particular cut-off, this was considered significantly different from the control mean.

When a set of the brain-injured subjects' scores on a measure were transformed into quasi z-scores using the mean and standard deviation of the control group, 'poor performance' so-defined ($p<0.1$), corresponds to <-1.64 or $> +1.64$, (depending on the direction of impaired performance). If (as was the case for most of the measures) a lower score meant less proficient performance, then a score below the lower cut-off (-1.64) defined poor performance. This transformation was applied to all brain-injured subjects' test scores to check whether they fell within this range. It is the transformed scores that are presented in all tables of results for individual subjects (Tables A.4., A.6., A.8., A.10. and A.12., see Appendix A.). Cells in those tables containing a score within the range of poor performance are shaded. (See Table A.1., in the Appendix A., for raw score means and standard deviations of the control group.) It is recognized that these scores are not z-scores in the normal sense. They are not based on the mean and standard deviation of the group containing the individuals whose performance is represented by those scores (i.e. the brain-injured subjects). Instead they are based on the mean and standard deviation of a different group, the control subjects. However, for sake of convenience, they will be referred to as z-scores in the write-up of this project.

The tests used to check for deficits are as follows. (They are described fully in the Method section.)

Motor and Visuo-Motor Tests

WAIS-R Digit Symbol

Trail Making Test

Rey-Osterrieth Figure, Copy

Visual Tracking and Reaction Time Assessment Task (referred to as the 'Computer Task')

Visual Processing Tests

Wisconsin Card Sorting Test –Revised (WCST-R)

WCST-R Category Score

WCST-R Perseverative Responses

WCST-R Conceptualization Index

Porteus Mazes

Memory Tests

RBMT Paragraph recall, immediate

RBMT Paragraph recall, delayed

RBMT Picture Recognition

Rey-Osterrieth Figure, Recall

Verbal Tests

Higher Level Language Screening Test (HLLST)

HLLST Yes/No questions

HLLST Vocabulary

HLLST Grammar

HLLST Auditory/Visual Comprehension

HLLST Reading Comprehension

HLLST Antonyms

HLLST Synonyms

HLLST Give Definitions

HLLST Provide a Word

HLLST Différences

HLLST Categories

HLLST Sentence Formulation

HLLST Analogies

HLLST Homonyms

HLLST Absurdities

HLLST Association Naming

HLLST Sequencing

WAIS-R Similarities

To minimize complexity in the presentation of these results, result presentation is confined to listing of tests thus associated with the circuit. A different set of tests was associated with each circuit. Results are presented in the Appendix A. as a separate set of tables for each. Two of the circuits were not associated in this way with any tests from the project battery (right dorsolateral prefrontal circuit and the right lateral orbital circuit). Consequently no tables are presented for those.

Results for a specific test are only presented when a majority of subjects within a circuit-lesion-group all performed poorly on it. Subjects involved and their lesion profiles were then subjected to closer scrutiny, following the Classification Tree Analysis approach. This is explained in more detail below. The pattern of brain involvement and demographic characteristics for each individual is set out in a separate companion table, immediately following the first. (These tables of results are presented in an Appendix A.) Reference is made to these individual subject characteristics when they have implications for further analysis and conclusions in the Result Section.

6.3.2. Deficits Present among Subjects with Lesions in the Dorsolateral Prefrontal Circuit

There were thirteen specific tests where a majority of subjects with lesions of this circuit, in either brain hemisphere, performed poorly (listed below). Individual scores on those tests for these subjects are shown in Table A.4. and Table A.5. (see Appendix A.). The pattern of brain involvement and demographic characteristics, for each individual, is set out in a separate companion table (Table A.5. and Table A.7. respectively, see Appendix A). There were six tests from within this set where a clear majority of other subjects, with lesions confined to different locations, did not perform poorly. These are written in bold. It was these, and these only, that were included in the further analysis, described in Phase 5.

Left Hemisphere Circuit	Right Hemisphere Circuit
HLLST Give Definitions	**CST Perseverative**
Trail Making Test, Part B	**Errors**
HLLST Auditory Visual	WAIS-R Digit Symbol
Comprehension	HLLST Sentence Formulation
HLLST Antonyms	
HLLST Absurdities	
HLLST Synonyms	
WAIS-R Digit Symbol	
HLLST Association Naming	
HLLST Provide a Word	
HLLST Sentence Formulation	

6.4. PHASE 3: Neuropsychological Deficits among Brain Injured Subjects with Verified Lesions of the Anterior Cingulate Circuit.

Objective: All subjects in the project were administered a battery of tests. It is the objective of this project to identify the ones from that battery which are sensitive to lesions of the anterior cingulate circuit.

There were twelve specific tests where a majority of subjects with lesions of this circuit, in either brain hemisphere, performed poorly (listed below). Individual scores on those tests for these subjects are shown in Table A.8. and Table A.10 (see Appendix A). The pattern of brain involvement and demographic characteristics, for each individual, is set out in a separate companion table (Table A.9. and Table A.11. respectively, see Appendix A.). There were three tests from within this set where a clear majority of other subjects, with lesions confined to different locations, did not perform poorly. These are written in bold. It was these, and these only, that were included in the further analysis, described in Phase 5.

Left	Right
Computer Tracking Task	WAIS-R Digit Symbol
Trail Making Test Part B	HLLST Synonyms
HLLST Auditory/Visual Comprehension	HLLST Sentence Formulation
HLLST Antonyms	
HLLST Synonyms	
HLLST Provide a Word	
HLLST Association Naming	
WAIS-R Digit Symbol	
HLLST Sentence Formulation	

6.5. PHASE 4: Neuropsychological Deficits among Brain-Injured Subjects with Verified lesions of other Language-Related Circuitry.

Objective: All subjects in the project were administered a battery of tests. It is the objective of this phase to identify the ones from that battery which are sensitive to lesions of the language-related circuitry identified by Crosson (1992).

This circuit occurred in the left hemisphere only. There were six specific tests where a majority of subjects with lesions of this circuit, performed poorly (listed below). Individual scores on those tests for these subjects are shown in Table A.12. (see Appendix A). The pattern of brain involvement and demographic characteristics, for each individual, is set out in a separate companion table (Table A.13., see Appendix A). There were two tests from within this set where a clear majority of other subjects, with lesions confined to different locations, did not perform poorly. These are written in bold. It was these, and these only, that were included in the further analysis, described in Phase 5.

Left
Trail Making Test, Part B
HLLST Synonyms
HLLST Antonyms
HLLST Association Naming
HLLST Provide a Word
HLLST Sent Formulation

6.6. PHASE 5: Broad Areas of Cognition Associated with Basal-Cortical Circuitry: An Integration of Findings from Phases 2 to 4.

Godefroy et al.'s method of analysing brain-behaviour relationships ('Classification Tree Analysis') involved three steps. For the first, measures were identified where a majority of subjects in a circuit-lesion group had a deficit and no more than a minority of subjects without a lesion in the same circuit also showed significantly impaired performance. This is essentially what was performed in Phases 2 to 4 and it yielded an initial pool of measures which were more likely to be sensitive to circuit lesions (summarized in Table 24).

Table 24

Tests Associated with Lesions of Basal-Cortical Circuitry

Neuropsychological Test (No. with a deficit out of 25)	Task
WAIS-R Digit Symbol (n=11)	Writing as many symbols next to numbers as possible in 90 seconds
Trail Making Test, Part B (n=10)	Dot-to-dot task, alternating between number and letter sequences
Computer Tracking Task (n=6)	Using a joystick to keep a 5mm circle inside a 15 mm square randomly moving around a computer screen
WCST-R Perseverative Responses (n=10)	Number of persistent card sorts made to wrong principle
HLLST Auditory/Visual Comprehension (n=10)	Following examiner's instructions in relation to a picture
HLLST Association Naming (n=15)	Naming as many items as possible in a category in 60 seconds
HLLST Antonyms (n=12)	Giving the opposite of a given word
HLLST Synonyms (n=13)	Giving another word that means the same as a given word
HLLST Give Definitions (n=7)	Explaining word meanings
HLLST Absurdities (n=9)	Explaining the absurdity of a story

The next step required closer comparison of the pattern of brain lesions for all subjects performing poorly on a particular measure and all those who did not on the same measure. This had to be done separately for each of the tests remaining in our 'potentially-sensitive-measure-pool' (i.e., those listed in Table 24). Where relationships were thus found to exist between certain deficits and circuit lesions, they were categorized according to Godefroy et al.'s four basic modes of brain-behaviour relationships. (Classification Tree Analysis is described in detail in section 6.3.1.1.) Those basic modes are:

1. *Unicity*, when the occurrence of a deficit depends on the lesion of a single structure, i.e. one deficit, one lesion.
2. *Equivalence*, when the occurrence of a deficit depends upon a single lesion within two possible structures. (In the context of this project, if a majority of deficit subjects had either

lesion A or B, sometimes in combination, and no more than one or two non-deficit subjects had lesion A or B, it was concluded that that deficit resulted from either lesion A or lesion B.)

3. *Association*, when the occurrence of a deficit requires the combined lesion of two different structures. (In the context of this project, if all deficit subjects had lesions A, B and C and no other subjects without the deficit had this combination of lesions, it was concluded that the deficit was a result of the combination.)

4. *Summation,* when a single lesion of two possible structures results in a minor deficit and the combined lesion of both structures results in a major deficit. This in fact seems to be a special case of equivalence. However, with the limitations on the data available (small numbers and possible additional, but undetected lesions), it was not possible to judge whether any instance of equivalence was in fact an instance of this special case.

When the poorly performing subjects showed no consistent lesions, the cause of their poor performance was unknown. The possibility could not be discounted that such subjects may in fact have had consistent lesions, but the neuro-imaging available, e.g., CT-scans, may simply not have revealed all lesions present.

For some forms of cognition, more than one circuit was involved. Some circuits were also associated with more than one type of cognition. Examination of findings for all circuits in combination (not just one-by-one as in Phases 2 to 4) should further clarify neuropsychological processing associated with these circuits. As further analysis of data yielded by the four previous phases (Phases 2 to 4) was required, this effectively became another phase (Phase 5). This analysis is presented for each area of cognition involved. Those areas were complex programs of motor activity, executive functions, verbal comprehension and verbal expression.

6.6.1. Complex Programs of Motor Activity

It was hypothesized in the literature review that this function would be associated with the dorsolateral prefrontal circuit.

6.6.1.1. WAIS-R Digit Symbol Subtest

6.6.1.1.1. Nature of the Task

This is a well known subtest from the well known WAIS-R. Subjects were required to write as many symbols next to numbers as they could within 90". An arbitrary correspondence between symbols and numbers is taught at the start of this test. The critical elements of this task have been investigated by Crowe, Benedict, Enrico, Mancuso, Matthews and Wallace (1999). They concluded that the ability to execute elementary motor tasks is a significant factor in this task, processing speed less so. Some variance in Digit Symbol performance remained unaccounted for however. Some combination of visuo-motor coordination, sustained attention and motor persistence, as proposed by Lezak (1995) are conceivably involved also. Abilities one might expect, that have been eliminated by research include: intellectual prowess, learning, memory or visual acuity.This was a well known subtest from the WAIS-R. The subject was required to write as many symbols next to numbers as they could within 90". An arbitrary correspondence between symbols and numbers is taught at the start of this test.

6.6.1.1.2. Analysis of Associated Brain Areas

Lesions present in a majority of the subjects with a deficit on the WAIS-R Digit Symbol subtest are shown in Table 25. Five out of the six subjects with the left dorsolateral prefrontal circuit involved had the deficit. The section of the circuit involved for four out of those five was either the caudate nucleus or the globus pallidus, i.e. the left basal ganglia.

Most subjects with one of the right hemisphere circuits involved (dorsolateral prefrontal, anterior cingulate and lateral-orbital) also had the other two circuits involved. For the majority of these subjects, again it was the basal ganglia (right) part of the circuit, either the caudate nucleus or the globus pallidus, that was affected, not the cortical sections. The proportions of subjects with the basal ganglia level of these circuits involved were: right dorsolateral prefrontal (6/7), right lateral orbital (4/6) and right anterior cingulate (4/6). Also, none of the subjects with any of the left circuits involved had any of the right circuits involved, and vice versa. In conclusion, deficit performance on the WAIS-R Digit Symbol subtest appears to be

associated with left or right basal ganglia, in particular the combination of the globus pallidus and the caudate nucleus within one hemisphere. This corresponds to what Godefroy et al. have termed equivalence.

As to whether lesions at the cortical level of these circuits would have produced the same deficit as the basal ganglia lesions, this data set is inconclusive. Only one or two subjects had lesions at the cortical level of these circuits. These numbers are too small to examine this possibility. The one subject with the left dorsolateral prefrontal lobe involved had a deficit on the Trail Making task (Part B). One with a lateral orbital cortex lesion had the deficit, while two other subjects with this cortical lesion did not. The two subjects with lesions of the anterior cingulate cortex did not have the deficit.

Comparison of all subjects with deficits on this task, with all those without, in terms of brain lesions revealed further information (see Table 25 & Table 26). Of all those who had this deficit, seven out of 14 had the right dorsolateral prefrontal circuit involved, compared with only two out of the 11 who did not have this deficit. A similar picture emerged for the same circuit in the left hemisphere. Five out of the 14 with this deficit had the left dorsolateral prefrontal circuit involved, while only one out of 11 without this deficit had that circuit involved. It was noteworthy that these two circuit-lesion subgroups had very few members in both groups (i.e., deficit group and the nondeficit group). The two circuit-lesion subgroups combined represented 12 out of the 14 subjects who showed difficulty with this task. This pattern of data is consistent with equivalence. The fact that two subjects did not have lesions in either of these circuits but still displayed the deficit suggests that additional brain areas again are associated with this task.

The range of correlations between this task and others from the neuropsychological test battery provide further information about cognitive requirements of this task. 19 other measures correlated significantly with the WAIS-R Digit Symbol subtest. They are listed in Table 27, in order of magnitude. Several important deductions can be drawn from these correlational data. Firstly, the other assessment task yielding the scores showing the strongest statistical relationship to scores on the WAIS-R Digit Symbol subtest was the short-term story-recall

task. This would suggest a significant verbal memory element within the WAIS-R Digit Symbol subtest. Then of the 10 most highly correlated other measures, seven involve high-level expressive language tasks. This, in combination with the correlation with the story-recall task suggests that a substantial proportion of the mental processing employed during execution of this task is verbally mediated. For instance, subjects may be remembering numbers by their verbal labels, and associating the labels with novel labels for the abstract symbols. Some of the latter do resemble other established symbols after all, e.g. symbols for mathematical computations.

Another noteworthy association involves the ten-most-correlated measures and right-sided motor signs. First of all, there is a correlation of -.44 ($p<.05$) between right-sided motor signs and WAIS-R Digit Symbol subtest scores. Then seven members of this set are also correlated with right-sided motor signs (see Table 27). Clearly the left hemisphere of the brain is important to this task. However, our comparison of lesion profiles of subjects with and subjects without a deficit also pointed to the involvement of the right hemisphere (the right dorsolateral prefrontal circuit). The Trail Making Test, Part A was highly correlated with WAIS-R Digit Symbol performance ($r=-.62$, $p<.001$) and it was also the one measure from the entire test-battery which correlated with left-sided motor signs ($r=-.56$, $p<.01$). Thus the two analyses (lesion-profile comparison and correlation matrix scrutiny) complement each other, in support of the conclusion of left and right dorsolateral frontal circuit involvement.

In conclusion, deficit performance on the WAIS-R Digit Symbol subtest appears to be associated with left or right basal ganglia, in particular the combination of the globus pallidus and the caudate nucleus within one hemisphere.

6.6.1.1.3. Brain Lesions Associated with this Task by other Research

Lezak (1995) concluded from a literature review, that while the WAIS-R Digit Symbol task is highly sensitive to general brain damage, it has little localizing significance. This adds a note of caution to the conclusion of this phase.

Table 25

Lesions of All Subjects with a Deficit on this Measure.

Measure 1: WAIS-R Digit Symbol

Brain Area	Subjects (ID No.s)													
	1	*5*	*6*	*13*	*24*	*25*	*26*	*36*	*40*	*41*	*45*	*48*	*53*	*56*
Left Subcortical Circuit Structures														
Caudate Nucleus		+						+			+			
Globus Pallidus		+									+	+		
Left Basal-Cortical Circuits														
Dorsolateral Prefrontal		+						+	+		+	+		
Lateral Orbital		+						+	+		+	+		
Anterior		+						+			+	+		
Lang Circuitry		+					+	+	+		+	+		
Other Left Hemisphere Areas														
		+					+	+	+		+	+		

Table 25 (Cont.)

Lesions of All Subjects with a Deficit on this Measure.

Measure 1: WAIS-R Digit Symbol

Brain Area	Subjects (ID No.s)													
	1	*5*	*6*	*13*	*24*	*25*	*26*	*36*	*40*	*41*	*45*	*48*	*53*	*56*
Right Subcortical Circuit Structures														
Caudate Nucleus	+		+			+				+			+	+
Globus Pallidus	+		+			+				+			+	
Right Basal-Cortical Circuits														
Dorsolateral Prefrontal	+		+	+		+				+			+	+
Lateral Orbital	+		+	+					+	+			+	
Anterior	+		+	+		+				+			+	
Other Right Hemisphere Areas														
	+		+	+		+	+		+	+			+	+

Table 26

Lesions of All Subjects WHO DO NOT HAVE a Deficit on this Measure.

Measure 1: WAIS-R Digit Symbol

Brain Area	Subjects (ID No.s)										
	3	*4*	*7*	*12*	*20*	*21*	*31*	*42*	*46*	*47*	*54*
Left Subcortical Circuit Structures											
Caudate Nucleus											
Globus Pallidus					+						
Left Basal-Cortical Circuits											
Dorsolateral Prefrontal					+						
Lateral Orbital					+	+	+			+	
Anterior					+				+	+	
Lang Circuitry						+	+			+	
Other Left Hemisphere Areas											
			+	+	+	+	+		+	+	

Table 26 (Cont.)

Lesions of All Subjects WHO DO NOT HAVE a Deficit on this Measure.

Measure 1: WAIS-R Digit Symbol

Brain Area	Subjects (ID No.s)										
	3	*4*	*7*	*12*	*20*	*21*	*31*	*42*	*46*	*47*	*54*
Right Subcortical Circuit Structures											
Caudate Nucleus	+	+									
Globus Pallidus	+	+									
Right Basal-Cortical Circuits											
Dorsolateral Prefrontal	+	+									
Lateral Orbital	+	+					+			+	
Anterior	+	+							+	+	
Other Right Hemisphere Areas											
	+	+					+	+	+	+	

See Appendix C. for a complete description of each individual subject's characteristics.

Table 27

Tests significantly correlated with the WAIS-R Digit Symbol subtest (WDSS)

Test	Correl-ation with WDSS	Correl-ation with Left sided Motor Signs	Correl-ation with Right sided Motor signs
WAIS-R Digit Symbol subtest			-.44*
Story Recall Task, delayed recall	.69***		
WAIS-R Similarities subtest	.68***		-.48*
Trail Making Test, Part B	-.67***		.54**
Trail Making Test Part A	-.62***	.56**	
HLLST Association Naming subtest	.58**		-.47*
HLLST Sequencing subtest	.56**		-.42*
HLLST Categories subtest	.54**		-.42*
HLLST Sentence Formulation subtest	.51**		
HLLST Grammar subtest	.49*		
HLLST Reading Comprehension subtest	.48*		-.73***
Porteus Mazes	.48*		
Wisconsin Card Sorting Test, Conceptual Level Responses	.46*		
Complex Figure of Rey, Recall	.44*		
HLLST Vocabulary subtest	.44*		-.44*
Story Recall Task, immediate recall	.43*		-.55**
Complex Figure of Rey, Copy	.42*		
HLLST Antonyms subtest	.41*		
HLLST Synonyms subtest	.41*		
HLLST Analogies subtest	.40*		

* **p<.05**
** p<.01
*** p<.001

6.6.1.2. Trail Making Test, Part B.

6.6.1.2.1. Nature of the Task

This is a very widely used neuropsychological assessment task. The subject is required to draw a continuous line along a series of small circles scattered across an A4 page, in sequence. Circles contained either numbers or letters and the sequence alternated between the two, ie 1 A 2 B 3 C etc. The performance index was time to completion. Various researchers have investigated the mental processing requirements of Part B of the Trail Making Test (TMT). Gaudino, Geisler and Squires (1995) concluded "that the TMT should best be conceptualized as reflecting a combination of several cognitive functions. Within the clinical setting, the greater time taken to complete Part B appears to reflect an increased demand on motor speed, visual search and higher cognitive processes. Additional slowing in brain-damaged patients could reflect deficits in any or all of these domains." (p. 534). Much debate has occurred within the literature as to the 'higher cognitive processes' that are involved. Suggestions include, ability to execute and modify a plan of action, to maintain two trains of thought simultaneously, attention, concentration, conceptual tracking, activity rate, not to mention receptive and expressive language functions. Crowe (1998) found that cognitive alternation measures and visual search uniquely contributed to variance on the TMT Part B.

6.6.1.2.2. Analysis of Brain Areas Associated with this Task

The pattern of circuit involvement in relation to poor performance on this measure was different from other measures considered so far. All five subjects with all three, left hemisphere, basal-frontal circuits involved performed poorly. None of the subjects with a lesser number of the left hemisphere, basal-frontal circuits involved did so (see Tables 28 & 29). This would be consistent with the Godefroy et al.'s definition of 'association'. The correlation with right-sided motor signs was $r=.54$ ($p<.01$). Furthermore, as was noted in examination of results for the WAIS-R Digit Symbol subtest, for all the subjects with all three, left hemisphere basal-frontal circuits involved, the lesions were primarily at the basal ganglia

level (globus pallidus and the caudate nucleus). See Tables 28 and 29. So it is possible that this deficit resulted from the basal ganglia lesions rather than a lesion of basal-cortical circuits.

However four other subjects, without any left hemisphere, basal-frontal circuits involved (according to the neuro-imaging available) also had a deficit on this task. Thus there are probably other lesions, not clear from this set of data, capable of causing this. This would be consistent with 'equivalence'.

The range of correlations between this task and others, from the neuropsychological test battery, are an indicator of task requirements and consequently a possible indirect indicator of associated brain areas. 18 other measures correlated significantly with the Trail Making Test, Part B. They are listed in Table 30, in order of magnitude. Of the four most strongly associated tests, three involved motor tasks, and the fourth was story-recall, delayed. Various high-level expressive language tasks were among the next-most-correlated tasks. This set of mental processes represented in the most-correlated-tests are arguably the key elements to the Trail Making Test, Part B. The implicit verbal processing and delayed verbal recall requirement is substantial. Presumably this is involved when subjects are mentally alternating between the two verbal sequences (numbers and letters). Another feature of these correlations is the lack of consistent correlation with right-sided motor signs. This might have been expected given the conclusions of the lesion-profile comparison (Tables 28 & 29). It leaves open the possibility of that the particular functional system serving performance of the Trail Making Test, Part B involves areas outside left basal-frontal circuits, e.g. the right hemisphere.

In conclusion, the brain areas subserving the Trail Making Task Part B are the combination of the globus pallidus and the caudate nucleus in the left hemisphere, thereby implicating all three circuits (dorslateral prefrontal, anterior cingulate and lateral orbital) or other unknown areas.

6.6.1.2.3. Brain Areas Associated with this Task by Other Research

As a variety of skills are involved in this task, so a variety of different impairments can lead to poor performance. Some studies have found correlations between test performance and general severity of brain condition (e.g., mild head trauma -Leininger, Gramling, Farrell, Kreutzer & Peck, 1990). Others have reported poor performance in association with very

specific parts of the brain. For example, a correlation of r=.80 with caudate atrophy in patients with Huntington's disease (Starkstein, 1988). Lezak (1995) reported that 'electrophysiological measures that appear to be "associated with frontothalamic functioning" -early stages of the Contingent Negative Variation (CNV) -correlate significantly with both TMT A and B, lending support to hypotheses linking the TMT to frontal activation (Segalowitz, Unsal & Dywan, 1992)' (p. 383).

While the findings of this phase are not identical to findings of other research, there is some approximate consistency. Some of the inconsistency could be attributed to the limitations of measures used in this project and all the others (neuro-imaging inaccuracy and imperfect test reliability).

Table 28

Lesions of All Subjects with a Deficit on this Measure.

Measure 2: Trail Making Test, Part B

Brain Area	Subjects (ID No.s)									
	5	*13*	*20*	*24*	*25*	*26*	*36*	*41*	*45*	*48*
Left Subcortical Circuit Structures										
Caudate Nucleus	+						+		+	
Globus Pallidus	+		+						+	+
Left Basal-Cortical Circuits										
Dorsolateral Prefrontal	+		+				+		+	+
Lateral Orbital	+		+				+		+	+
Anterior Cingulate	+		+				+		+	+
Language circuitry	+					+	+		+	+
Any Left Hemisphere Areas										
	+		+	+		+	+		+	+
Right Basal-Cortical Circuits										
Dorsolateral Prefrontal		+			+			+		
Lateral Orbital		+						+		
Anterior		+			+			+		
Other Right Hemisphere Areas										
		+		+	+			+		

Table 29

Lesions of All Subjects WHO DO NOT HAVE a Deficit on this Measure.

Measure 2: Trail Making Test, Part B

Brain Area	Subjects (ID No.s)														
	1	*3*	*4*	*6*	*7*	*12*	*21*	*31*	*40*	*42*	*46*	*47*	*53*	*54*	*56*
Left Subcortical Circuit Structures															
Caudate Nucleus															
Globus Pallidus															
Left Basal-Cortical Circuits															
Dorsolateral Prefrontal									+						
Lateral Orbital							+	+	+			+			
Anterior Cinguate											+	+			
Language Circuitry							+	+	+			+			
Other Left Hemisphere Areas															
					+	+	+	+	+		+	+			
Right Subcortical Circuit Structures															
Caudate Nucleus	+	+	+	+									+		+
Globus Pallidus	+	+	+	+									+		
Right Basal-Cortical Circuits															
Dorsolateral Prefrontal	+	+	+	+									+		+
Lateral Orbital	+	+	+	+				+	+			+	+		
Anterior	+	+	+	+							+	+	+		
Other Right Hemisphere Areas															
	+	+	+	+				+	+	+	+	+	+		+

Table 30

Tests Significantly correlated with Trail Making Test, Part B (TMTB)

Test	Correl-ation with TMTB	Correl-ation with Left Sided Motor Signs	Correl-ation with Right Sided Motor Signs
Trail Making Test, Part B			.54**
Porteus Mazes	-.81***		
Trail Making Test Part A	.79***	.56**	
Story Recall Task, delayed recall	-.74***		
WAIS-R Digit Symbol subtest	-.67***		-.44*
HLLST Reading Comprehension subtest	-.66***		-.73***
HLLST Sequencing subtest	-.62**		-.42*
WAIS-R Similarities subtest	-.57**		-.48*
HLLST Grammar subtest	-.57**		
HLLST Antonyms subtest	-.56**		
Complex Figure of Rey, Copy	-.56**		
HLLST Association Naming subtest	-.55**		-.47*
Complex Figure of Rey, Recall	-.51**		
Wisconsin Card Sorting Test, Number of Categories achieved	-.49*		
Wisconsin Card Sorting Test, Conceptual Level Responses	-.47*		
HLLST Sentence Formulation subtest	-.47*		
HLLST Synonyms subtest	-.46*		
HLLST Vocabulary subtest	-.45*		-.44*
HLLST Absurdities subtest	-.45*		

* **p<.05**
** p<.01

6.6.1.3. Computer Tracking Task

6.6.1.3.1. The Nature of the Task

This involved the subject using a joy stick to keep a 5mm square inside a 15 mm square that was randomly shifting around a computer screen.

6.6.1.3.2. Analysis of Brain Areas Associated with this Task

All six subjects having significant difficulty with this task had lesions within the anterior cingulate circuit (either left or right), compared to only eight from the19 who did not have this deficit (see Table 31 & Table 32). Furthermore, when the level of circuit lesion was examined for all the subjects performing poorly on this task, all levels of the circuits were represented. This is consistent with the circuit as a whole being important, and not just any one element of the circuit. Another important implication, assuming the neuro-imaging was reasonably accurate, is that the right and left hemispheres are equally important. Consistent with the latter conclusion, neither left or right-sided motor signs were significantly correlated with performance of this task, and neither were any of the other measures in the neuropsychological test battery. It is concluded that the left or right anterior cingulate circuit is important to this task.

6.6.1.3.3. Brain Areas Associated with this Task by Other Research

This task is a new variant on the pursuit-tracking task, which has been studied extensively since the 1920s (Eysenck & Frith, 1977). The difficulty that subjects with Parkinson's Disease (PD) have with this task has been well established (e.g., Frith, Bloxham & Carpenter, 1986). Playford, Jenkins, Passingham, Nutt, Frackowiak and Brooks (1992) found that PD subjects, whose performance of this task was slowed, displayed attenuated increases in regional-cerebral-blood-flow (PET) in a number of significant brain areas. Those included, the contralateral lentiform nucleus (i.e., the putamen & globus pallidus), supplementary motor area, anterior cingulate cortex and the dorsolateral prefrontal cortex. Furthermore, Dick, Benecke, Rothwell, Day and Marsden (1986) observed that patients with isolated lesions of the supplementary motor area and the anterior cingulate cortex can show motor deficits very similar to PD patients. Ceballos-Baumann, Marsden, Passingham, Stephan, Frackowiak and Brooks (1994) compared regional cerebral activation, of intact subjects, when paced joystick movements were either imagined or performed in freely chosen directions. Imagination of movement led to significant activation of the dorsolateral prefrontal cortex, supplementary motor area and lentiform nucleus (i.e., the putamen & globus pallidus). Actual performance of movement led to no significant change in the level of striatal activation but significant increases in contralateral sensorimotor cortex, caudal supplementary motor area and cerebellar

regional-cerebral-blood-flow were observed. This led Brooks (1995) to the conclusion that the basal ganglia play a critical role in preparation and execution of movement for this task, and possibly monitoring and optimizing motor movement needed to achieve a particular goal, but not in the determination of basic parameters of movement. Thus while these findings are consistent with the anterior cingulate circuits of either hemisphere being involved (the conclusion of this phase), they suggest that other circuits would be as well, for example the dorsolateral prefontal circuit.

Table 31
Lesions of All Subjects with a Deficit on this Measure.
Measure 3: Computer Tracking Task

Brain Area	Subjects (ID No.s)					
	13	*20*	*46*	*47*	*48*	*53*
Left Basal-Cortical Circuits						
Dorsolateral Prefrontal		+			+	
Lateral Orbital		+		+	+	
Anterior		+	+	+	+	
Language Circuit				+	+	
Other Left Hemisphere Areas						
		+	+	+	+	
Right Basal-Cortical Circuits						
Dorsolateral Prefrontal	+					+
Lateral Orbital	+			+		+
Anterior	+		+	+		+
Other Right Hemisphere Areas						
	+		+	+		+

See Appendix B. for a complete description of each individual subject's characteristics.

Table 32

Lesions of All Subjects WHO DO NOT HAVE a Deficit on this Measure.

Measure 3: Computer Tracking Task

Brain Area	Subjects (ID No.s)																		
	1	*3*	*4*	*5*	*6*	*7*	*12*	*21*	*24*	*25*	*26*	*31*	*36*	*40*	*41*	*42*	*45*	*54*	*56*
Left Basal-Cortical Circuits																			
Dorsolateral Prefrontal				+									+	+			+		
Lateral Orbital				+				+				+	+	+			+		
Anterior Cingulate				+									+				+		
Language Circuit				+				+			+	+	+	+			+		
Other Left Hemisphere Areas																			
				+		+	+	+			+	+	+	+			+		
Right Basal-Cortical Circuits																			
Dorsolateral Prefrontal		+	+		+					+					+				+
Lateral Orbital		+	+		+							+		+	+				
Anterior Cingulate		+	+		+					+					+				
Other Right Hemisphere Areas																			
		+	+		+					+	+	+		+	+	+			+

6.6.2. Executive Functions

From the literature review it was hypothesized that the dorsolateral prefrontal circuit subserved these functions.

6.6.2. Wisconsin Card Sorting Test –Revised (WCST-R) Perseverative Responses

6.6.2.1.1. The Nature of this Task

This is a very well-known, almost 'classic', neuropsychological assessment task. The subject is presented with a series of 128 cards, one by one, and asked to 'match' them with one of four stimulus cards. Designs on each of the latter include, a single red diamond, two green stars, three yellow crosses and four blue circles. Designs on the matching cards involved every possible combination of the four categories in each of the three dimensions (shape, colour and number). The subject is told simply whether his/her placement was right or wrong, not the basis for sorting. Once they have correctly sorted ten cards in a row according to one of shape, colour or number, the criterion is changed. This task yields several indices of test performance. The one used here was persistence at sorting according to an incorrect criterion ('perseveration').

6.6.2.1.2. Analysis of Brain Areas Associated with this Task

Five out of the nine subjects with the right dorsolateral prefrontal circuit involved had a deficit on this task. There was no other brain lesion where most subjects with that lesion had a deficit. See Table 33 and Table 34. Thus while evidence for a link between this task and the dorsolateral prefrontal circuit is not strong, it is suggestive. Table 35 lists significant correlations found between this measure and other tests from the project battery. It is not surprising that the two most strongly related measures are both from the same task (Wisconsin Card Sorting Test, conceptual level responses and categories). Interestingly, of the six other tasks significantly correlated, three are memory tasks (Complex Figure of Rey, Recall, Delayed story recall and Picture Recognition). Two of the others have a major verbal recall component (HLLST Categories subtest and HLLST Association Naming subtest). The

only one remaining was the HLLST Absurdities subtest. When the level of circuit lesion was examined for all the subjects performing poorly on this task, all levels of the circuits were represented. This is consistent with the circuit as a whole being important, and not just any one element of the circuit.

In conclusion, data suggested a possible link between the right dorsolateral circuit and perseveration on this task.

6.6.2.1.3. Brain Areas Associated with this Task by Other Research

A large body of research has been conducted using this test (see Lezak, 1995). Although the task achieved widespread acceptance as a measure of frontal dysfunction, this has been seriously challenged by more recent authors (e.g., Reitan & Wolfson, 1994). Furthermore a range of neurological disorders have been associated with impaired performance (e.g., long term alcoholism, diffuse injury, posterior lesions, as well as frontal ones, see Lezak, 1995 for review). This provides more reason to be cautious about accepting the suggestion above, of a link between perseveration on this task and lesions of the right dorsolateral prefrontal circuit.

Table 33

Lesions of All Subjects with a Deficit on this Measure.

Measure: 4 Wisconsin Card Sorting Test, % Perseverative Responses

Brain Area	Subjects (ID No.)									
	3	*4*	*13*	*21*	*24*	*25*	*26*	*36*	*48*	*56*
Left Basal-Cortical Circuits										
Dorsolateral Prefrontal								+	+	
Lateral Orbital				+				+	+	
Anterior								+	+	
Language circuit				+				+	+	
Other Left Hemisphere Areas										
					+	+	+	+	+	
Right Basal-Cortical Circuits										
Dorsolateral Prefrontal	+	+	+			+				+
Lateral Orbital	+	+	+							
Anterior	+	+	+			+				
Other Right Hemisphere Areas										
	+	+	+		+	+				+

Table 34

Lesions of All Subjects WHO DO NOT HAVE a Deficit on this Measure.

Measure: 4 Wisconsin Card Sorting Test, % Perseverative Responses

Brain Area	Subjects (ID No.)														
	1	*5*	*6*	*7*	*12*	*20*	*31*	*40*	*41*	*42*	*45*	*46*	*47*	*53*	*54*
Left Basal-Cortical Circuits															
Dorsolateral Prefrontal		+				+		+			+				
Lateral Orbital		+				+	+	+			+		+		
Anterior		+									+	+	+		
Language circuit		+					+	+			+		+		
Other Left Hemisphere Areas															
		+		+	+	+	+	+			+	+	+		
Right Basal-Cortical Circuits															
Dorsolateral Prefrontal	+		+						+					+	
Lateral Orbital	+		+				+	+	+				+	+	
Anterior	+		+						+			+	+	+	
Other Right Hemisphere Areas															
	+		+				+	+	+	+		+	+	+	

Table 35

Tests Significantly correlated with Wisconsin Card Sorting Test, % Perseverative Responses (%Pers)

Test	Correl-ation With (%Pers)	Correl-ation with Left Motor Signs	Correl-ation with Right Motor Signs
Wisconsin Card Sorting Test, Conceptual Level Responses	-.80***		
Wisconsin Card Sorting Test, Number of Categories achieved	.78***		
Complex Figure of Rey, Recall	.53**		
HLLST Absurdities subtest	.52**		
Story Recall Task, delayed recall	.48*		-.55**
HLLST Categories subtest	.46*		-.42*
HLLST Association Naming subtest	.41*		-.47*
Picture Recognition	.40*		

* **p<.05**
** p<.01 *** p<.001

6.6.2.2. HLLST Association Naming

6.6.2.2.1. Nature of the Task

This task required the subject to say as many words as they could beginning with the letter "L" within one minute, and a second item, where they had to name as many items of clothing as they could, also within one minute. As this task was very similar (although not identical) to the very well studied 'word fluency task', (otherwise known as the FAS) the body of literature generated by that task is relevant here.

Estes (1974) analysis of the task requirements is still as clear as any. Key elements include organizing output in terms of clusters of meaningfully related words. More specifically, organization of thinking to guide a search for words that satisfy specified contraints (starting with the same letter, or, belonging to the same category). Examples of search strategies

include words with the same initial consonant, variations on a word, variations on a theme. Then there are the memory aspects of access to the stored representations in semantic memory and keeping keep track of what has been already said. Warburton et al. (1996) also argue (as have various previous researchers) that initial letter fluency is more dependent on a phonologically based word store whereas category fluency (e.g. naming as many items of clothing as possible in one minute) is dependent upon access to intact representations in semantic memory. Hence this task involved both forms, unlike the FAS task.

Another approach to analysing the task components was taken by Parks et al. (1992). They based their approach on the principle that the word fluency task (in all its variations), and the Wisconsin Card Sorting Test supposedly require the same area of the brain, the frontal lobes. They start by proposing a parallel distributed processing model of Wisconsin Card Sorting Test (WCST) performance. Then they argue that essentially similar mental processing is required for the verbal fluency task. One such similarity being attention. 'The subject is asked to "attend to" words beginning with the given letter selectively (even though, in this case, the "attention" is to stored memories of previous stimuli rather than to current stimuli).' (p. 221). They go on to cite experimental evidence. Another supposedly similar element is instrumental learning ("the reinforcement-bias pathway"). The examiner's tolerance, praise, for certain types of words, and rejections of others, being analogous to reinforcement of correct card placements and rejection of incorrect ones, as occurs on the WCST. However this argument is weakened somewhat by data of this thesis. Subjects with poor performance on the HLLST Association Naming subtest did not consistently perform badly on the WCST.

Another review (Reitan & Wolfson, 1994) casts serious doubt on the proposition that performance on either the WCST or the word fluency task involves the frontal lobes. This undermines the common neuro-anatomy argument for parallels between a model of WCST performance and a model of word fluency performance. Nonetheless, as another yet-to-be-disproved hypothesis about the information processing involved on the word fluency task, it is still of interest.

6.6.2.2.2. Analysis of Brain Areas Associated with this Task

From Table 36 and Table 37, the proportions of subjects with lesions in a particular circuit who had the deficit, compared to those who did not were as follows. Dorsolateral prefrontal circuit (6/0), Lateral Orbito-frontal circuit (8/1), Anterior Cingulate circuit (5/2) and Language Circuitry (8/1). However fifteen subjects had the deficit, indicating a number of subjects with the deficit did not have involvement of any of these circuits (as far as the available neuro-imaging indicated). The type of brain lesion whose presence or absence coincided most directly with the presence or absence of the deficit, was general left hemisphere injury. Eleven out of the fifteen subjects with the deficit had a left hemisphere injury (of various kinds, cortical and subcortical), compared to only three out of the ten without the deficit. Thus, from the neuroimaging data available, this deficit seems to be associated with general left hemisphere injury. This conclusion is consistent with the significant negative correlation between right sided motor signs and HLLST Association Naming subtest scores ($r=-.47$, $p<.05$) among the complete group of brain-injured subjects. That correlation reflects more motor impairment ('motor signs') being associated with lower (less proficient) scores on this measure. There was no correlation with left sided motor signs ($r=-.09$ ns).

The analysis reported in Phase1 ("Resolution of Data Issues") revealed another issue that is relevant to this part of the data analysis.

Table 57 shows that 71% (5/7) of all CVA subjects have this deficit. This raises the possibility that poor performance on the HLLST Association Naming task reflects the general effects of a CVA rather than any focal lesions. However comparison of the number of CVA subjects who have this deficit, with the number of CVA subjects who do not, revealed that the proportions were the same (5/15 and 2/10 respectively).

Further light is shed on the task requirements of this task by the range of correlations between this task and others from the neuropsychological test battery. Table 38 lists all 21, significantly correlated measures, from within the project battery, in order of magnitude. Not surprisingly, of the highest 11 out of this group, nine were other measures of higher-

level expressive language skills. However the two non-language tasks within this group of 11 are noteworthy (WAIS-R Digit Symbol and Trail Making Test, Part B). A further complementary finding was the significant negative correlation between right-sided motor signs and performance proficiency on all three measures (WAIS-R Digit Symbol, $r=-.44$, $p<.05$, Trail Making Test, Part B, $r=.54$, $p<.01$, and HLLST Association Naming, $r=-.47$, $p<.05$). This is consistent with significant areas of the left hemisphere being involved with all three tasks.

In conclusion, the closer scrutiny of lesions among those brain-injured subjects with and without this deficit (Table 36 & Table 37), and the correlations with other measures (Table 38), and motor signs, support the conclusion that poor performance on this measure is associated with lesions of the left hemisphere.

6.6.2.2.3. Brain Areas Associated with this Task in other Research

A critical and insightful review of neuropsychological findings using the word fluency task was contributed by Reitan and Wolfson (1994). They were critical of neuropsychologists' widespread acceptance of impaired word fluency as an indicator of left frontal damage. Pendleton, Heaton, Lehman and Hulihan (1982) found subjects with damage in a variety of other areas also had impaired word fluency. The other brain areas included right frontal lobe damage, non-frontal focal damage in either hemisphere, and diffuse brain damage.

A recent functional MRI study (Schlosser et al. 1998) found that the left prefrontal cortex and the right cerebellum were activated among normal subjects during performance of this task. Those authors also reviewed previous PET studies. These consistently showed activation of the dorsolateral prefrontal cortex and variable deactivation in the temporal areas and the posterior cingulate cortex during word fluency task performance.

The apparent inconsistency between results from this project (a lesion study) and results from PET studies of unimpaired subjects, on the same task, raises important questions. Could the subjects with subcortical lesions in this circuit conceivably all have undetected

disruption to the dorsolateral prefrontal cortex? Another possibility might be that certain areas are primarily involved in mediating this task (i.e., the prefrontal cortex) while other, nonactivated ones (caudate nucleus or globus pallidus) still form part of a larger, but necessary neural context (at least during task performance by intact individuals). Peterson and Fiez (1993) cautioned in their review of PET work that a functional (activated) area is not necessarily a task-mediating area. Likewise, is there overwhelming evidence that non-activated areas are necessarily uninvolved in task-mediation? For instance, there are also the findings of Pendleton et al. (1982) referred to earlier, that right frontal lobe damage, non-frontal focal damage in either hemisphere, and diffuse brain damage were also associated with impaired performance on this task. Thus the integrity of larger sections of the brain may be as important to task performance as the integrity of the activated area by itself (i.e. the dorsolateral prefrontal cortex). PET scanning of subjects with any of these lesions during word-fluency-task performance might help us discover the reason for this discrepancy. What alternative sets of brain areas seem to be employed by those subjects?

While the general convergence of results from PET and lesion studies has been noted by Bradshaw and Mattingley (1995, p. 63), discrepancies like these, across neuropsychological research findings in general are frustratingly common. Pulvermuller (1996) has drawn attention to this as a general issue, not just in relation to the verbal fluency task. In this author's opinion, how language loss can occur after a relatively confined focal lesion of Wernicke's area, while intact individuals will display widespread cortical activation during various language tasks, has not been adequately explained. Resolving these discrepancies will probably require a future generation of imaging technology, more sophisticated than our present one. Implications of this type of discrepancy are explored further in the Discussion section.

Table 36

Lesions of All Subjects with a Deficit on this Measure.

Measure 5: HLLST Association Naming

Brain Area	Subjects (ID No.)														
	4	*5*	*12*	*13*	*20*	*21*	*24*	*25*	*26*	*31*	*36*	*40*	*45*	*48*	*53*
Left Basal-Cortical Circuits															
Dorsolateral Prefrontal		+			+						+	+	+	+	
Lateral Orbital		+			+	+				+	+	+	+	+	
Anterior		+			+						+		+	+	
Language circuit		+				+			+	+	+	+	+	+	
Other Left Hemisphere Areas															
		+	+		+	+	+		+	+	+	+	+	+	
Right Basal-Cortical Circuits															
Dorsolateral Prefrontal	+			+				+							+
Lateral Orbital	+			+						+		+			+
Anterior	+			+				+							+
Other Right Hemisphere Areas															
	+			+			+	+		+		+			+

Table 37

Lesions of All Subjects WHO DO NOT HAVE a Deficit on this Measure.

Measure 5: HLLST Association Naming

Brain Area	Subjects (ID No.)									
	1	*3*	*6*	*7*	*41*	*42*	*46*	*47*	*54*	*56*
Left Basal-Cortical Circuits										
Dorsolateral Prefrontal										
Lateral Orbital								+		
Anterior							+	+		
Language circuit								+		
Other Left Hemisphere Areas										
				+			+	+		
Right Basal-Cortical Circuits										
Dorsolateral Prefrontal	+	+	+		+					+
Lateral Orbital	+	+	+		+			+		
Anterior	+	+	+		+		+	+		
Other Right Hemisphere Areas										
	+	+	+		+	+	+	+		+

Table 38

Tests Significantly correlated with HLLST Association Naming Subtest (HANS)

Test	Correl-ation With HANS	Correl-ation with Left Motor Signs	Correl-ation with Right Motor Signs
HLLST Association Naming subtest			-.47*
WAIS-R Similarities subtest	.67**		-.48*
HLLST Categories subtest	.66**		-.42*
HLLST Definitions subtest	.60**		-.45*
WAIS-R Digit Symbol subtest	.58**		-.44*
HLLST Sequencing subtest	.57**		-.42*
HLLST Synonyms subtest	.56**		
Trail Making Test, Part B	-.55**		.54**
HLLST Provide a Word subtest	.55**		
HLLST Homonyms subtest	.54**		
HLLST Antonyms subtest	.53**		
HLLST Reading Comprehension subtest	.51**		-.73***
Complex Figure of Rey, Recall	.50**		
HLLST Analogies subtest	.50*		
HLLST Porteus Mazes	.49*		
Trail Making Test Part A	-.48*	.56**	
Story Recall Task, immediate recall	.47**		-.55**
HLLST Sentence Formulation subtest	.45*		
HLLST Audio/Visual Comprehension subtest	.44 *		-.70**
HLLST Absurdities subtest	.44*		
Wisconsin Card Sorting Test, Number of Categories achieved	.42*		
Wisconsin Card Sorting Test, % Perseverative Responses	.41*		

* **p<.05**
** p<.01
*** p<.001

6.6.3. Verbal Comprehension

6.6.3.1. HLLST B. Auditory/Visual Comprehension

6.6.3.1.1. Nature of the Task

On this subtest, the subject had to follow the examiner's instructions (5 in all) in relation to a picture. It represented a family engaged in various domestic activities in a garden setting. The specific instructions were:

'Point to the combustion' *(the subject had to point to a barbeque appliance, that was emitting smoke)*

'Point to the liquid refreshment' *(the subject had to point to a drink in the hand of a person in the picture)*

'Point to the smaller door' *(the subject had to identify that a car door was smaller than a house door and point it out)*

'Point to the paw off the ground *(a dog in the picture had three paws on the ground and one off)*

'Point to the ball, the sprinkler, the door and the fire.' *(all items were in the picture and the subject had to point them out, in sequence).*

As the Higher Level Language Screening Test (HLLST) is a new test, the subtests have not been the subject of extensive published analysis, or investigation. Several elements are clearly involved. Auditory comprehension of words and phrases, that represent various levels of abstraction. The words were either nouns or adjectives, sometimes incorporated within an adjectival phrase. Then there is visual search for, and recognition of, the pictured object that corresponds to the spoken label. Finally the last item has an additional sequential memory component. While some comprehension of syntax is involved, this is not a major part of the task.

6.6.3.1.2. Analysis of Brain Areas associated with this Task

A comparison of brain lesions shown by subjects who had difficulty with this task and lesions shown by those who did not, revealed a picture very similar to that described above in relation to HLLST Association Naming. There was a correlation of r=.44 ($p<.05$) between the two measures. Likewise correlation with motor signs suggested brain areas engaged during performance on this task were strongly lateralized in the left hemisphere. The correlation with right motor signs was highly significant (r=-.70, $p<.001$), unlike the correlation with left motor signs (r=.23, ns).

Five out of six of those with the Left Dorsolateral Prefrontal circuit involved had difficulty with this testing task and the 14 subjects who did not, included only one with a lesion of this circuit (see Table 40). However this 14 included four and three respectively with lesions in the Left lateral orbital circuit and Left Anterior Cingulate circuits. This suggests that the Left Dorsolateral Prefrontal circuit is important to this skill while the other two left hemisphere circuits, and all the right hemisphere ones, were not. However as a further six subjects who did not show lesions in that circuit (with the neuro-imaging available) also showed this deficit, it might be associated with lesions of other kinds (see Table 39). This too is consistent with equivalence. Four out of the five subjects, with a lesion in the left dorsolateral prefrontal circuit, (who also had a deficit in this task) had their lesions at the basal ganglia level (caudate nucleus or globus pallidus). The one subject in the sample with a lesion of the dorsolateral prefrontal circuit also had the deficit. This is modest support for the whole circuit, rather than just one element, being important to the task.

Table 41 reveals high correlations between the HLLST Audio/Visual Comprehension subtest and 15 other measures of high-level language functioning. The two other, and more noteworthy, inclusions in Table 41 involve immediate and delayed paragraph recall. This supports the interpretation of a significant verbal memory element to this task. The high, negative correlation with right-sided motor signs (-.70, $p<.001$), indicates performance of this task is strongly lateralized in the left hemisphere.

In conclusion, the left dorsolateral prefrontal circuit is important to this task.

6.1.3.1.3. Brain Lesions Associated with this Task by other Research

There is no previous neuropsychological research available using this task. Caplan, Hildebrandt and Makris (1996) studied the effect of various brain lesions on the ability of stroke patients to visually demonstrate, by pointing to and manipulating domestic objects, the meaning of sentences spoken by an examiner. Findings were 'consistent with the conclusion that several parts of the left perisylvian cortex (Wernicke's area) form critical parts of a neural system responsible for syntactic processing. Other data suggest some degree of localization of this function within the pars opercularis. (Broca's area)' (p. 946). Pulvermuller (1996) contributed a very comprehensive review of data from psychophysiological investigations of language processing. He reported that processing of nouns evoking visual associations (like items from this task) would involve a combination of Wernicke's area and the visual cortex (occipital lobes). In the context of this project, this set of structures suggested by other research correspond to 'other language-related circuitry.' However, this analysis points to the involvement of left dorsolateral prefrontal circuit in mediating performance of this assessment task.

The presenting of the verbal material in written form however adds another element to this task, not covered in the other research (above). For example, De Nil, Kroll, Kapur and Houle (2000) performed PET scans on neurologically intact subjects while silently reading a set of 25, serially presented, low-imagery words. No demonstration of understanding was required. A large number of areas showed activation, including bilateral activation of the cerebellum (L>R), extending into the primary occipital region. Other activation noted included the bilateral precentral motor cortex (insula level) and the left medial frontal gyrus. These could be summarized as areas mediating visual and motor processing, which generally do not involve the basal cortical circuits. This would tend to exclude the act of silent reading from the set of functions mediated by the basal cortical circuits.

Table 39

Lesions of All Subjects with a Deficit on this Measure.

Measure 6: HLLST B Auditory Visual Comprehension

Brain Area	Subjects (ID No.)									
	5	*6*	*13*	*20*	*24*	*25*	*36*	*40*	*45*	*46*
Left Basal-Cortical Circuits										
Dorsolateral Prefrontal	+			+			+	+	+	
Lateral Orbital	+			+			+	+	+	
Anterior	+			+			+		+	+
Language circuit	+						+	+	+	
Other Left Hemisphere Areas										
	+			+			+	+	+	+
Right Basal-Cortical Circuits										
Dorsolateral Prefrontal		+	+			+				
Lateral Orbital		+	+					+		
Anterior		+	+			+				+
Other Right Hemisphere Areas										
		+	+		+	+		+		+

Table 40

Lesions of All Subjects WHO DO NOT HAVE a Deficit on this Measure.

Measure 6: HLLST B Auditory Visual Comprehension

Brain Area	Subjects (ID No.s)														
	1	*3*	*4*	*7*	*12*	*21*	*26*	*31*	*41*	*42*	*47*	*48*	*53*	*54*	*56*
Left Basal-Cortical Circuits															
Dorsolateral Prefrontal												+			
Lateral Orbital						+		+			+	+			
Anterior Cing.										+	+	+			
Language circuit						+	+	+			+	+			
Other Left Hemisphere Areas															
				+	+	+	+	+			+	+			
Right Basal-Cortical Circuits															
Dorsolateral Prefrontal	+	+	+						+				+		+
Lateral Orbital	+	+	+					+	+		+		+		
Anterior	+	+	+						+		+		+		
Other Right Hemisphere Areas															
	+	+	+				+	+	+	+	+		+		+

See Appendix B. for a complete description of each individual subject's characteristics.

Table 41

Tests Significantly correlated with HLLST Audio/Visual Comprehension subtest (HA/VCS)

Test	Correl-ation with HA/VCS	Correl--ation with Left Motor Signs	Correl-ation with Right Motor Signs
HLLST Audio/Visual Comprehension subtest			-.70***
HLLST Definitions subtest	.74***		-.45*
HLLST Vocabulary subtest	.72***		-.44*
HLLST Reading Comprehension subtest	.63**		-.73***
HLLST Antonyms subtest	.58**		
WAIS-R Similarities subtest	.55**		-.48*
HLLST Provide a Word subtest	.53**		
HLLST Homonyms subtest	.51**		
Story Recall Task, immediate recall	.51**		-.55**
HLLST Sentence Formulation subtest	.49*		
HLLST Categories subtest	.48*		-.42*
HLLST Sequencing subtest	.48*		-.42*
HLLST Synonyms subtest	.47*		
Story Recall Task, delayed recall	.46*		
HLLST Analogies subtest	.44*		
HLLST Association Naming subtest	.44*		-.47*
HLLST Absurdities subtest	.43*		
HLLST Yes/No subtest	.40*		-.41*

* $p<.05$
** $p<.01$
*** $p<.001$

6.6.4 Verbal Expression

6.6.4.1 HLLST Give Definitions

6.6.4.1.1. The Nature of the Task

This task required the subject to explain the meaning of four words (i.e., rehearsal, consequences, persist and oppose).

6.6.4.1.2. Analysis of Brain Areas Involved in this Task

While Table 44 shows a consistent association between this measure and right-sided motor signs, (suggesting a left hemisphere focus), verified lesions among subjects with a deficit on this task suggest either hemisphere can be involved. Five of the six subjects with lesions in the (left or right) dorsolateral prefrontal circuit had a deficit on this task. Only two of the eighteen without the deficit had a lesion in that circuit. Only one of the seven subjects with this deficit did not have a lesion of that circuit. Thus, unless lesions of the same circuit were present but undetected in this one subject, then the deficit was associated with a different structure(s). This would be consistent with equivalence. Furthermore the lesions causing circuit-disruption for the subjects with this deficit, were spread across all levels of the circuit (e.g. cortical and subcortical).

In conclusion, lesions of the left or right dorsolateral prefrontal circuit can impair performance of this task.

6.6.4.1.3. Brain Areas Associated with this Task by Other Research

This task is similar to another which has been considered in many studies, the Vocabulary subtest of the Wechsler Adult Intelligence Scale (WAIS). Even now that the WAIS is into a third revision (the WAIS-III), this task is little changed. Lezak (1995) reviewed findings with that task. Essentially she concluded that performance is typically affected by left hemisphere

damage and increased glucose metabolism (i.e., the activation revealed by PET scanning) occurs in and around the left temporal lobe when this test is taken.

The stimulus words for this task (rehearsal, consequences, persist and oppose) are a mixture of abstract nouns and verbs. Pulvermuller (1996) contributed a very comprehensive review of data from psychophysiological investigations of language processing. He reported that processing of abstract content words (i.e. nouns) was not as strongly lateralized to the dominant (usually left) hemisphere because they would tend to be visualized during verbal-cognitive processing. The greater the visualization, the more the nondominant (usually right) hemisphere was involved. This could account for the link found with both hemispheres above. Clearly research into localization of word processing is difficult. Identifying the pertinent features that distinguish words associated with one area from those linked to another area has been a very difficult enterprise.

Table 42

Lesions of All Subjects with a Deficit on this Measure.

Measure 7: HLLST Give Definitions

Brain Area	Subjects (ID No.s)						
	5	*13*	*24*	*25*	*36*	*40*	*45*
Left Subcortical Circuit Structures							
Caudate Nucleus	+				+		+
Globus Pallidus	+						+
Left Basal-Cortical Circuits							
Dorsolateral Prefrontal	+				+	+	+
Lateral Orbital	+				+	+	+
Anterior Cingulate	+				+		+
Lang Circuitry	+				+	+	+
Any Left Hemisphere Areas							
	+		+		+	+	+
Right Basal-Cortical Circuits							
Dorsolateral Prefrontal		+		+			
Lateral Orbital		+				+	
Anterior Cingulate		+		+			
Other Right Hemisphere Areas							
		+	+	+		+	

Table 43

Lesions of All Subjects WHO DO NOT HAVE a Deficit on this Measure.

Measure 7: HLLST Give Definitions

Brain Area	Subjects (ID No.s)																	
	1	*3*	*4*	*6*	*7*	*12*	*20*	*21*	*26*	*31*	*41*	*42*	*46*	*47*	*48*	*53*	*54*	*56*
Left Subcortical Circuit Structures																		
Caudate Nucleus																		
Globus Pallidus							+								+			
Left Basal-Cortical Circuits																		
Dorsolateral Prefrontal							+								+			
Lateral Orbital																		
Anterior Cingulate							+	+		+				+	+			
Language Circuitry								+	+	+				+	+			
Any Left Hemisphere Areas																		
					+	+	+	+	+	+			+	+	+			
Right Basal-Cortical Circuits																		
Dorsolateral Prefrontal	+	+	+	+							+					+		+
Lateral Orbital	+	+	+	+						+	+			+		+		
Anterior Cingulate	+	+	+	+							+		+	+		+		
Other Right Hemisphere Areas																		
	+	+	+	+						+	+	+	+	+		+		+

Table 44

Tests Significantly correlated with HLLST Give Definitions subtest (HGDS)

Test	Correl-ation with HGDS	Correl-ation with Left Motor Signs	Correl-ation with Right Motor Signs
HLLST Give Definitions subtest			-.45*
HLLST Audio/Visual Comprehension subtest	.74***		-.70***
WAIS-R Similarities subtest	.73***		-.48*
HLLST Homonyms subtest	.69***		
HLLST Association Naming subtest	.60**		-.47*
HLLST Synonyms subtest	.59**		
HLLST Reading Comprehension subtest	.58**		-.73***
HLLST Categories subtest	.56**		-.42*
HLLST Analogies subtest	.54**		
HLLST Sentence Formulation subtest	.54**		
HLLST Sequencing subtest	.52**		-.42*
HLLST Antonyms subtest	.49**		
HLLST Provide a Word subtest	.49**		
HLLST Vocabulary subtest	.48**		-.44*
HLLST Absurdities subtest	.47*		
Story Recall Task, immediate recall	.45*		-.55**
Story Recall Task, delayed recall	.45*		
HLLST Grammar subtest	.42*		

* $p<.05$
** $p<.01$
*** $p<.001$

6.6.4.2. HLLST Absurdities

6.6.4.2.1. The Nature of the Task

The task for this subtest was a bit different from most tasks used in the traditional investigation of aphasia. The subject was presented with three statements, one at a time. They were asked to tell the examiner if there was anything ridiculous about each statement. (For example, 'A large company was anxious to increase its sales. It decided to print and distribute catalogues to a large number of potential customers. On the bottom of each catalogue was printed, "If you have not yet received a copy of this catalogue, please phone or write to us.".')

6.6.4.2.2. Analysis of Brain Areas Associated with this Task

From Tables 45 and 46, seven out of the nine subjects with a deficit on this task had lesions in the dorsolateral prefrontal circuit (left or right), while only seven out of the sixteen subjects without this deficit had a lesion in the same circuit. Furthermore the level of the circuit where the lesions occurred (among the deficit subjects) was variable, not just cortical, or subcortical for example. This suggests that this circuit, left or right, is important to this task. Correlations with other measures, and correlations between those measures and our indirect measure of lateralization (severity of motor signs) further clarify laterality (or lack thereof) for this skill (see Table 47). Essentially the nine, most-strongly-correlated tests did not show any clear correspondence with laterality of motor signs at all. This is consistent with the conclusion with Godefroy et al's principle of equivalence.

In conclusion, lesions in either the left or right dorsolateral prefrontal circuit are associated with poor performance of this task.

6.6.4.2.3. Brain Areas Associated with this Task by other Research

Pulvermuller's (1996) review of psychophysiological investigations of language processing clearly showed how difficult it is to precisely localize processing of specific word-types. He reported that almost the entire cortex "lights up" in imaging studies when, for example,

meaningful stories are being comprehended. Stories are a composite of a diverse set of verbal phenomena. The absurdity items are essentially meaningful stories. This is consistent with the lack of lateralization found in this project. This is another instance where it is difficult to reconcile PET data with the findings of this project.

Table 45

Lesions of All Subjects with a Deficit on this Measure.

Measure 8: HLLST Absurdities

Brain Area	Subjects								
	3	*13*	*20*	*24*	*25*	*26*	*36*	*40*	*48*
Left Basal-Cortical Circuits									
Dorsolateral Prefrontal			+				+	+	+
Lateral Orbital			+				+	+	+
Anterior Cing.			+				+		+
Language Circuitry						+	+	+	+
Other Left Hemisphere Areas									
Other Left hemisphere areas			+	+		+	+	+	+
Right Basal-Cortical Circuits									
Dorsolateral Prefrontal	+	+			+				
Lateral Orbital	+	+						+	
Anterior	+	+			+				
Other Right Hemisphere Areas									
Other Right hemisphere areas	+	+		+	+			+	

Table 46

Lesions of All Subjects WHO DO NOT HAVE a Deficit on this Measure.

Measure 8: HLLST Absurdities

Brain Area	Subjects (ID No.s)															
	1	*4*	*5*	*6*	*7*	*12*	*21*	*31*	*41*	*42*	*45*	*46*	*47*	*53*	*54*	*56*
Left Basal-Cortical Circuits																
Dorsolateral Prefrontal			+								+					
Lateral Orbital			+				+	+			+		+			
Anterior			+								+	+	+			
Language Circuitry			+				+	+			+		+			
Other Left Hemisphere Areas																
Other left hemisphere areas			+				+	+			+	+	+			
Right Basal-Cortical Circuits																
Dorsolateral Prefrontal	+	+		+					+					+		+
Lateral Orbital	+	+		+				+	+				+	+		
Anterior	+	+		+					+			+	+	+		
Other Left Hemisphere Areas																
Other Right hemisphere areas	+	+		+				+	+	+		+	+	+		+

Table 47

Tests Significantly correlated with HLLST Absurdities subtest (HAS)

Test	Correlation with HAS	Correlation with Left Motor Signs	Correlation with Right Motor Signs
HLLST Absurdities subtest			
HLLST Antonyms subtest	.70***		
Rey Figure, Recall	.64**		
HLLST Yes/No questions	.62**		-.40*
Trail Making Test, Part A	-.59**	.56**	
WCST-R Perseverative Responses	.52**		
HLLST Sequencing subtest	.50*		-.42*
Story Recall Task, delayed recall	.49*		
HLLST Grammar subtest	.48*		
HLLST Give Definitions subtest	.47*		-.45*
Trail Making Test, Part B	-.45*		.54**
HLLST Association Naming subtest	.45*		-.47*
HLLST Audio/Visual Comprehension subtest	.43*		-.70***
HLLST Categories subtest	.43*		-.42*
WCST-R Conceptual Level Responses	-.40*		

* p<.05
** p<.01
*** **p<.001**

6.6.4.3. HLLST Antonyms

6.6.4.3.1. Nature of the Task

For each of the four items involved on this task, the subject was told a word and asked to give a word which meant the opposite. The actual words *(and correct reponses)* were: ignorant *(clever, intelligent, smart, knowledgeable, polite),* prosperity *(poverty, poorness, adversity),* mournful *(happy, joyful, cheerful)* and courageously *(cowardly, fearful).* Again, as the Higher Level Language Screening Test (HLLST) is a new test, this subtest has not been the subject of extensive published analysis, or investigation. However, the task is

straightforward. The subject has to recognize the word spoken by the examiner, then scan their semantically based, word-memory store to retrieve a word that constitutes a semantic opposite (instead of a match) and then speak it out loud.

6.6.4.3.2. Analysis of Brain Areas involved in this Task

The starting point for analysis of lesions associated with a deficit on this measure was identification of those lesions clearly occurring more often among the deficit subjects. Four of the subjects with a deficit had a lesion in the left dorsolateral prefrontal circuit, compared to only two of the subjects without this deficit. Lesions within this circuit for deficit subjects occurred at various levels of this circuit, consistent with the circuit as a whole being important, not just any particular part of it. Also, six of the subjects with a deficit on this measure had a lesion in the right frontal lobe, compared to only three of the subjects without this deficit. Together, subjects with lesions in either of these locations accounted for 9/12 (75%) of the subjects with a deficit, compared to only 5/13 (38%) among the subjects without this deficit. Furthermore only one of the deficit subjects had lesions in both places (right frontal lobe and left dorsolateral prefrontal circuit). This pattern of data is consistent with equivalence. However the fact that a further four subjects did not have lesions in either of these locations but still displayed the deficit suggests two possibilities. Either lesions in these areas were present, but undetected, or further brain areas again are associated with this task.

With reference to the set of other measures significantly correlated with the HLLST Antonyms subtest (see Table 50), an unexpected result is the type of task most strongly correlated of all. This was Part A of the Trail Making Test. This is despite the fact that several, apparently much more similar tasks were included in the analysis (i.e. HLLST Antonyms and Homonyms, not to mention all the other high-level expressive language tasks), and that the Trail Making Test, Part A correlated significantly with left-sided motor signs. As it is not plausible to interpret a significant motor requirement in the HLLST Antonyms subtest, the most likely reason would be a common underlying brain structure, i.e. within the right hemisphere. Furthermore, of the five most strongly correlated other

tests (from Table 50), none display a significant correlation with right motor signs. All this would be consistent with the involvement of the right hemisphere in the functional system of brain regions involved in the performance of this task, e.g. the right frontal lobe, as suggested by the scrutiny of Table 48 & 49 (below).

In conclusion, deficits on this task were associated with either the right frontal lobe or the left dorsolateral prefrontal circuit.

6.6.4.3.3. Brain Lesions Associated with this Task by other Research

A search of the literature was unable to locate a neuropsychological study of antonym naming specifically. However it is arguably comparable to generation of single words semantically related to a stimulus word. One commonly used task of this type is articulation of a verb, related to a heard noun. After a carefully designed series of studies, Warburton et al. (1996) found extensive activation (via PET in normal subjects) of the left dorsolateral prefrontal cortex and medially, the anterior cingulate cortex and the supplementary motor area (SMA) in association with this task.
The stimulus words for this task (ignorant, prosperity, mournful and courageously) are a mixture of abstract nouns and adjectives. Pulvermuller (1996) contributed a very comprehensive review of data from psychophysiological investigations of language processing. He concluded that verbal processing generally involved Wernicke's area but certain word types involved additional areas as well. In particular, the more the meaning of a word could be visualized, the more likely it was that brain areas involved would extend beyond the dominant (usually left) hemisphere. Abstract nouns and adjectives were used as stimulus material for this task. Unlike function words (e.g., pronouns, auxilliary verbs and conjunctions), most people probably find them easier to visualize. This would be consistent with the link to the right frontal lobe suggested by this phase.

Table 48

Lesions of All Subjects with a Deficit on this Measure.

Measure 9: HLLST Antonyms

Brain Area	Subjects (ID No.s)											
	6	*13*	*20*	*24*	*25*	*26*	*31*	*36*	*40*	*41*	*45*	*46*
Left Basal-Cortical Circuits												
Dorsolateral Prefrontal			+					+	+		+	
Lateral Orbital			+				+	+	+		+	
Anterior			+					+			+	+
Language Circuit						+	+	+	+		+	
Other Left Hemisphere Areas												
Frontal Lobes							+		+			+
Other Left Hemisphere areas			+					+			+	
Right Basal-Cortical Circuits												
Dorsolateral Prefrontal	+	+			+					+		
Lateral Orbital	+	+					+		+	+		
Anterior	+	+			+					+		+

Table 48 (Cont.)

Lesions of All Subjects with a Deficit on this Measure.

Measure 9: HLLST Antonyms

Brain Area	Subjects (ID No.s)											
	6	*13*	*20*	*24*	*25*	*26*	*31*	*36*	*40*	*41*	*45*	*46*
Other Right Hemisphere Areas												
Frontal Lobes					+	+	+		+	+		+
Other Left Hemisphere areas	+	+			+		+			+		

Table 49

Lesions of All Subjects WHO DO NOT HAVE a Deficit on this Measure.

Measure 9: HLLST Antonyms

Brain Area	Subjects												
	1	*3*	*4*	*5*	*7*	*12*	*21*	*42*	*47*	*48*	*53*	*54*	*56*
Left Basal-Cortical Circuits													
Dorsolateral Prefrontal				+						+			
Lateral Orbital				+			+		+	+			
Anterior				+					+	+			
Language Circuit				+			+		+	+			
Other Left Hemisphere Areas													
Frontal Lobes							+		+				
Other Left hemisphere areas				+	+	+	+		+	+			
Right Basal-Cortical Circuits													
Dorsolateral Prefrontal	+	+	+								+		+
Lateral Orbital	+	+	+						+		+		
Anterior	+	+	+						+		+		
Other Right Hemisphere Areas													
Frontal Lobes		+						+	+				
Other Right hemisphere areas	+	+	+					+	+		+		+

Table 50

Tests Significantly correlated with HLLST Antonyms subtest (HAS)

Test	Correl-ation with HAS	Correl-ation with Left sided Motor signs	Correl-ation with Right sided Motor signs
HLST Antonyms subtest			
Trail Making Test Part A	-.74***	.56**	
HLLST Synonyms subtest	.71***		
HLLST Absurdities subtest	.70***		
Complex Figure of Rey, Recall	.62**		
HLLST Vocabulary subtest	.59**		-.44*
HLLST Grammar subtest	.58**		
HLLST Sequencing subtest	.57**		-.42*
HLLST Audio/Visual Comprehension subtest	.57**		-.70***
Trail Making Test, Part B	-.56**		.54**
Story Recall Task, delayed recall	.54**		
HLLST Homonyms subtest	.53**		
HLLST Association Naming subtest	.53**		-.47*
HLLST Definitions subtest	.49*		-.45*
HLLST Categories subtest	.46*		-.42*
HLLST Sentence Formulation subtest	.45*		
HLLST Provide a Word subtest	.44*		
WAIS-R Similarities subtest	.43*		-.48*
HLLST Analogies subtest	.42*		
WAIS-R Digit Symbol subtest	.41*		-.44*

*** p<.05**
**** p<.01**

6.6.4.4. HLLST Synonyms

6.6.4.4.1. Nature of the Task

On this task, the subject was presented with a single word at a time (4 in all) and asked to give a word that means the same. The words *(and correct responses)* were frequent *(often, common regular),* tranquil *(serene, calm, peaceful, quiet),* entirely *(wholly, all, totally, completely, altogether)* and scheme *(plan, plot, idea)*. As the Higher Level Language Screening Test (HLLST) is a new test, the subtests have not been the subject of extensive investigation. However, the task is straightforward. The subject has to recognize the word spoken by the examiner, then scan their semantically based, word-memory store to retrieve a word that constitutes a semantic match and speak it out loud.

6.6.4.4.2. Analysis of Brain Areas associated with this Task

7/13 (54%) of subjects with a left, language-related circuit lesion showed difficulties with this task, compared to 2/12 (17%) of those without involvement of this circuit. This analysis is complicated by language-circuit-lesion subjects often having lesions in either or both of, two of the left basal-frontal circuits (dorsolateral prefrontal and lateral orbito-frontal). Close scrutiny of Table 51 however, reveals that none of the lesions in these other two circuits ever occurred (as far as our neuro-imaging reveals) in the absence of a lesion in the language-related circuitry. Whenever a lesion in the left dorsolateral prefrontal circuit occurred, there were also lesions in both the language-related circuitry and the lateral orbito-frontal circuit. In two instances a lesion in the lateral orbito-frontal circuit occurred without one being present in the dorsolateral prefrontal circuit, but lesions were still present in the language-related circuitry. In conclusion, the language-related circuit will be taken as the one of these three most probably involved. Close scrutiny of deficit subjects indicated that lesions in this circuit were spread across all levels of this circuit except for the Thalamus. This is consistent with this circuit as a whole being important, not just any particular part of it. (See Table A.12. in Appendix A, all subjects except No. 47 and No.48 also had a deficit on the HLLST Synonyms subtest).

However Tables 51 and 52 reveal there is more to the picture. 7/13 (54%) of subjects with a right frontal lobe lesion showed difficulties with this task, compared to 2/12 (17%) of those

without involvement of this circuit. Together, subjects with either of these lesions account for 11/13 (85%) of subjects with this deficit. Furthermore, only three out of the eleven deficit subjects with either of these two lesions had both of them. It was generally one or the other. This pattern of data is consistent with equivalence. Of the subjects without this deficit, only 3/12 (25%) had lesions in either of these locations. The fact that a further two subjects did not have lesions in either of these locations but still displayed the deficit suggests two possibilities. Either lesions at these locations were present, but undetected, or further brain areas again are associated with this task ('association').

The pattern of correlations with other measures is shown in Table 53. The ten most-highly-correlated other tests are all relatively similar, high-level expressive language tasks. The three out of these showing the highest correlations of all (HLLST Homonyms, Antonyms and Analogies) all lacked any significant correlation with right-sided motor signs, unlike nearly all of the remaining members of the set-of-ten, most-correlated-tests.

In conclusion, subjects with this deficit tended to have lesions in either the language-related circuit (left hemisphere) or the right frontal lobe.

6.6.4.4.3. Brain Lesions Associated with this Task by other Research

One consistent finding of recent PET studies of language processing is that very minor variations in task requirements can involve quite different regions of the brain (e.g., Wise, Chollett, Hadar, Friston, Hoffner & Frackowiak, 1991; Fiez, Raichle, Balotoa, Tallal & Petersen, 1996). There is not yet any body of research available with this task or very similar ones. Thus the difference between previous findings (that link verb-noun association to the left dorsolateral prefrontal cortex and medially, the anterior cingulate cortex and the supplementary motor area. –Warburton, et al. 1996), and those of this project, might just reflect differences in task requirements. Therefore, no one has so far has reported findings inconsistent with the conclusion of this phase, that deficits on this task result from lesions to the left language circuitry, or the right frontal lobe and other, unknown areas.

A search of the literature was unable to locate a neuropsychological study of Synonym naming specifically. However important evidence is provided by Pulvermuller's (1996) work. He concluded that verbal processing generally involved Wernicke's area but certain word types involved additional areas as well. In particular, the more the meaning of a word could be visualized, the more likely it was that brain areas involved would extend beyond the dominant (usually left) hemisphere. Wernicke's area is a part of the language-related circuitry (as defined in this project). Most people can probably visualize the stimulus words for this task easily (frequent, tranquil, entirely and scheme). This would be consistent with the link to the right frontal lobe suggested by this phase. Pulvermuller's conclusions are consistent with the conclusions of this phase.

The examination of results from other studies, documented for the HLLST Antonyms subtest above, also applies to the HLLST Synonyms subtest. The task requirements of both subtests are arguably comparable to generation of single words semantically related to a stimulus word. One commonly used task of this type is articulation of a verb, related to a heard noun. From PET with normal subjects, Warburton, et al. (1996) found that this particular experimental task was associated with extensive activation of the left dorsolateral prefrontal cortex and medially, the anterior cingulate cortex and the supplementary motor area (SMA). While this set of circuits do not coincide with language-related circuitry, there is some overlap, particularly at the basal ganglia level. Furthermore, a consistent finding from recent PET studies is that very minor variations in task requirements can involve very different regions of the brain (e.g., Wise et al.1991; Fiez et al. 1996). This Synonym-naming task and the verb-articulation task are not identical afterall, which could therefore account for the different pattern of PET activation.

Table 51

Lesions of All Subjects with a Deficit on this Measure.

Measure 10: HLLST Synonyms

Brain Area	Subjects												
	3	*5*	*13*	*21*	*24*	*25*	*26*	*31*	*36*	*40*	*41*	*45*	*46*
Left Basal-Cortical Circuits													
Dorsolateral Prefrontal		+							+	+		+	
Lateral Orbital		+		+				+	+	+		+	
Anterior		+							+			+	+
Language Circuit		+		+			+	+	+	+		+	
Other Left Hemisphere Areas													
Frontal Lobes				+				+		+			+
Other Left hemisphere areas		+					+	+	+	+		+	+
Right Basal-Cortical Circuits													
Dorsolateral Prefrontal	+		+			+					+		
Lateral Orbital	+		+					+		+	+		
Anterior	+		+			+					+		+
Other Right Hemisphere Areas													
Frontal Lobes	+					+	+	+		+	+		+
Other Right hemisphere areas	+		+		+	+		+		+	+		+

Table 52

Lesions of All Subjects WHO DO NOT HAVE a Deficit on this Measure.

Measure 10: HLLST Synonyms

Brain Area	Subjects (ID No.s)											
	1	*4*	*6*	*7*	*12*	*20*	*42*	*47*	*48*	*53*	*54*	*56*
Left Basal-Cortical Circuits												
Dorsolateral Prefrontal						+			+			
Lateral Orbital						+		+	+			
Anterior						+		+	+			
Language Circuit								+	+			
Other Left Hemisphere Areas												
Frontal Lobes								+				
Other left hemisphere areas				+	+	+		+	+			
Right Basal-Cortical Circuits												
Dorsolateral Prefrontal	+	+	+							+		+
Lateral Orbital	+	+	+					+		+		
Anterior	+	+	+					+		+		
Other Right Hemisphere Areas												
Frontal Lobes							+	+				
Other Right hemisphere areas	+	+	+				+	+		+		+

Table 53

Tests Significantly correlated with HLLST Synonyms subtest (HSS)

Test	Correlation with HSS	Correlation with Left Motor Signs	Correlation with Right Motor Signs
HLLST Synonyms subtest			
HLLST Homonyms subtest	.71***		
HLLST Antonyms subtest	.71***		
HLLST Analogies subtest	.70***		
HLLST Sequencing subtest	.60**		-.42*
HLLST Grammar subtest	.60**		
HLLST Definitions subtest	.59**		-.45*
HLLST Association Naming subtest	.56**		-.47*
HLLST Vocabulary subtest	.56**		-.44*
WAIS-R Similarities subtest	.55**		-.48*
Trail Making Test Part A	-.54**	-.56**	
Complex Figure of Rey, Copy	.49*		
HLLST Sentence Formulation subtest	.48*		
HLLST Audio/Visual Comprehension subtest	.47*		-.70***
HLLST Categories subtest	.47*		-.42*
Trail Making Test, Part B	-.46*		.54**
HLLST Provide a Word subtest	.44*		
Complex Figure of Rey, Recall	.42*		
WAIS-R Digit Symbol subtest	.41*		-.44**

* **p<.05**
** p<.01
*** p<.001

6.6.5. Summary of Circuit-lesions associated with Assessment tasks

The conclusions of Phase 5 are summarized in Table 55.

Table 55

Summary of Circuit-lesions associated with Assessment Tasks

Neuropsychological Test	***Task***	**Lesions associated with deficit performance**
WAIS-R Digit Symbol	*Writing as many symbols next to numbers as possible in 90"*	Combination of globus pallidus & caudate nucleus in either L or R hemisphere, (involved in all 3 circuits)
Trail Making Test, Part B	*Dot-to-dot task, alternating between number and letter sequences*	As above

The correlation between the above two measures was: r=.67 (p <.001)

Computer Tracking Task	*Using a joystick to keep a 5mm circle inside a 15 mm square randomly moving around a computer screen*	Left or Right anterior cingulate circuit

WCST-R Perseverative Responses	*Persistence at sorting cards according to an incorrect principle*	Right dorsolateral prefrontal circuit
HLLST Auditory/Visual Comprehension	*Following examiner's instructions in relation to a picture*	Left dorsolateral prefrontal circuit, and other, unknown areas

The correlation between the above two measures was: r=.02 (n.s.)

HLLST Give Definitions	*Explaining word meanings*	Left or right dorsolateral prefrontal circuit
HLLST Absurdities	*Explaining the absurdity of a short story*	As above

The correlation between the above two measures was: r=.47 (p <.05)

Table 55 (Cont.)

Summary of Circuit-lesions associated with Assessment Tasks

Neuropsychological Test	*Task*	Lesions associated with deficit performance
HLLST Association Naming	*Naming as many items as possible in a category in 60 seconds*	General Left hemisphere
HLLST Antonyms	*Giving the opposite of a given word*	Right frontal lobe, Left Dorsolateral Prefrontal circuit or other, unknown areas
HLLST Synonyms	*Giving another word that means the same as a given word*	Right frontal lobe, Left Language circuitry or other, unknown areas

The correlation between the above two measures was: r=.78 (p <.01)

It is the first objective of the present project to identify measures that are sensitive to circuit lesions. Table 55 shows the ten out of the original 31which were potentially sensitive. From closer scrutiny of lesion profiles for each test, one of the ten were excluded (HLLST Association Naming), leaving nine tests arguably sensitive to circuit lesions. Another part of the first objective is to see if there is any evidence for links between each of these and individual circuits. Such evidence would suggest possible differentiation of roles between the circuits. Five out of the seven circuits were linked to specific measures.

Left Hemisphere

- Combination of globus pallidus and caudate nucleus (invclved in all three basal-frontal circuits) (WAIS-R Digit Symbol, Trail making Test, Part B)
- Left dorsolateral prefrontal circuit (HLLST Auditory/Visual Comprehension, HLLST Give Definitions subtest, HLLST Absurdities subtest, HLLST Antonyms subtest)
- Left anterior cingulate circuit (Computer Tracking Task)
- Left language circuitry (HLLST Synonyms subtest)

- General left hemisphere (HLLST Association Naming)

Right Hemisphere

- Combination of globus pallidus and caudate nucleus (involved in all three basal-frontal circuits) (WAIS-R Digit Symbol, Trail making Test, Part B)
- Right anterior cingulate circuit (Computer Tracking Task)
- Right dorsolateral prefrontal circuit (HLLST Give Definitions subtest, HLLST Absurdities subtest, WCST-R Perseverative responses)
- Right frontal lobe (HLLST Synonyms subtest and HLLST Antonyms subtest)

Clearly some suggestion of role differentiation is present. More functions were linked to the dorsolateral prefrontal circuit than any other. Some small degree of verbal/visual differentiation of function for the left and right hemispheres of this circuit is evident. Otherwise the main role for this circuit in both hemispheres appears to be select, higher-level language functions. Two other circuits were associated with one measure only. The anterior cingulate circuit with a visual-motor attention task and the language-related circuit with synonyms. Then two complex motor programme activities were associated with the combination of globus pallidus and caudate nucleus in either hemisphere. Two high-level language tasks (Antonyms and Synonyms) were associated with both the right frontal lobe and a left hemisphere, basal-cortical circuit. Unexpectedly, equal involvement of a basal-cortical circuit in either hemisphere was found for several measures. These were complex motor functions, and select higher-level language tasks (HLLST subtests of, Give definitions and Absurdities, Antonyms and Synonyms).

However the very real limits on the precision of both neuroimaging and neuropsychological tests, limit interpretation of findings presented in Table 55. For all of the neuropsychological assessment tasks, successful performance requires the integrated exercise of a variety of cognitive processes. It may be only one, or a subgroup of, those cognitive processes that are associated with the respective circuit.

Table 56

Correlations between Circuit-Lesion-Sensitive Tests and Motor Signs for All Brain-Injured Subjects only (N=25)

Circuit-Lesion-Sensitive Tests	Motor Signs	
	Left	Right
Trail Making Test, Part B	.22	**.54****
WAIS-R Digit Symbol Subtest	-.28	**-.44***
Computer Tracking Task	**-.01**	.05
WCST-R Perseverative Responses	**-.002**	-.04
HLLST Auditory/Visual Comprehension Test	**.24**	**-.70****
HLLST Association Naming Test	-.09	**-.47***
HLLST Antonyms Test	-.24	-.24
HLLST Synonyms Test	-.07	-.25
HLLST Give Definitions	.39	**-.45***
HLLST Absurdities	-.08	-.26

* $p<.05$
** $p<.01$

6.6.6. Examination of Alternative Explanations for Deficits

6.6.6.1. Undetected Brain Injury

A certain proportion of brain disruption will probably not be revealed by the neuro-imaging available (see '4.3 Lesion Verification' in the Method section). Some of that undetected disruption (i.e. diffuse injury, smaller lesions, full extent of larger lesions, axonal injury, etcetera) could reasonably be inferred from the typical pattern of brain involvement associated with the cause of each subject's brain impairment (i.e., Closed Head Injuries, Cerebrovascular Accidents, Tumours, Parkinson's Disease, Other). For example, people who have suffered closed head injuries (CHIs) have a distinctive pattern of primary and secondary damage. This is associated with an equally distinctive set of neuropsychological difficulties (Reilly & Bullock, 1997). The same can be said about cerebrovascular accidents (CVAs) (Hom & Reitan, 1990). Checking whether any deficits are consistently associated

with cause of the brain impairment should reduce the erroneous attribution of deficits to more detectable, focal lesions (e.g. those within the basal-cortical circuits).

This possibility that neuropsychological difficulties were really only general effects of CHI, CVA etcetera was checked by further analysis. For each deficit listed in Table 55, incidence was examined for each diagnostic group in turn (see Table 57). If a clear majority of subjects in a particular diagnostic category had one of these deficits, then that deficit was held to be a potential feature of that diagnostic category, rather than a consequence of one of the focal lesions.

In Table 57, there were six instances where more than two thirds (>67%) of subjects within a diagnostic category performed poorly. Cells containing these results are shaded in grey. It is proposed that such deficits are a general consequence of membership of the respective diagnostic category. This possibility will be considered for each one in turn (see later phases). However another possibility needs to be eliminated. Lesion A could be over-represented within a Diagnostic Category (X) in this project. If Lesion A consistently resulted in Deficit B, we might erroneously conclude that Deficit B was associated with Diagnostic Category X. This is checked by compilation of another table (Table 57).

In Table 58, the CHI subjects showed an over-representation of right-sided lesions, in contrast to the CVAs, who showed an over-representation of left-sided lesions. However this does not have any obvious correspondence to the distinctive neuropsychological difficulties associated with diagnostic categories (see Table 57).

Table 57

Relationship between Circuit Deficits and Diagnostic Categories

Neuropsychological Test *(No. with a deficit out of 25)*	***Task***	**% of Ss within a Diagnostic Category showing a deficit**		
		CHI *n=15*	**CVA** *n=7*	**Other** **n=3*
WAIS-R Digit Symbol *(n=11)*	*Writing as many symbols next to numbers as possible in 90 seconds*	47%	71%	33%
Trail Making Test, Part B *(n=10)*	*Dot-to-dot task, alternating between number and letter sequences*	29%	57%	33%
Computer Tracking Task *(n=6)*	*Using a joystick to keep a 5mm circle inside a 15 mm square randomly moving around a computer screen*	12%	43%	33%
WCST-R Perseverative Responses *(n=10)*	*Number of persistent card sorts made to wrong principle*	29%	43%	67%
HLLST Auditory/Visual Comprehension *(n=10)*	*Following examiner's instructions in relation to a picture*	35%	43%	33%
HLLST Association Naming *(n=15)*	*Naming as many items as possible in a category in 60 seconds*	41%	71%	100%
HLLST Antonyms *(n=12)*	*Giving the opposite of a given word*	47%	43%	33%
HLLST Synonyms *(n=13)*	*Giving another word that means the same as a given word*	53%	29%	67%
HLLST Give Definitions *(n=7)*	*Explaining word meanings*	24%	29%	33%
HLLST Absurdities *(n=9)*	*Explaining the absurdity of a story*	29%	43%	33%
HLLST Sentence Formulation *(n=18)*	*Generating a sentence that included three set words*	65%	57%	100%

** 'Other' included subjects with neurological diagnoses recorded in medical notes as: 'abscess' (1), 'tumour' (1) and 'astrocytoma' (1).*

Table 58

Overview of Brain Lesions by Diagnostic Category

Brain Area Involved	CHI *(N=15)*	CVA *(N=7)*	Other *(N=3)*
Left Prefrontal Dorsolateral Circuit	2	4	
Left Lateral Orbital Circuit	4	4	1
Left Anterior Cingulate Circuit	3	4	
Language-related circuitry	5	3	1
Left Cortex	7	4	
Left subcortex	3	4	2
Right Prefrontal Dorsolateral Circuit	6	2	1
Right Lateral Orbital Circuit	8	1	1
Right Anterior Cingulate Circuit	8	1	1
Right Cortex	8	2	
Right subcortex	8	2	1

NB The same subject is often counted in more than one cell as individual subjects typically showed a range of lesion.

6.6.6.2. Brain Level, rather than Brain Circuits

The basal-cortical circuits straddle four levels of the brain (cortex, striatum, pallidum & substantia nigra and the thalamus). They also straddle a more basic differentiation of brain levels, cortex and subcortex. There is a long tradition in neurology and neuropsychology of associating different neuropsychological functions with these different levels of brain organization. This suggests the possibility that deficits apparently associated with a circuit, might in fact be associated with one of the levels of the brain included in the circuit. Particularly so if any level is over represented (e.g. the cortex) in the lesions of subjects within a group, assembled on the basis of circuit involvement.

Of the 25 brain lesion subjects, the numbers of subjects with involvement at each of the four levels were, frontal lobes (9), striatum (11), pallidum and substantia nigra (11) and the thalamus (2). In terms of cortical/subcortical, numbers were 15 and 19 respectively. Significant numbers of subjects were counted in more than one category. When subjects were grouped this

way, instead of by circuit (as they were in Phases 2 to 4), far fewer deficits were associated with any of the groups. This gave significant support for the circuit concept as an explanation for neuropsychological functions.

The method used to check association between particular deficits and lesions of a certain brain level was the same as that described in "6.3.1. Data Analysis and Rationale". Tests were identified where a majority of subjects in a particular lesion group (defined by one of the above brain levels) had a deficit, and where a majority of subjects without that lesion, did not have a deficit. It could be argued that performance on those tests were associated with that level of brain lesion. The tests thereby linked to each level were,

Frontal Lobes
HLLST Antonyms
HLLST Synonyms
(The right frontal lobe, that was over-represented among this group, was found to be associated with these measures. See sections 6.6.4.3.2. HLLST Antonyms, and 6.6.4.4.2. HLLST Synonyms.)

Striatum
WAIS-R Digit Symbol

Pallidum & Substantia Nigra
Trail Making Test, Part B
(These findings are consistent with findings reported elsewhere for these tasks. See sections 6.6.1.1. WAIS-R Digit Symbol and 6.6.1.2. Trail Making Test, Part B).

Thalamus

(Only two subjects had the thalamus involved and this was not enough for this kind of informal group data analysis.)

Cortex

HLLST Association Naming

HLLST Synonyms

SubCortex

HLLST Antonyms

HLLST Synonyms

HLLST Association Naming

It should be noted that of the 15 and 19 subjects respectively that were in the cortical and subcortical groups, 14 subjects were in both. Thus the two groups could hardly be regarded as different. Relatively few deficits were clearly associated with particular brain levels. Clearly level of brain lesion, as distinct from circuit involvement, is not strongly linked to the pattern of deficits revealed among subjects in this thesis.

6.7. PHASE 6: Neuropsychological Deficits of Parkinson's Disease Subjects

Objective: Subjects with PD potentially have degenerative changes in all circuits. Phase 5 identified a set of ten measures (see Table 55), arguably sensitive to lesions in some of the circuits. Support from further investigation would significantly extend our understanding of the role of these structures. A survey of another group of subjects, with presumed basal ganglia impairments, (early-stage PD subjects), is an example of the type of investigation which would test the conclusions of Phase 5. Support required PD subjects to demonstrate comparable deficits. The objective of Phase 6 was establishing the correspondence between the PD subjects' and circuit-lesion subjects' deficits.

The first issue when making such a comparison is; which of the basal-cortical circuits are likely to be affected in PD? PD is a progressive, multi-system disease which varies considerably both within and between individuals (Kelly, 1995). Brooks (1995) concluded from a review of PET studies done with PD subjects that loss of striatal dopmaine is associated with functional deafferentation of the supplementary motor area, anterior cingulate cortex and the dorsal prefrontal areas but appears to spare primary motor and lateral premotor cortex activity. The key disease-process in PD is profound Dopamine depletion both in the striatum, and, to a lesser extent, in the prefrontal cortex (Scatton, Javoy-Agid, Rouquier, Dubois & Agid, 1983; Agid, Ruberg, Dubois & Pillon, 1987; Kish, Sannak & Hornykiewicz 1988). However the action of dopamine in these areas is not yet fully understood (Owen, Doyon, Dagher, Sadikot & Evans, 1998; Groves, Garcia-Munoz, Linder, Manley, Martone & Young, 1995). The PD subjects involved with this project had not received any neurological investigations like CT or MRI and all the six circuits include a part of the striatum (e.g. the caudate nucleus). Thus all circuits were potentially, but not necessarily, involved in all the PD subjects. The distinctive neuropsychological difficulties found with PD have been interpreted as effects of circuit-disruption, rather than as effects of degeneration of structures forming the individual links making up those circuits. The circuit-disruption hypothesis would suggest that people with PD, and people with circuit disruption due to brain damage, would have similar cognitive impairments.

The PD subjects' results were first analyzed in the same way as the brain-injured subjects' results (see section "6.3.1. Data Analysis and Rationale"). However proceeding with this analysis first required resolving certain methodological difficulties. The PD subjects were significantly different from the controls in terms of characteristics known to affect neuropsychological test performance (see Table 59). They were significantly older and had higher pre-morbid intelligence. (They also showed significantly less depression on the non-somatic items of the Beck Depression Inventory. However even the highest group average on this measure [brain-injured] was well below the minimum threshold for clinically significant depression. Therefore these depression differences were not considered a problem from a methodological point of view.)

See Table A.15. (in Appendix A.) for more detailed background information about the PD subjects. Old age is associated with various cognitive changes. There is a very extensive and somewhat inconsistent literature addressing this issue. However another comprehensive review is beyond the scope of this thesis. Therefore reliance will have to be placed on the conclusions of others, in this case Lezak (1995). According to her analysis, psycho-motor slowing is possibly the most prominent cognitive change associated with aging. This is closely allied to impairment of sustained and selective attention. Memory tasks involving effortful processes such as mental manipulation, active search or categorization or memorizing despite distractions also tend to be more difficult for older people. Other memory tasks known to be affected include verbal recall (e.g., recall of word lists involving nine or more items, delayed recall, verbal fluency tasks) visual recall and recognition. Success at novel problem solving tasks and visuo-perceptual judgement have been found to decline with aging, e.g. less accurate copying of the Rey-Complex Figure (Ska, Dehaut & Nespoulous, 1987 -in Lezak, 1995) and more perseverative errors on the Porteus Mazes (Daigneault, Braun & Whitaker, 1992b).

Table 59

Background Information.

Mean (SD) for each parameter

Variable	Measure	Controls N=11	Brain-injured N=25	PD N=13
Age	Age (Yrs) **	31.8 (11.1)	34.80 (15.61)	63.08 (4.84)
Pre-morbid IQ	NART-R IQ **	106.3 (8.5)	101.76 (13.53)	115.15 (6.68)
Depression	Beck Deprsn Inv *	6.55 (4.03)	5.74 (5.93)	1.58 (2.35)

* *Significantly different between groups, p<.04, Oneway ANOVA*

** *Significantly different between groups, p<.001, Oneway ANOVA*

Age-related normative data (including both means and standard deviations) are available for some of the measures. Measures, publications reporting normative data, type of scores used, average performance for all PD subjects, are shown in Table A.14. (see Appendix A.).

A further strong predictor of post-traumatic ability is pre-morbid intelligence (Grafman et al. 1988). Thus it is arguable that the higher pre-morbid intelligence of the PD subjects could have masked possible effects of basal ganglia degeneration. Adams et al. (1985) performed statistical simulations of typical lesion-group comparisons while controlling for differences in things like age and education by entering them as co-variates in analyses of co-variance (ANCOVA). They concluded that this methodology did not successfully eliminate consideration of the co-variate as an explanation for results. Thus although that technique is often used to deal with issues like controlling for extraneous variables (e.g. premorbid IQ), it would not be appropriate here.

Possibly the best, if a less precise, approach with these data would be comparison of each PD subject's pre-morbid (NART-R) IQ z-score with their z-scores on the neuropsychological tests. The latter z-scores to be based on age-related norms reported elsewhere in the literature (see Table A.14. in Appendix A.). Significant discrepancies suggest neuropsychological deficits. This is similar to the analysis used with the brain-injured subjects, except that the NART-R IQ z-score is replacing the control group mean as definition of normal performance. The other important difference from the analysis of brain-injured subjects' data in Phase 2 is the use of published, age-related normative data for the calculation of PD subjects' z-scores, instead of the control group data. Otherwise, the structure of the data presentation follows that used for the brain-injured subjects (see section "6.3.1. Data Analysis and Rationale").

There are some methodological shortcomings to this approach. For example there may be variations in level and type of sample bias across normative samples providing the age-related data for each measure (e.g. in terms of socio-economic status or educational levels). There is also the lack of information about how performance on each measure is related to general intelligence. Performance on some cognitive tasks is more strongly related to general IQ than others. For those, smaller IQ score-test score discrepancies would be significant, while with tasks less strongly related, larger discrepancies would be needed to achieved significance. However this crude analysis does at least provide some way of exploring possible patterns within a data set where considerable practical constraints prevent more substantial data collection and analysis.

For practical reasons, we will proceed with the questionable assumption that IQ and individual neuropsychological performance are perfectly correlated in the unimpaired population. NART-R IQ will be transformed into a z-score (i.e. 100 = a z-score of 0, and 115 = a z-score of +1.0). If a majority of the PD subjects showed less proficient performance than what would have been obtained by fewer than one in 10 people with their IQ, it was concluded that the PD group was characterized by a deficit on this measure. The 'fewer than 1-in-10' criterion corresponds to a discrepancy between their IQ z-score and a z-score from a specific test of 1.64. **The PD group was so-found to be characterized by deficits on four of the measures (out of 25). Two involved prose recall (Paragraph recall, Immediate and Delayed) another, oral construction of sentences requiring inclusion of set words, or a set sentence length (HLLST Sentence Formulation) and fourth, a computer-based tracking task.**

In Table 60, results for a specific test are only presented when a majority of the subjects with Parkinson's Disease (PD) all performed poorly on it. One of those four tests had also been linked to particular types of lesions in Phase 5 (see Table 55). This was the right or left anterior cingulate circuit (Computer Tracking task). The two other tests (Paragraph recall, Immediate & Delayed) were suggested by the literature review to be associated with the left dorsolateral prefrontal circuit, but this was not found in Phase 5.

Medications used by PD subjects of this phase did not include anticholinergic drugs, sometimes used as a treatment for PD, which have also been associated with memory impairments (Barbosa, Limongi & Cummings, 1997). The difficulty with constructing a sentence around three set words (HLLST Sentence Formulation) is consistent with other cognitive impairments reported among PD subjects, e.g. reduced speed of cognitive processes (Barbosa et al.).

However the number of measures revealing a deficit for the PD group was small, only four (see Table 60). This was much fewer than the number among the brain injured group (ten, see Table 55). This probably reflects more severe brain impairments among the brain-injured subjects, compared to the PD subjects. This was supported by a comparison of the motor signs evident

among each group. The extent of motor signs among the brain-injured group was clearly more severe, and included a wider range of such impairment across subjects. The score for total motor impairments (left and right combined) among the brain-injured group was 6.45 (SD: 5.95) and the Parkinson's Disease (PD) group was 3.08 (SD: 1.98). Significantly different on t-test, ($p<.05$).

Table 60
Results for PD subjects on Tests revealing Deficits

Skill Area linked to Circuit	Test of Skill Area	Subjects (N=13)												
	bject ID No.s	*8*	*9*	*10*	*11*	*14*	*15*	*16*	*17*	*18*	*19*	*35*	*38*	*39*
Attention & Motor response	*Computer Tracking Task**	-3.77	-3.57	-3.67	-1.45	1.05	-1.77	-2.0	**-3.0**	.73	-2.24	-1.43	-2.10	-1.83
Expressive Syntax	*HLLST Sentence Formulation*	-1.13	-1.13	-1.13	-1.13	-1.80	-2.14	-2.5	**-1.8**	-1.80	-1.80	0.89	-1.13	0.89
Verbal Recall	*Paragraph recall, immediate*	-1.59	0.29	-1.27	1.24	-0.33	-1.70	-1.9	-0.33	-2.53	-0.96	-0.69	-1.90	-1.45
	Paragraph recall, delayed	-2.36	0.78	-0.79	0.78	0.15	-1.34	-1.1	-0.79	-2.36	-2.36	-0.25	-2.36	-0.79

* Age-related normative data were not available for this measure. In the absence of anything better, despite their shortcomings, normative data generated by the control group were used to calculate z-scores.

Other researchers have reported significant correlations between level of motor impairment and cognitive difficulties among people with PD, which has been interpreted as reflecting a common underlying brain structure. Indices of cognitive function so-associated include visual-spatial reasoning and psychomotor speed (Mortimer, Pirozzolo, Hansch & Webster, 1982) and memory (Viitanen, Mortimer & Webster, 1994).

However Table 61 shows only one significant correlation between motor signs of the PD subjects and the measures that had revealed neuropsychological deficits among the brain injured subjects. (The latter were listed in Table 55.) If the alpha=0.05 criterion is used, one correlation among 45 being significant could be expected by chance only. Thus it will not be considered a noteworthy result. This is in contrast to the result of calculating the same correlation matrix with the brain-injured subjects' data (see Table 62).

The subtle nature of cognitive impairments in early-stage PD subjects has been reported by other researchers (e.g., Bennett, Waterman, Scarpa & Castiello, 1995). The deficit-criterion used in the brain-injured subjects' analysis and the PD subjects' analysis (in Table 60), would be less likely to identify smaller deficits. Consequently, additional, more sensitive, analysis was performed on the PD subjects' data to see if evidence for those deficits was in fact present. PD data based on age-norms were used. PD subjects' performance (on the measures revealing deficits in Phase 5), were compared with a measure of pre-morbid ability. The National Adult Reading Test –Revised (NART-R) was considered the most suitable measure of pre-morbid ability for this group. It is the most well accepted test of pre-morbid ability in the absence of aphasic disturbances (Lezak, 1995). The prediction that performance on each of these measures would be significantly lower than NART-R IQ was tested with a series of T-tests (see Table A.16. in Appendix A). Nine out of the ten comparisons revealed a significant difference in the direction predicted. This supported the proposition that the PD group had the same difficulties as the circuit-lesion, brain injured groups, albeit of a smaller magnitude. Of the two comparisons not revealing a significant difference, one was in the predicted direction (HLLST Association Naming).

A further complementary analysis involved correlations between the deficit measures (from Phase 5) and the four measures revealing deficits among the PD subjects (The Computer Tracking Task, HLLST Sentence Formulation, immediate paragraph recall and delayed paragraph recall). This allowed exploration of possible relationships between the two, apparently dissimilar, sets of deficits. The correlation matrix is shown in Table 61. Only data from the PD subjects was used in calculation of these correlations. The pattern of correlations in Table 61. gave some clarification to cognitive difficulties of the PD subjects. The clarification is twofold. Delayed story recall is associated with three HLLST subtests, Association Naming, Synonyms and Give Definitions. One of those tasks is associated with Immediate Story Recall as well. Declarative semantic memory is arguably the common thread running through these tasks. In the literature review it was concluded that this was associated with the left dorsolateral prefrontal circuit.

Then there was the clearly inverse relationship between immediate story recall and the task requirements of the HLLST Auditory/Visual Comprehension subtest. The latter required the subject to follow the examiner's oral instructions in relation to a picture, which would seem to include a verbal recall component. Other requirements are clearly present though, primarily visual. Specifically, the latter ones included scanning, searching, and recognition within the stimulus picture. This different direction of correlation suggests dissociation between these visual tasks and declarative, verbal semantic memory, and that the visual task requirements might be the main ones of that task. This task was strongly associated with right motor signs, suggesting strong lateralization in the left hemisphere ($r=-.70$), unlike the other two, HLLST Synonyms subtest (no significant correlation with motor signs of either side) and HLLST Give Definitions subtest (with right motor signs, $r=-.47$). The analysis in Phase 5 concluded that the HLLST Auditory/Visual Comprehension subtest was associated with the left dorsolateral prefrontal circuit, HLLST Synonyms subtest with the right frontal lobe and left, language-related circuitry, and the HLLST Give Definitions subtest with the left or right, dorsolateral prefrontal lobe.

Table 61

Correlations between Lesion-sensitive Tests and Motor Signs for PD Subjects only

	Motor Signs		
	Left	**Right**	**Total**
Tests Sensitive to circuit-lesions (from Phase 2)			
WAIS-R Digit Symbol Subtest	-.36	.24	-.12
Trail Making Test, Part B	.09	.22	.12
Computer Tracking Task	**.32**	.11	.19
WCST-R Perseverative Responses	**-.56***	-.06	-.30
HLLST Auditory/Visual Comprehension Test	**.17**	-.14	.07
HLLST Association Naming Test	.10	.34	.36
HLLST Antonyms Test	.07	.13	.18
HLLST Synonyms Test	.03	.03	.10
HLLST Sentence Formulation	-.07	-.40	-.33
HLLST Give Definitions	-.15	.12	.02
HLLST Absurdities	-.23	.19	.02
Tests Sensitive to PD Deficits			
Computer Tracking Task	**.32**	.11	.19
Sentence Formulation	-.07	-.40	-.33
Story Recall, Immediate	-.01	.21	.02
Story Recall, Delayed	-.08	-.13	-.001

Table 62

Correlations between Lesion-sensitive Tests and Motor Signs for All Brain-Injured Subjects only (N=25)

	Motor Signs		
	Left	**Right**	**Total**
Tests Sensitive to circuit-lesions (from Phase 2)			
WAIS-R Digit Symbol Subtest	-.28	**-.44****	**-.55*****
Trail Making Test, Part B	.22	**.54*****	**.63*****
Computer Tracking Task	**-.01**	.05	.11
WCST-R Persevertive Responses	**-.002**	-.04	-.07
HLLST Auditory/Visual Comprehension Test	**.23**	**-.70*****	**-.39***
HLLST Association Naming Test	-.09	**-.47****	**-.41***
HLLST Antonyms Test	-.24	-.24	**-.40***
HLLST Synonyms Test	-.07	-.25	-.26
HLLST Sentence Formulation	.12	-.33	-.23
HLLST Give Definitions	.39	**-.47***	-.03
HLLST Absurdities	-.08	-.26	-.27
Tests Sensitive to PD Deficits			
Computer Tracking Task	**-.01**	.05	.11
Sentence Formulation	.12	-.33	-.23
Story Recall, Immediate	-.05	**-.55*****	**-.48****
Story Recall, Delayed	-.04	**-.38***	**-.40***

* p<.1
** p<.05
*** p<.01

From what is understood about the effects of PD in the early stage (the stage of subjects in this project), it could be expected that subjects with brain injuries to the pallidum and substantia nigra would have cognitive impairments similar to the PD subjects. However, the analysis reported in section "6.6.6.2. Brain Level, rather than Brain Circuits" found that the only measure revealing a deficit for subjects with brain injuries at this level was Part B of the Trail Making Test. Although other studies have reported deficits on this instrument for PD subjects, PD subjects of this project did not show that deficit.

In conclusion, apart from the common difficulty with the computer-presented pursuit tracking task, convergence between the findings from the PD subjects and the lesion subjects is weak at best. The only other common element that could be argued, tentatively, is a verbal declarative memory deficit. This is possibly a common requirement for short term, verbal prose recall (a deficit for the PD subjects) and search and retrieval from a much larger store of word knowledge (in the case of the lesion subjects).

7. DISCUSSION

7.1. General Overview of Results Analysis and Findings

Investigation of neuropsychological functions presents many methodological challenges. Critical preliminary issues required substantial analysis in their own right (Phase 1) before the central objective of this project could be addressed. The data gathered from the spinal injury control group was found to be reasonably representative of the general population. The general accuracy, within limits, of the neuroimaging (CT and MRI) used to establish lesion location, was verified. Resolution of those issues made possible the further analysis required for the main objective of this project (Phases 2 to 5).

Clearly some suggestion of role differentiation between circuits was found. More functions were linked to the dorsolateral prefrontal circuit than any other. There was a small degree of verbal/visual differentiation of function for the left and right hemispheres of this circuit. Two other circuits were associated with one measure only, the anterior cingulate circuit with a computer-presented pursuit tracking task and the language-related circuit with synonyms. Two complex motor programme activities were associated with the combination of globus pallidus and caudate nucleus in either hemisphere. A pair of high-level language tasks (generation of antonyms and synonyms) were associated with both the right frontal lobe and a left hemisphere, basal-cortical circuit. Unexpectedly, equal involvement of a basal-cortical circuit in either hemisphere was found for several measures. These were complex motor functions, and select higher level language tasks (HLLST Give Definitions, HLLST Absurdities, HLLST Antonyms and HLLST Synonyms). See section "6.6.5. Summary of Circuit Lesions Associated with Assessment Tasks".

When subjects were grouped according to level of brain involvement (e.g., frontal lobes, striatum etc., or cortex, subcortex), instead of by circuit (as they were in Phases 2 to 4), far fewer deficits were associated with any of the groups. This gave significant support for the circuit concept as an explanation for neuropsychological functions. (See section "6.6.6.2. Brain Level, rather than Brain Circuit").

These conclusions from Phase 5 were tested with another set of (presumably) circuit-impaired subjects, people with early-stage Parkinson's Disease (Phase 6). However, apart from the common difficulty with the computer-presented pursuit tracking task, convergence between the findings from the PD subjects and the lesion subjects was weak at best. The only other common element that could be argued, tentatively, is a verbal declarative memory deficit. Some uncertainty remained about whether the lack of clear consistency reflected extraneous group-differences. The latter included more mild general neurological impairment of the PD subjects (reflected in motor signs), and the higher premorbid intelligence and age of the PD subjects. Although some control for these differences was possible, future research comparing PD subjects to other basal-ganglia groups with fewer differences could resolve this question. See section "6.7. Phase 6: Neuropsychological Deficits of Parkinson's Disease Subjects". There are two further possible reasons for nondetection of impairments among the subjects with PD. One is that the abnormal processes leading to cognitive impairment in PD and basal-cortical circuit brain lesions are substantially different, hence the cognitive impairments are also substantially different. The second is that the dopaminergic medications being taken may have prevented some of the cognitive and language effects of PD (Murray, 2000). See Table B.6 in Appendix B. for a list of the medications taken by the subjects with PD. However, broadly speaking, the types of impairments associated with PD in Phase 6 have been associated with basal-cortical lesion subjects in other studies, and likewise, the types of impairments associated with the latter group in Phase 5 have been associated with PD subjects in other research (See Literature Review.). This is probably another illustration of limitations of current research methodology, which are discussed further below.

7.1.1. Qualitative Examination of Deficits associated with Lesions

Phase 5 identified a set of tests on which poor performance was associated with lesions of basal-cortical circuitry (see Table 55). However, these tests each involved a variety of cognitive processes. The general pattern of results described in section 7.2 'General Overview of Results Analysis and Findings' included some suggestion of functional specialization for different circuits. Tests associated with deficits, listed in Table 55, could be divided into three categories.

The first of these was tests of conscious attention and performance of complex programs of motor activity (see Table A.18. in Appendix A.). The second was tests of language functions (see Table A.20. and Table A.21. in Appendix A.) and the third was tests of executive functions (see Table A.19. in Appendix A.). Links between circuits and functions will be discussed separately for each test-category in turn.

Three tests involving conscious attention and performance of complex programs of motor activity were associated with lesions of basal cortical structures. Of these three, the computer based tracking task was associated with the anterior cingulate circuit (in either hemisphere). The remaining two, the Trail Making Test, Part B, and WAIS-R Digit Symbol subtest, were both associated with the globus pallidus and the caudate nucleus (also in either hemisphere). The rostrolateral part of the globus pallidus is a part of the anterior cingulate circuit (See Figure 2). Thus it is possible that impaired performance of all three tests of conscious attention and performance of complex programs of motor activity were linked to the anterior cingulate circuit.

Of the processes involved in complex programmes of motor activity, one was consistently required by the tests associated with lesions, and consistently not required by the tests not associated with lesions. **This was dynamic allocation of attention between competing inputs**. In the case of the Computer task, one input was the small square randomly moving around the computer screen, and the second, in competition with the first, was the small circle controlled by the subject's joystick. For Part B of the Trail Making Test, one of the inputs corresponded to the circles identified with numbers, and the second was the set identified with letters. In the case of the WAIS-R Digit Symbol task, competing inputs were provided by the numbers and symbols respectively. Nothing comparable was involved in the other three tasks. These were the Trail Making Test, Part A, the Rey-Osterrith Figure and the Porteus Mazes. Therefore, it is proposed that this function (dynamic allocation of attention between competing inputs) is associated with the anterior cingulate circuit. Notably, performance of the computer based tracking task was also impaired among the PD subjects, suggesting that the anterior cingulate circuit is the main one affected by this condition.

This is consistent with Bennett et al.'s (1995) finding that early-stage PD subjects took more time than controls to complete a complex spatial-attention task. Bennett et al interpreted this finding according to a theory previously advanced by Brown and Marsden (1990). This theory held that a depletion of (cognitive) processing resources occurs in PD. The mildness of the effect would be consistent with the very early stage of their PD at the time of testing (Hoehn & Yahr stages 1 & 2, the same as PD subjects in this project). Sprengelmeyer et al's (1995) study of Huntington's Disease (HD) subjects obtained a similar finding. This is not inconsistent with recent research into skills associated with another part of the brain that includes the cortical sections of the basal-cortical circuits, the frontal lobes. Shallice et al. (1998) reported activation of the left anterior cingulate cortex and the left dorsolateral prefrontal cortex during dual-task performance. The importance of this type of processing is underlined by a finding reported by Alderman (1996). He found that capacity for dual-task performance differentiated brain injured clients who responded to operant conditioning methods from those who did not.

In reference to Table 55, it is striking that on five of the remaining six tests associated with basal cortical circuits impaired performance is linked to the dorsolateral prefrontal circuit. Those tests were the WCST Perseverative Responses index, and four subtests from the HLLST. These included Auditory/Visual Comprehension, Give Definitions, Absurdities and Antonyms. A common lesion raises the possibility of common impairment(s) underlying impaired performance across this set of tests.

Two of the four language measures associated with lesions of the dorsolateral prefrontal circuit required **verbal expression of an abstract idea.** The HLLST Absurdities subtest required the subject to explain how an orally presented scenario was absurd. The second of the two tasks (HLLST Give Definitions) involved the subject explaining the meaning of a series of words (e.g., rehearsal, consequences). None of the language subtests not associated with this circuit required the same kind of verbal expression (see Table A.20. & Table A.21.). Formulation of expression and abstraction together, suggest this function can be viewed as the culmination of a set of prior processes, possibly in sequence. For example. they could include effective comprehension and interpretation of certain life experiences (possibly including verbal communication from others) and analysis of this experience leading to conclusions. These

conclusions would have to be represented verbally, prior to articulation. The successful culmination of various prior processes implies two things. One is the likelihood that various brain structures, including some more substantial, more complex ones are involved (e.g., the cortex). The second is that there is some kind of orchestration, or synchronization of the sub-processes to ensure an effective outcome, namely the coherent and incisive expression of an abstract idea.

This is not inconsistent with Murray's (2000) finding that, compared to control subjects, subjects with HD made shorter utterances, had a smaller proportion of grammatical utterances, a larger proportion of simple sentences, and fewer embeddings per utterance. The HD subjects produced utterances that were shorter and syntactically more simple than those of a PD group. These impairments would be consistent with difficulty expressing abstract ideas verbally. HD, unlike PD, involves degeneration of the caudate nucleus, and the dorsolateral head of the caudate nucleus is part of the dorsolateral prefrontal circuit. This would therefore be consistent with the dorsolateral prefrontal circuit mediating these language functions. We have argued that PD probably does not involve this circuit, at least in the early stages of the disease.

However, the other three subtests linked to the dorsolateral prefrontal circuit in Table 55, (WCST-R Perseverative Responses, HLLST Auditory/Visual Comprehension and HLLST Antonyms) do not appear to involve a unifying process that could not be argued, just as strongly, to be present among the tests not associated with lesions.

Another issue relevant to this point in the discussion is the association between two tests (the Trail Making Test, Part B, and WAIS-R Digit Symbol subtest) and two basal ganglia structures (the globus pallidus and the caudate nucleus, in either hemisphere). It has already been argued that performance on these two tests is mediated by another basal-cortical circuit (the anterior cingulate), because part of the globus pallidus is part of this other circuit (the rostrolateral segment). However, other parts of these two basal ganglia structures (the dorsolateral head of the caudate nucleus and the lateral dorsomedial globus pallidus) are also part of the dorsolateral prefrontal circuit (See Figure 2 in section "2.3. Circuitry of the Basal Ganglia"). From the scanning available (usually CT), it was not possible to identify which sub-areas of the

globus pallidus and caudate nucleus were involved. Thus the possible involvement of additional segments of these basal ganglia structures (the lateral dorsomedial globus pallidus and the dorsolateral head of the caudate nucleus) which are part of the dorsolateral prefrontal circuit, cannot be ruled out. In fact it is when we allow for this possibility that the picture starts to fit together. On this basis it is proposed that the Trail Making Test, Part B, and WAIS-R Digit Symbol subtest are also associated with the dorsolateral prefrontal circuit. These two tasks involve various forms of mental processing, and it is argued that one form, (dynamic allocation of attention between competing inputs) is associated with the anterior cingulate circuit, while another (manipulation of information from working memory, see below) is associated with the dorsolateral prefrontal circuit. The association of these two circuits and these functions is supported by a PET study. Shallice et al, (1998) reported activation of the left anterior cingulate cortex and the left dorsolateral prefrontal cortex during dual-task performance. In fact the common co-activation of these two areas of cortex (Shallice, 2001) suggest forms of cognition proposed here for their respective circuits are closely related. As both cognitive processes correspond to sections of Normal and Shallice's model of executive processing, the respective circuits are probably both integral to this processing.

There are noteworthy similarities between two of the three remaining tests associated with the dorsolateral prefrontal circuit (the WCST-R Perseverative Responses and the HLLST Auditory/Visual Comprehension subtest) and the two tests linked to the globus pallidus and the caudate nucleus, in either hemisphere. These two tests were the Trail Making Test, Part B, and WAIS-R Digit Symbol subtest. **They all involve the ability to manipulate several items of information at once to complete a task, when those items are novel, available to awareness from working memory only, and not represented in concrete form.** This is consistent with executive functions, or an aspect thereof.

It is noteworthy that this conclusion is not inconsistent with the assertion by Cummings (1993), that executive processing is one of the two markers for the dorsolateral prefrontal circuit: the other was motor programming. There is an even stronger consistency between this conclusion and Shallice's (2001) one that the dorsolateral prefrontal cortex is activated (on PET scanning)

when 'information held in short term storage is operated upon' and not when memory alone is involved (i.e., simple retrieval without manipulation).

For instance, in relation to the WCST-R, Perseverative Responses Index, the subject had to retain (in working memory) the administrator's feedback on a series of previous card sorts, and deduce the sorting principle. Continually testing new hypotheses against the previous feedback demanded significant concentration. Part B of the Trail Making Test required the subject to retain (in working memory) the point in one series (number or letter) they had got to, while searching visually under time pressure for the next item in the other series. Thirdly, the WAIS-R Digit Symbol subtest required the subject to either learn, or continually refer back to, seven novel pairings of a single-digit-number with an abstract symbol, to identify and write the correct symbol, under time pressure, against each new digit presented in a random sequence. Fourthly, for the HLLST Auditory/Visual Comprehension subtest, the subject had to retain a sequential verbal instruction while scanning a picture of a complex domestic scene, and carry out that instruction.

On the other hand, two tasks widely regarded as tests of executive functions (the Rey-Osterrieth Figure copying task and the Porteus Mazes), that were not associated with lesions, did not make the same kinds of demands on subjects. (See Table A.19. in Appendix A.) Neither of these required working memory, the pencil manipulation was guided solely by stimulus material (e.g., the stimulus figure, or the outline of the maze) continually in the subject's view. Another possibly simplifying feature of those tasks was the greater likelihood that processing was confined to the visual modality. While the other tests (WAIS-R Digit Symbol etc) were primarily visual, it is arguable that each one has particular features which make subjects likely to incorporate some verbal representation of the internal process, as they perform the task. For example, with the WCST-R, there is the likelihood that the subject was applying verbal labels to sorting criteria (e.g., shape, colour etc.). For the Trail Making Test, Part B, each sequence is normally referred to by the verbal labels (e.g., 1, A, 2, B, 3, C, etc). For the WAIS-R Digit Symbol task, numbers have verbal labels and the abstract symbols arbitrarily paired with them often resemble symbols which have verbal labels (e.g., the letter

V). Finally, the HLLST Auditory/Verbal Comprehension subtest has a major explicit verbal component. The subject has to carry out a verbal instruction in relation to a picture.

Norman and Bobrow (1975) argued that brain damage of any kind tends to reduce an individual's information processing capacity, thereby producing what has been labeled, the 'resource artefact'. Consequently a patient may tend to perform normally on one task and poorly on another because the latter is simply more difficult, irrespective of the location of the damage. This conclusion that more complex tasks (manipulation of information from working memory and dynamic allocation of attention between competing inputs) are associated with basal-cortical circuit lesions, is reminiscent of the 'resource artefact'. Bradshaw and Mattingley (1995) have argued that the presence of 'double dissociation' is required to discount the resource artefact possibility. Double dissociation involves one group of subjects being impaired on task A, but normal on task B, and another group is normal on task A and impaired on task B.

To check for this possibility, numbers of subjects with an impaired performance on any of the tests listed in Table 55 were counted. By implication, if the resource artefact had been present, subjects would tend to fall within either of two groups, one of subjects impaired on most tests, and the other of subjects unimpaired on most tests. This pattern was not present. Numbers of subjects for each possible number of impaired-test-performances were, 1 impaired performance (n=4/22), 2 impaired performances (n=1/22), 3 (n=5/22), 4 (n=2/22), 5 (n=0/22), 6 (n=4/22), 7 (n=2/22), 8 (n=0/22), 9 (n=3/22) 10 (n=1/22). Furthermore, a strong differentiation of brain areas associated with different tests was arguable from the data. See section "6.6 PHASE 5: Broad Areas of Cognition Associated with Basal-Cortical Circuitry: An Integration of Findings from Phases 2 to 4".

Interestingly, data gathered for this project suggested that what had previously been identified as a general consequence of brain injury, (the resource artefact) may in fact have reflected the specific involvement of basal-cortical circuitry. The extensiveness of the structures involved may make them particularly vulnerable to disruption from some of the more common types of brain injury.

Impaired expressions of anontyms and synonyms (HLLST Antonyms and HLLST Synonyms) was clearly associated with lesions to some of the brain subdivisions employed in the analysis. However the tasks involved are essentially different from others considered so far. Furthermore their close similarity to other HLLST subtest tasks which were not linked to lesions (e.g. HLLST Homonyms, HLLST Differences and HLLST Analogies), suggest that the essential process linked to lesions is more subtle and specific. However, beyond the explicit task (identification of antonyms or synonyms), there are no suggestions as to what the distinctive underlying process tapped by these subtests might be.

7.1.2. Neuropsychological Significance of Excitation and Inhibition

Neural circuits have been characterized as a balance of excitation and inhibition. It has been argued (e.g., by Crosson, 1992) that lesions at different points within a circuit could result in different forms of imbalance, hence different forms of cognitive impairment. (See Section "2.3 Circuitry of the Basal Ganglia.") However, this concept has not been widely employed in modeling of cognitive functions (Kapur, 1996). Jackson and Houghton (1995) have probably contributed the most serious attempt to date, in their modeling of the basal ganglia's involvement in spatial attention. Kapur (1996) has concluded that while speculation in individual cases might be plausible, present knowledge is not sufficient for us to draw conclusions about how the balance of excitation and inhibition affects cognitive processes.

Only four of the ten measures linked to lesion-areas in Phase 5 were associated with particular elements within a circuit, rather than a circuit as a whole. Poor performance on the Trail Making Test, Part B and the WAIS-R Digit Symbol subtest were associated with lesions of the caudate nucleus and globus pallidus (combined) in either hemisphere. These two structures operate as adjacent consecutive stages within the basal-cortical circuits described by Alexander et al. (1986). After receiving excitatory input from the cortex, the striatum (which includes the caudate nucleus) sends inhibitory impulses directly to the globus pallidus, and excitatory ones indirectly, via a subthalamic loop. The globus pallidus, in turn, sends inhibitory input to the thalamus thereby moderating onward excitatory input from the thalamus, to the cortex. It has been argued that the critical process within those two testing tests is the dynamic allocation of

attention between competing inputs. (See section 7.1.1. "Qualitative Examination of Deficits associated with Lesions" above.) This provides the basis for some speculation about correspondence between neural processes and information processing models. Both of the implicated structures provide inhibition to subsequent structures within the circuits. The dynamic allocation of attention involves deliberately inhibiting attention from one competing input (e.g., the series of numbers in Part B of the Trail Making Test), and directing it toward the other input (e.g., the series of letters in Part B of the Trail Making Test). Could the neural inhibition correspond to attentional inhibition?

This is an issue for future, very carefully designed, research. Close scrutiny of correlation between cognitive processes and relative activation of brain structures on PET would probably be required to answer this question. For example, on Part B of the Trail Making Task, comparison of areas of brain activation when the subject has reached one of the small circles, and is deciding which one to draw to next, with areas of brain activation during the actual time of drawing to the next circle. The time spent at the circle is probably spent inhibiting the inclination to continue with one series, e.g. letters, and searching for the next circle to draw to, while the time spent drawing to the next one involves the more simple, execution of that decision. This difference might be more pronounced during the earlier part of Trail Making Test (Part B) performance, when it is still more novel and the subject is working out his/her ongoing strategy for effective task completion. Other assessment tasks may also be worth exploring to identify a more 'pure' test of the critical requirements of Part B of the Trail Making Test.

Two other measures were associated with particular elements within a circuit, rather than a circuit as a whole. The HLLST Antonyms subtest and the HLLST Synonyms subtest were both associated with the right frontal lobe, as well as specific circuits. An association between verbal tasks like these with an area of the right hemisphere is less common, hence noteworthy. Pulvermuller (1996) concluded from an extensive review of electrocortical studies of language processing that meaningful-content words tended to involve both hemispheres (as opposed to grammatical function words, which tended to involve the left hemisphere only). Only one of the 25 subjects had frontal lobe involvement confined to the left hemisphere only. This was

subject 21, who had a deficit on the HLLST Synonyms subtest, but not the HLLST Antonyms subtest. (See Table 48, Table 49, Table 51 and Table 52.) One subject is not sufficient for drawing general conclusions about the role of an area of the brain, e.g., in this case, the left frontal lobe. Thus the data set did not allow us to rule out the possibility that the left as well as the right frontal lobe may be important to these tasks.

HLLST Antonyms and Synonyms both involve comprehension of a stimulus word presented orally by the examiner, memory search for another word, meaningfully related to the stimulus, (in a form defined at the outset) then completed with the articulation of that word (see Table A.20.). However this description is equally accurate for at least three other tasks, which were not found to be related to lesions, (the HLLST subtests of Differences, Homonyms and Analogies), implying that the critical requirement of the first two testing tasks is more subtle. The lesion-associated process involved in generation of antonyms and synonyms, is therefore possibly the explicit content of those tests (retrieval of antonyms and synonyms). There may not be a common subtle process at all, but rather two more specific ones, which both involve the right frontal lobe. The other three subtests presumably involve different brain areas, despite their superficially similar task requirements.

This provides the basis for speculation about correspondence between neural processes and cognitive processing. Generation of synonyms or antonyms conceivably involves five micro-stages. First there is recognition of the stimulus word [1]. Then there is retrieval of word meaning, which may not be a purely verbal process (e.g. images from other modalities could be involved) [2]. As the examiner is requiring a verbal response, the subject is required to represent this meaning in words, so he/she will need to generate a verbal description of that meaning [3]. A further stage of micro-processing is the selection from this newly generated pool of verbal material, the word(s) that satisfy the definition of 'antonym' or 'synonym' [4]. To complete the task, the subject then needs to communicate his/her answer to the examiner by verbal articulation [5]. From an intuitive point of view, micro-stages [2] and [3] seem to manifest a more 'excitatory' process, while micro-stage [4] seems to involve a more 'inhibitory' one. Houk (1995) has explained how the cortical areas such as the right frontal lobe, play an excitatory role in the circuitry described by Alexander et al. (1986). Thus it could

be suggested that the cortical areas associated with these tasks (the right frontal lobe and the cortical sections of the specific circuits involved with either antonyms or synonyms) involve word-meaning retrieval and verbal representation of that meaning.

Saint-Cyr et al. (1992), have provided another example of how researchers have drawn intuitive parallels between neuro-anatomy and subjective experience, in an effort to expand our knowledge. They were attempting to describe the different roles of the cortex and the striatum in completing motor tasks. They argued that the cortex played a greater role in conscious processing and the striatum was involved with unconscious, routinized processing because the cortex was a more complex neural structure than the striatum. This argument has an intuitive appeal, and it seems to increase our understanding. However their intuitive leap is no more than that.

As has often been pointed out, most if not all brain structures have multiple connections to other structures. Functions apparently associated with structure X in one study may be apparently associated with a connected structure (Y) in another. The basis for this speculation is tenuous (intuition), and the possibility that the actual role played by these neural structures is much more obscure and subtle cannot be ruled out. Speculation about parallels raises other questions. For example, does the overall intensity of excitation have to equal the overall intensity of inhibition for effective processing? Structures connected within a circuit clearly vary in size and in their connections with other, noncircuit structures. For example the lack of cognitive impairment following removal of the globus pallidus (Scott et al. 1998), compared to the significant impairments following frontal lobotomy (Walsh, 1987) suggest some structures, especially the larger, more complex ones, are more important to the overall operation of a circuit. These uncertainties underline the need for caution when attempting to interpret any association between test scores and the inhibitory/excitatory function of intact or impaired structures. Nonetheless, limited as the basis for this conjecture is (about parallels between neural processing and cognition), generation of a new idea that is consistent with the limited evidence is a starting point for further research. Kapur's (1996) review of evidence and explanations for 'paradoxical functional facilitation', resulting from brain injury, suggests

exploration of the interplay of excitatory and inhibitory processes may considerably advance our understanding of brain behaviour relationships.

7.2. Toward a New Theory of the Function of the Basal-Cortical Circuits

7.2.1. Brain-Cognition Relationships, Reconsideration of some Basic Assumptions

Why do different subjects performing identical tasks show different patterns of activation on PET scans, or why can different subjects with identical brain lesions show quite different patterns of impairment?

This phenomenon has been well known for some time. Caramazza and Badexker (1991) and McCloskey (1993) have pointed out there is always some variation between individuals. Caplan (1994) has drawn attention to it in the context of language functions, and Stuss, Eskes and Foster (1994) in relation to frontal lobe functions. This is also a feature of results from this project.

For each of the measures in Table 55, conclusions were drawn about the critical brain lesions. However, for all of the measures, there were subjects with the deficit where the lesion was not detected. For example, it was concluded that lesions of the globus pallidus or caudate nucleus in either hemisphere were associated with impaired performance of the WAIS-R Digit Symbol subtest (see Section 6.6.1.1.2.). However, Table 25 shows that four of the 14 subjects with a deficit on that task did not show either lesion. While non-detection of lesions among those four subjects cannot be ruled out, there is another possibility. These subjects may have had this processing mediated by other structures.

This variation between individuals opens up an important possibility. This is that at some point in processing, people are choosing different mental approaches to a task. People with more sophisticated visuo-analytic skills who have trained for a career in graphic design might tend to prefer the visuo-spatial modality for problem solving, for example. It is well known that people

can read either phonetically or by a whole-word approach. This possible explanation appears little recognized by other researchers.

There is often more than one set of mental processing that could allow completion of a task. In much the same way that two people of very different physique will approach the task of moving house very differently. Someone who is stronger will not feel the need to pack items in smaller containers. They can physically cope with larger ones. They could combine items from the one room together as a unit, or all similar items (e.g., all chairs, all cushions, etc) as sets of items. A person's preferred style would be determined by a combination of their abilities, and what methods they had been taught by others, or learnt from their own experience, that seemed to work best. It does not seem odd that two people could approach, and very effectively complete, the same task in quite different ways. Inconsistency across subjects may simply reflect different mental processing pre-dispositions. However, researchers have interpreted different people apparently using different brain areas to perform the same tasks as a failure of methodology. There is this notion that the brain must be like other bodily systems, e.g., the digestive system, where each and every part has a very fixed role in the overall system. If our investigative methods tell us not all people use the same parts of their brains when performing the same activities, then these methods are seen to be just not detecting all the brain activity that is going on.

The brain-plasticity phenomenon also lends support to the notion of active choices being made between options. Plasticity is defined as the brain's capacity to modify its structure as a reaction to learning and to brain damage. For example, some children with extraordinarily large brain cavities due to hydrocephalus have been observed to acquire skills thought impossible (Lebeer, 1998). In fact, there is even a significant literature describing subjects in whom brain damage led to clear skill improvements, summarized by Kapur (1996). For example, Miller et al. (1998) described five patients in whom the onset of dementia led to the development of new artistic skills. There is also the phenomenon of so-called *idiots savants* (Treffert, 1988). A variety of mechanisms have been proposed to account for these phenomena. They include, (1) intensive training in compensatory mental strategies; (2) unmasking of 'silent synapses' or latent anatomical connections, perhaps due to disinhibition; (3) reduced

interference/competition between cortical-sensory areas; (4) synaptic supersensitivity; or (5) new connections being formed by way of anatomical sprouting. After reviewing evidence and explanations, Kapur (1996) raised the possibility that they could be mediated by other 'superordinate' changes. It is argued by this author that the latter is the neural analogue of executive processing.

Cowan's (1988) model of memory functions described in the Introduction included a 'Central Executive that directs attention and controls voluntary processing'. Nielson et al.'s (1997) model of motor function included a stage called 'response planning'. Conceptually, these parallel executive functions could be involved in choosing between alternative processing options in their respective modalities. In fact each might be no more than a separate facet of the same executive process. Another issue is whether such a decision-making function is centralized in a certain brain region and actively decides, separately, for each and every mental processing event, how the person's mental processing will proceed. Some general theories of intelligence have conceptualized such a single, overarching process. For example an influential model from Campione and Brown (1979) included an elaborate executive system.

One subsystem of executive functions, according to Campione and Brown, was metacognition. This term refers to thought about thoughts or awareness of one's own thought processes and strategies of thought. Metacognition helps to inform and regulate cognitive routines and strategies. The integration of metacognitive knowledge with strategic behaviours results in more effective problem solving. Metacognition aids in inventiveness, planning, and self monitoring, and may lead to strategy selection, self criticism, and generation of new strategies.

Examples of metacognition include knowing that a strategy that has worked for one task might need to be slightly modified for a new task, knowing that some strategies will work for a variety of different tasks, knowing how to retrieve information from memory, and knowing how to deal with puzzlement when one encounters a logical dilemma. Puzzlement is an experiential aspect of metacognition and may be "both a source of new metacognitive knowledge and a cue for utilizing stored knowledge about appropriate strategies to confront the problem at hand" (Borkowski, 1985, p. 135)."

These concepts of metacognition and executive function seem well accepted in the context of information processing models. Shallice et al. (1989) have contributed what is probably the most effective modeling of executive functions. (See Figure 8, section 2.8.1.2.2.1. 'Modeling of Executive Functions'.) Clearly this kind of process could result in different individuals engaging in quite different cognition during completion of the same task. However, the evidence cannot be denied, of consistent use of brain areas during completion of particular tasks across individuals. For instance the long recognized and relatively consistent role of Wernicke's or Broca's areas in language processing (Benson, 1993). This suggests some kind of hard limits on this flexibility, and these could take a different form for different mental processes. It is proposed that for specific functions, the brain is able to exercise a limited but significant, flexibility in deployment of neural circuitry. A challenge for future research is identify the 'pool' of circuits available for deployment by the brain's executive areas for mental operation A, as distinct from those available to perform mental operation B.

Therefore, it is proposed the brain possesses at least some limited **flexibility** in allocation of neurological structures to mental processing. Another source of evidence for this proposition comes from research into the effects of removal of the globus pallidus (Scott et al. 1998). This procedure has not been found to result in significant cognitive deficits, despite an important PET study of PD subjects (Owen et al. 1998) and a detailed review of anterograde tract-tracing studies in primates (Parent & Hazrati, 1995a) reporting that this structure is a vital link for all the basal-cortical circuits. Parent and Hazrati argued that the globus pallidus influences neural activity in connected cortical areas through an inhibitory process, which 'sets the excitability' of those cortical areas. So, even though intact individuals probably employ this structure for important mental processing, if it isn't there, they manage to find other neurological structures to perform the same job. Another example has been provided by Weiller, Chollet, Friston, Wise and Frackowiak (1992) who assessed patients with left sided subcortical striatocapsular infarcts. They gave their patients a simple motor task to perform with their recovered right hand. Compared with control subjects, these subjects showed increased blood flow in both insulae, in the inferior parietal, prefrontal and anterior cingulate cortices, in the ipsilateral premotor cortex and basal ganglia, and in the contralateral cerebellum.

This brings us to the point where we need to consider a new theory of brain function. One which allows for flexibility and consistency. The limits on flexibility is an important research question, which seems to have received little systematic research attention so far. It is conceivable that some forms of mental processing (e.g., those identified earliest, like language and Wernicke's and Broca's areas) are less flexible than others. For instance those associated with a more diverse set of brain areas (e.g., memory) may be the types of mental processing where greater flexibility of brain structure mediation is possible.

7.2.2. A Possible New Theory

As research methodology improves and data accumulates, information processing models should eventually correspond exactly to the neuro-anatomical systems for mental activity. All mental activity ultimately involves, and is only made possible by, neuronal activity, after all. Afferent and efferent neurological connections between brain structures, and the variable density of those connections, suggest how such a set of structures may operate together in a unified network. Afferent/efferent status sets the direction of information transmission, and the density of connection determines the potential strength and volume of that transmission. These features of neural circuitry correspond fairly directly to elements of classical information processing models. However, neural circuitry includes other features as well such as excitatory and inhibitory functions. These are less familiar to information processing theorists (Parent & Hazrati, 1995a, Kapur, 1996). PET has revealed consistent activation of particular sets of brain structures during well-defined activities. Therefore it is feasible that as our knowledge of these networks improves and our information processing models become more refined, description of the network and the models will converge, and we will have arrived at a 'true' model of a particular cognitive process. In fact, neural-network modeling (Parks et al. 1991) is an established method, based on this idea, for exploring models of cognitive processing and brain-behaviour relationships. If functions of basal-cortical circuits do not neatly coincide with sections of established information processing models, then this points the direction for model revision.

The whole cortex projects to the striatum, and the striatum in turn projects to the smaller-still pallidum. An important PET study of PD subjects (Owen et al. 1998) and a detailed review of

antereograde tract-tracing studies in primates (Parent & Hazrati, 1995a), both concluded that the pallidum, sometimes referred to as the globus pallidus, was a particularly vital link for all the basal-cortical circuits. The section of the globus pallidus providing the connecting link was different for different circuits. Parent and Hazrati argued that the globus pallidus influences neural activity in connected cortical areas by means of an inhibitory process, which 'sets the excitability' of those cortical areas.

This set of serial projections (cortex to striatum, which projects to the pallidum, which in turn projects on to the thalamus, which finally projects back to the cortex) has led some writers (e.g., Percheron & Filion, 1990; Gerfen, 1992) to argue that the basal ganglia process information in a serial fashion, resulting in a massive convergence of information at the site of the basal ganglia (Graybiel, 1991). However this view has its critics. Alexander and colleagues (Alexander DeLong & Strick, 1986; Alexander Crutcher & DeLong, 1990; Alexander & Crutcher, 1990) have argued the primary form of neural processing within the basal ganglia occurs within five identifiable, parallel circuits, three of which have been a focus of this project (dorsolateral prefrontal circuit, lateral orbitofrontal circuit and the anterior cingulate circuit). The other two making up the complete set of five are the motor circuit and the oculomotor circuit, (Cummings, 1993). Other important basal-cortcial circuits have been proposed, including the language-related circuitry outlined by Crosson (1992). The debate is not yet concluded, however. Joel and Weiner (1994) have proposed a qualification to the parallel view: They consider the various circuits to be "interconnected". For example, despite assertions of the pallidum's importance to basal ganglia regulation of cortical cognition (Owen et al. 1998; Parent & Hazrati, 1995a), surgical removal of this structure does not result in major cognitive deficits (Scott et al. 1998). This suggests that critical information can be relayed by other links, and would suggest some degree of interconnectedness.

To review the outcome of this examination and discussion of results so far. Three types of processing have been associated with lesions of the basal-cortical circuitry by this project.

- The ability to manipulate several items of information at once to complete a task, when those items were novel, available to awareness from working memory only and not represented in concrete form.

- Verbal expression of an abstract idea.
- Dynamic allocation of attention between competing inputs.

The first two types of processing were associated with the dorsolateral prefrontal circuit, and the third with the anterior cinglate circuit.

The mental manipulation of several items of information to successfully complete a task is analogous to a large subset of the executive function processes described in Norman and Shallice's model of executive functions, for example, if not the complete set of them. The other type of processing associated with the dorsolateral prefrontal circuit was verbal expression of an abstract idea. Formulation of expression and abstraction, together suggest this function can be viewed as the culmination of a set of prior processes, possibly in sequence. For example, they could include effective comprehension and interpretation of certain life experiences (possibly including verbal communication from others) and analysis of this experience leading to conclusions. These conclusions would have to be represented verbally, prior to articulation. The successful culmination of various prior processes implies two things. One is the likelihood that various brain structures, including some more substantial, more complex ones are involved (e.g., the cortex). The second is that there is some kind of orchestration, or synchronization of the sub-processes to ensure an effective outcome, namely the coherent and incisive expression of an abstract idea.

The third type of processing (dynamic allocation of attention between competing inputs) is analogous to a subprocess in Normal and Shallice's model of executive functions, labelled as 'the supervisory attentional system'. Thus, dynamic allocation of attention could be one within the full set executive processes.

Even though the three mental processes associated with lesions of the basal-cortical circuitry were not linked to the same circuits, they shared something in common. This was the combination of several sub-processes, fluidly and effectively synchronized, necessary for the person to perform more complex tasks. Confinement of processing by any basal-cortical circuit to a single modality, such as visual processing only, seems unlikely. For instance, the tasks most sensitive to basal-cortical lesions all involved varying combinations of visual, verbal,

memory and motor processing (see Tables A.18., A.19., & A.20. in Appendix A.). This was a very clear feature of the results of this project. The tests involved were, the computer-presented tracking task, Part B of the Trail Making Test and the WAIS-R Digit Symbol subtest.

It is proposed that the basal-cortical circuits provide a point of integration for separate processing systems. For instance, in relation to the WCST-R, Perseverative Responses Index, several mental operations need to be integrated. There is the memory for the administrator's feedback on a series of previous card sorts, reference to them to deduce the sorting principle, and then guessing the most likely correct card sort for the next trial. Thus while the results of this project suggest the dorslateral prefrontal circuit is important to executive functions, the anterior cingulate circuit performs a closely related complementary function.

The particular pattern of neural involvement (as seen for instance in the activation displayed by PET) employed by a person to complete mental processing task X, could be potentially idiosyncratic to some degree, and reflect a set of individual propensities (e.g. genetic makeup), and past reinforcement (in the form of efficient task completion) of particular patterns of neural activity. It is conceivable that this could be the way particular patterns of thinking become established as that individual's 'personal style'. For example, there is the well established enhancement of texture identification, (Walker & Moylan, 1994) olfaction (Smith, Doty, Burlingame & MsKeown, 1993) odour identification (Murphy & McCaine, 1986) and auditory function (Muchnik, Efrati, Nemeth, Malin & Hildeshiemer, 1991) among blind subjects.

It is further proposed that there is a differentiation between two key cognitive processes. The first is the **orchestration** of sub-processes to complete a more complex mental processing event. This includes choosing between an array of neural-processing options according to circumstances. This would correspond to a more complex type of processing linked to the frontal lobes under the heading of 'executive functions' by past research, although identification of the brain areas involved in executive functions is not yet conclusive. For example, the limitations on the evidence for this widely accepted proposition have been highlighted by some careful reviewers of the literature (e.g., Tranel, Anderson & Benton, 1994).

Craik et al. (1998) drew attention to several related concepts, which all show some resemblance to the one advanced here, orchestration. Concepts involved were "attentional resources" (e.g., Craik & Byrd, 1982), "self-initiated processing" (Craik, 1983) and "strategic conscious control" (Jacoby, 1991; Hasher & Zacks (1979) and Moscowvitch & Umilta, 1990). Craik et al.'s discussion of possible underlying common elements in these concepts suggests a fruitful direction for further research into this important mental function. For example, could lesions result in loss of control of specialized cognitive functions, rather than a reduction in the resources needed to fuel cognitive operations? Such loss of control could mean that the cognitive system will not adapt sensitively to changing conditions but must fall back on undifferentiated routine procedures of a more automatic type. This argument has been developed by various researchers (e.g. Jacoby, 1991; Jennings & Jacoby, 1993; Moscowvith & Umilta, 1990).

The second of these two processes is the **integration** of outputs from these subprocesses. This includes the transmission of the orchestration to various subsystems and feedback from its implementation, back to the 'conduction centre'. It is proposed that the second process (integration) is primarily mediated by the subcortical sections of the basal-cortical circuitry.

At least four well-accepted models of information processing (attention, language, memory and executive function) include a stage that involves integration of input from more than one (sometimes considerably more than one) source. Posner's model of attention (see Table 3 in the introduction) includes a stage he labels 'II Selective Attention, A, Preconscious', which is involved in the 'parallel processing of multiple-input codes and simultaneous pathway activation.' Crosson (1992) describes four parallel processes which need to occur simultaneously as an individual engages in linguistic communication: semantic monitoring, release of formulated language, phonological monitoring and release of motor programmes. He even goes further to link each process to a different chain of subcortical and cortical structures, very similar but not identical to Alexander et al.'s (1986) basal-cortical circuits. Cowan's (1988) model of memory functions includes the idea of a person attending to multiple stimuli that are selectively dealt with to before being stored. Norman and Shallice's model of

executive function (Shallice et al., 1989) included a section labeled 'special-purpose cognitive subsystems' which collaborate to produce a single action. These subsystems presumably involve processes like memory, motor functions or verbal expression. The modularity concept, central to much theorizing in contemporary neuropsychology (Shallice, 1988), involves cognitive processes being organized into distinct processing units, or modules, analogous to subsystems. Then the output from these modules is combined in the service of more complex cognitive operations.

Ballard et al. (1995) have contributed some very detailed speculation about how the basal ganglia might integrate specific working memory into a more comprehensive, orchestrated mental processing event. They propose that the basal ganglia are the 'keeper of the context' for visual memory recall. 'Context' is conceivably the complete set of mental processing orchestrated by the executive processes to complete the task that includes some working memory processing. Furthermore, such a context determines how identical retinoptic images are processed, through the use and loading of short term visual memory. This kind of close integral association between working memory and executive functions has previously been argued by Fuster (1989).

In this discussion of the results and their implications, we have developed two critical concepts to describe the role played by the basal-cortical circuitry. They are the orchestration of sub-processes, and the integration of the outputs from these, as needed to complete a more complex mental processing event. These processes are not confined to any of the areas covered by those information processing models. Although each separate model includes a process analogous to these, it is argued that it is the same, single process occurring in all these areas. Modalities where such processes have been identified, within this project, include visual, verbal and motor. Norman and Shallice's model is perhaps the most comprehensive, in its coverage of diverse forms of mental processing, and is therefore perhaps the best available theoretical framework for explaining the role of the basal-cortical circuitry (see Figure 8, in section 2.8.1.2.2.1. Models of Executive Functioning'). Those authors included six main elements in their model. It is argued that the orchestration process identified here is analogous to the element labeled the 'supervisory attentional system'. Within their model, that element sends

input to another element labeled 'special purpose cognitive subsystems'. It is argued that this input corresponds to orchestration. The single arrow pointing to that next element, relayed on further to 'trigger data base', represents the overall balance of inhibition and excitation within the complete configuration of cortex/striatum/palidum/thalamus.

While the brains of intact individuals may tend to involve certain subcortical structures for certain types of cognition (as shown by PET scanning), some authors, (Caramazza & Badexker, 1991; McCloskey, 1993), have reported some variation in the brain structures employed between individuals. Furthermore, Crosson (1992) and Scott et al. (1998) have reported a lack of cognitive impairments following circumscribed lesions of those same basal ganglia structures. This suggests another level of brain organization possesses the capacity to choose between alternative basal-cortical circuitry. The basis for such choices might include past effective use of particular structures for similar mental activities, or idiosyncratic variations in neurophysiology, resulting in certain circuits being more effective for specific operations than others.

We have argued for the possibility that brain areas are not rigidly, uniformly specialized for functional purposes (see section 7.2.1. "Brain-Cognition Relationships, Reconsideration of some basic assumptions"); that there is some flexibility, limited perhaps, but there nonetheless. Thus, a variety of sub areas of the brain could be available, for a given mental processing event. Perhaps future role definitions of functional roles of particular brain areas would be more like 'pool of connections between complex analytic module A and limited, secondary, module B.' Possible dimensions of such complexity could be number of modalities involved, number of processing stages, amount of information elements manipulated within a single processing stage. Possible relationships between neurophysiological parameters of specific structures (e.g., types of neurons) and dimensions of mental processing during activation could be explored. Each would be networked by neural connection, to other modules.

Much more probably needs to be learnt about mental processing (including cognition and language) and neurophysiology before there can be a conclusive convergence of these two areas of knowledge. Clear shortcomings in our research methodology must be recognized.

These involve psychometric instruments (imperfect reliability and diverse cognitive processing demands within individual tests), and inaccuracies of neuroimaging. Then there is our current conceptualization of mental processing. Design of our present crop of psychometric instruments has been based on this. However, correspondence between contemporary theories of mental processing and brain activity is hazy at best. The former is purely a manifestation of the latter after all. Thus this conceptualization must contain some errors and distortions. It is probably these combined limitations which prevent us achieving a more detailed knowledge of the functions of these circuits at the present time.

7.3. Weaknesses of the Present Study

The study was not without its weaknesses. Every effort has been made to deal with these throughout the study, but the study certainly would have been more conclusive without them.

Assessment instruments have developed considerably since the study was planned. Some areas identified in more recent literature were not included either, for example visual neglect.

Subjects available were relatively few, and tended to have multiple lesions, some outside the areas of interest. More subjects, with more discrete lesions, would have allowed an analysis that was more conclusive, and more powerful.

Among the subjects with verified brain lesions, there was very unequal representation of subjects with discreet lesions at each of the brain levels involved in the circuits, that is, cortical, striatal, pallidal and thalamic. This made it more difficult to identify possible contributions of circuit components versus the circuit as a whole.

Subjects with Parkinson's Disease (PD) were used as a second experimental group. However, the demographic profile of this group, in terms of age and general intelligence was significantly different from that of the subjects with closed-head injuries. To a lesser

Furthermore, the normative data used to compare the PD subjects' performance came from a samples that varied considerably in terms of size and representativeness of the general population.

The quality of the neuroimaging available was variable, resulting in less-than-ideal precision in lesion identification. Furthermore, the ideal method of neurological investigation would have involved complementary PET analysis. This was not available. These shortcomings are examined in some detail in section 5.5 'Lesion Verification'. A heavy reliance was placed on the clinical judgement of the two medical experts who rated the scans. This falls short of the ideal level of experimental rigor in such investigation, and many researchers regard more precise methods as a basic requirement in neuropsychological research. It would be quite precarious to argue that, in this project, possible misclassification of lesion involvement has been conclusively ruled out for all subjects.

7.4. Implications for Further Research

There is still a substantial lack of clarity in our knowledge about the role of the basal-cortical circuitry, and the basal ganglia specifically. One of the main limitations on this kind of research is the low numbers of subjects available with relevant lesions. Furthermore those that are available tend to have a range of additional lesions/pathology, which create difficulties for result interpretation. Lesion studies, like this project can add considerable new knowledge. More so if the findings can be replicated in the future by other researchers. However, the subtractive control PET technique of Petersen et al. (1989) with intact individuals is a major advance in our research technology. This creates a different set of disadvantages to overcome, not least being expense. There are also the general difficulties with the PET technology, described earlier (see Introduction section 1.1.2 'Positron Emission Tomography (PET) Studies'). One is defining and establishing a 'resting state'. Perhaps biofeedback technology could be applied to this issue, e.g. cultivation of alpha rythyms, galvanic skin response, or just heart rate. This author is not aware of any research investigating correlation between those indices and PET imaging. Examining effects on PET scans of extraneous variables, frequently present during these examinations, would greatly assist the elimination of 'noise' from research

results. The significant effect on PET scans of very minor variations in task requirements has been known for some time (e.g., Wise et al. 1991, Fiez et al. 1996). Things worth investigating for possible effects on PET scanning could include a wide range, e.g., alpha rythyms, blood pressure, level of arousal, mental focus, self control, comfort with examination setting, relationship with research staff, understanding of the procedure, age, IQ, personality variables, other health factors etc. Any of these might even be found to account for some of the subject-variability which has long confounded data interpretation!

Kapur's (1996) review of evidence and explanations for 'paradoxical functional facilitation', resulting from brain injury, suggests exploration of the interplay of excitatory and inhibitory processes may considerably advance our understanding of brain behaviour relationships. However, firing of both excitatory and inhibitory neurons may increase cerebral blood flow, hence show up as activated areas on PET scans (Kapur, 1996), so it will probably require a future generation of imaging technology to pursue this line of research.

During PET examinations, task mediation is routinely attributed to activated areas only. What then of non-activated areas, particularly when they show a very strong neuro-anatomical connections to the activated areas? Furthermore, lesions in the non-activated, but connected areas may even be associated with impaired task performance, as was found in this and previous studies using the word-fluency task (see section '6.2.1.1.3 Conclusions as to Brain Areas involved in the HLLST Association Naming Task'). Arguably the non-activated areas may therefore be involved in some task-mediation which is not detected with PET. Given the considerable, current popularity of PET as a preferred neuropsychological research tool, excluding brain areas from those potentially involved on the basis of nonactivation on PET could result in an extensive new body of misinformation about neuropsychological processes. This could have important implications for neuropsychological research in general. It suggests that conclusions about brain areas and task-mediation should not be made on the basis of PET findings alone.

A new line of research, which seems to show promise for reducing this lack of clarity, involves four stages. Firstly we would need to develop assessment tasks which were as 'pure' as

possible. A number of dimensions of word variability have been established, which affect how they are processed, e.g., 'imagability,' concreteness and abstraction (Toglia & Battig, 1978; Battig & Montague, 1969; Paivio, Yuille & Madigan, 1968). These dimensions need to be controlled.

Then, as the second stage, a task protocol, based on this task needs to be developed for a PET study of a group of intact subjects. For instance, during PET studies, a control task is given first to establish the activation associated with the irrelevant elements of a task, for comparison with the actual task to identify activation associated with the critical elements alone. More than one critical element could entail more than one experimental version of the task. (This closely resembles the refinement of PET methodology developed by Petersen et al. 1989.) A frequent problem with the PET methodology and language studies is the production, by even relatively simple verbal tasks, of generalized, nonspecific activation of large areas of the brain (e.g., the whole brain or one hemisphere) (Pulvermuller, 1996). Defining tasks that result in more specific activation, hence some localization of brain functions, involves a trial and error process of development. The aim of this second stage would be to arrive at PET definition of areas of brain activation associated with critical verbal functions. Data generated by this stage would include the mean scores and standard deviation of a group of intact subjects on this more 'pure' measure of a critical language function. This second stage would provide the information needed for the next one.

The third part of this line of research involves assembling a group of subjects with relatively circumscribed lesions of the areas, identified by the PET study, as tending to be activated during performance of this critical language task. The PET findings would suggest that performance of subjects in this lesion-group would be significantly impaired on this task. This hypothesis could be tested by comparing their performance on this task(s) with the performance of the intact subjects. This third stage could enable us to combine the methodologies of lesion studies and PET, and thereby minimize the limitations of both. So far, no studies like this seem to have been published.

If some (or all) of this lesion group do not show the predicted poor performance, this suggests a further PET study (the fourth stage). Areas of activation among these subjects could suggest which connected structures are also important to performance of this task. Another issue would be the variability of activated areas among these subjects. Could some degree of idiosyncratic neural processing be possible? If it can occur, what are the limits on it? Furthermore, data would need to be closely scrutinized to see if they suggest any explanation for discrepancies between the PET and lesion studies. So far, researchers tend to treat this as a product of methodological shortcomings, e.g., inaccuracy of neuro-imaging (PET, MRI, CT etc) compounding imperfect reliability, and diverse processing requirements of psychometric instruments. Could it reflect some real differences in the functioning of intact and damaged brains? This could even suggest a further line of research into brain plasticity (and other function-recovery processes) among the lesion subjects, which might account for their unimpaired test performance. For example, further PET studies of the lesion subjects. What structures do they use now that the previous ones are damaged? Although not yet fully understood, some reports suggest the capacity of some brains for neural plasticity is extensive. For example, as already noted, some children with large brain cavities have been observed to acquire skills thought impossible (Lebeer, 1998). See section 7.2.1. Further fine-grained exploration of these issues could involve neurospychological surveying and PET studies of subjects with lesions in different points within a circuit. For example, the types of issues that could then be examined might include, effects of release of inhibition, or reduction in stimulation on overall function associated with a circuit. Subjects suitable for these kinds of studies might occasionally present at a large, centralized neuro-diagnostic facility, serving a large population. The small number who might be located in this way are very unlikely to be sufficiently homogeneous for a group study.

Plasticity itself could have major implications for neuropsychological processing. For instance, if more than one structure could potentially mediate a particular cognitive process, do all neurologically intact people tend to have the same first preference for a structure? Do they consistently use the same one for a particular function even, or does it vary from occasion to occasion? Could selection of the structure be a role for 'executive processing' for instance, or could simple learning play a part? For example in the case of the latter, reinforcement (e.g.

successful task completion) might make a subject more likely to use the same instrumental processing next time they needed to achieve the same end. Exploring the frequency and variety of PET activation within individuals on separate occasions (e.g., morning versus evening, distraction versus non-distraction etc.) could reveal new information about flexibility of brain processing. So too could comparing groups with known variations in skills and abilities. For example people with Verbal IQs significantly higher than Performance IQs and vice versa, and skilled 'visual processors' (e.g., Graphic Designers or Architects) versus skilled word smiths (e.g., journalists).

Could a little-recognized dimension of human variability, level of neural flexibility in information processing, predict other important human parameters, like creativity, effectiveness of problem solving or even capacity for skill recovery after brain injury? A first challenge to such a line of research would be devising a measure of flexibility-level.

There were some major omissions among the testing tasks used for this project, largely a reflection of the long time interval between commencement and completion. Clearly future research could endeavour to include more of those. Another important, complementary area for future research of this kind is measurement of personality variables that some have argued to be associated with the basal cortical circuits, like obsessive compulsive disorder, and features of the frontal lobe syndrome (apathy, irritability and aggression). For instance, Cummings (1993) proposed that irritability, and disinhibition are markers for involvement of the orbitofrontal circuit, and apathy is a marker for involvement of the anterior cingulate circuit. Furthermore, the dorsolateral prefrontal prefrontal or orbitofrontal –subcortical circuits were candidates for the mediation of depression, while the orbito frontal or anterior cingulate circuits were implicated in the mediation of Obsessive Compulsive Disorder (OCD).

Methodology for investigating executive functions and metacognition also has room for development. A first step would be clear and comprehensive, operational definition of these functions. This would be a prelude to the development of testing tasks, in line with Tranel et al.'s (1994) analysis, quoted above. This doesn't apply only to executive functions. It applies to all candidates for inclusion in a definition of the role of the basal ganglia. (See section 4.

'Project Objectives', Table 15.) The goal of this part of the process should be development of testing tasks that neatly capture elements of, or stages within, information-processing models. Ideally they would include no more than an absolute minimum of extraneous requirements. Finally, to maximize beneficial clinical application of assessments including these tasks, they should emphasize functional relevance. Good examples of assessments attempting to achieve this include: Behavioural Assessment of the Dysexecutive Syndrome (Wilson, Alderman, Burgess, Emslie & Evans, 1996) and The Test of Everyday Attention (Robertson, Ward, Ridgeway & Nimmo-Smith, 1994). These are ambitious goals indeed. It would be these kinds of tasks that should be presented to neurologically intact people undergoing PET scanning.

The more simple such tasks are, arguably the less idiosyncratic variation there would be across people in terms of cognitive processes, hence brain areas, employed during task completion. Thus the lower the variation across people in terms of PET imaging of brain areas involved, the more likely that task is to have captured a basic element of the cognitive process.

APPENDIX A.

Results Tables

List of all Tables in Appendix A

List of all Tables in Appendix A.

Table A.1.

Means and Standard Deviations for the Spinal Injury Control Subjects and Normative Groups

Skill Area	Test of Skill Area	Controls N=11	Normative Sample Means *	t-test of difference
		Mean (SD)	**Mean (SD)**	
Orienting to a verbal stimulus	HLLST Yes/No Questions	3.36 (0.50)	3.60 (0.61) *(Clarke et al, 1998, N=82)*	not significant (ns)
	HLLST Vocabulary	3.64 (0.81)	3.51 (0.67) *(Clarke et al, 1998, N=82)*	n.s.
	HLLST Grammar	2.18 (0.75)	2.34 (0.74) *(Clarke et al, 1998, N=82)*	n.s.
	HLLST B Aud/Vis Comprehension	4.91 (0.54)	4.90 (0.34) *(Clarke et al, 1998, N=82)*	n.s.
Orienting to a visual stimulus	HLLST C Reading Comprehension	3.09 (0.94)	3.61 (0.58) *(Clarke et al, 1998, N=82)*	n.s.
Voluntary movements, motor speed	Trail Making Test, Part A	36.73 (12.76)	37.8 (19.8) *(Ernst et al, 1987, N=114)*	n.s.
	WAIS-R Digit Symbol	7.70 (2.50)	10 (3) *(Wechsler, 1981N=300)*	p<.01
	Computer Tracking Task	55.84 (12.81)	*Not available*	-
	Rey Figure Copy	34.73 (1.42)	33.20 (6.1) *(Spreen & Strauss, 1981, N=26)*	n.s.

Table A.1. (Cont.)

Means and Standard Deviations for the Spinal Injury Control Subjects and Normative Groups

Skill Area	Test of Skill Area	Controls N=11	Normative Sample Means *	t-test of difference
Verbal recall	Paragraph recall, immediate	7.55 (2.34)	9.76 (3.96) *(Wilson et al, 1989, N=118)*	p<.01
	Paragraph recall, delayed	6.36 (2.01)	8.60 (4.06) *(Wilson et al, 1989, N=118)*	p<.01
Verbal Expression	WAIS-R Similarities	9.83 (2.52)	10 (3) *(Wechsler,1981N=300)*	n.s.
	HLLST Antonyms	3.36 (0.92)	3.73 (0.59) *(Clarke et al, 1998, N=82)*	n.s.
	HLLST Synonyms	3.45 (0.82)	3.67 (0.57) *(Clarke et al, 1998, N=82)*	n.s.
	HLLSTGive Defns	6.55 (2.02)	6.98 (1.46) *(Clarke et al, 1998, N=82)*	n.s.
	HLLST Prov a Word	4.91 (0.30)	4.84 (0.43) *(Clarke et al, 1998, N=82)*	n.s.
	HLLST Differences	3.64 (0.67)	3.55 (0.77) *(Clarke et al, 1998, N=82)*	n.s.
	HLLST Categories	2.73 (0.65)	2.87 (0.34) *(Clarke et al, 1998, N=82)*	n.s.

Table A.1. (Cont.)

Means and Standard Deviations for the Spinal Injury Control Subjects and Normative Groups

Skill Area	Test of Skill Area	Controls N=11	Normative Sample Means *	t-test of difference
Verbal Expression	HLLST Sent Formul	4.45 (1.21)	4.67 (0.72) *(Clarke et al, 1998, N=82)*	n.s.
	HLLST Analogies	3.18 (0.87)	3.46 (0.85) *(Clarke et al, 1998, N=82)*	n.s.
	HLLST Homonyms	2.91 (1.58)	3.77 (0.75) *(Clarke et al, 1998, N=82)*	p<.05
	HLLST Absurdities	2.91 (0.30)	2.83 (0.41) *(Clarke et al, 1998, N=82)*	n.s.
	HLLST Assoc Name	31.64 (4.95)	35.17 (6.78) *(Clarke et al, 1998, N=82)*	p<.05
	HLLST Sequencing	1.64 (0.81)	1.71 (0.58) *(Clarke et al, 1998, N=82)*	n.s.
Executive Functions, visual	WCST Conceptualization	83.0 (4.88)	78.76 (14.34) *(Heaton et al, 1993, N=63)*	n.s.
	Porteus Mazes (yrs)	15.8 (1.0)	Not available	-
Selection of targets from competing inputs	Trail Making Test, Part B	83.36 (30.33)	103.2 (66.0) *(Ernst et al, 1987, N=163)*	n.s.
	WCST Persev Errors	1.18 (1.47)	8.29 (7.0) *(Heaton et al, 1993, N=63)*	p<.01**

Table A.1. (Cont.)

Means and Standard Deviations for the Spinal Injury Control Subjects and Normative Groups

Skill Area	Test of Skill Area	Controls N=11	Normative Sample Means *	t-test of difference
Selection of targets from competing inputs	WCST Categories	6.0 (0)	5.62 (1.08) *(Heaton et al, 1993, N=63)*	*no signif test due to zero variance in one group*
Visual Recall	Rey Figure Recall	20.73 (5.57)	19.50 (6.70) *(Spreen & Strauss, 1981, N=26)*	n.s.
	Picture Recognition	9.82 (0.40)	*9.99 (0.99) (Wilson et al, 1989, N=118)*	n.s.

For those tests where performance is affected by age (see section 6.7), only those sections of the normative samples with the same mean age as the control group were used.

*** Significant differences in the direction of the spinal-injury control group being more able, in comparison with the available normative sample mean. Otherwise significant differences indicated where the spinal-injured controls were less able.*

Table A.1. (Cont.)

Means and Standard Deviations for the Spinal Injury Control Subjects and Normative Groups

Other Demographic information

Variable	**Measure**	**Controls N=11**	**Normative Sample Means ****	**t-test of difference**
Age	Age (Yrs) **	31.8 (11.1)		
Pre-morbid IQ	NART-R IQ **	106.3 (8.5)	100 (15)	n.s.
Depression	Beck Deprsn Inv (Affective/cogniti ve subscale)	6.55 (4.03)	15.55 (9.96) -for depressives *(Beck & Steer 1987, N=248)*	p<.009*

**Data for a 'non-depressed' normative group was not available for the Affectve/cognitive subscale of the Beck Depression Inventory. Thus the best available test of the normality of the control group was to verify that they showed a significantly lower score on this scale than a diverse group of depressive subjects.*

Table A.2.: Predicted Deficits and Actual Deficits among Brain-injured Subjects (N=25)

Skill Area	Test of Skill Area	Lesions associated with poor perform.	Proportion of Ss with those lesions showing deficit perform.	Lesion side of all Ss with this deficit
Orienting to a verbal stimulus	HLLST Yes/No Questions	Language Areas *(Caplan, 1994)* (LAs) *	1/7	Left: 2 Right: 0 Both: 1
	HLLST Vocabulary	LAs	3/7	Left: 4 Right: 1 Both:2
	HLLST Grammar	LAs	0/7	Left: 1 Right: 2
	HLLST B Aud/Vis Comprehension	LAs	3/7	Left: 4 Right: 3 Both: 2
Orienting to a visual stimulus	HLLST C Reading Comprehension	LAs	0/7	Left: 3 Right: 1 Both: 1
Voluntary movements, motor speed	Trail Making Test, Part A	Any Brain Injury *(Lezak, 1995)*	7/25	Left: 3 Right: 3 Both: 1
	Trail Making Test, Part B	Any Brain Injury *(Lezak, 1995)*	10/25	Left: 6 Right: 3 Both: 1

* Language Areas as derived from a comprehensive literature review by Caplan, 1994. Within the dominant hemisphere of left-hemisphere dominant people, they included the association cortex in the region of the Sylvian fissure -specifically, the posterior half of the pars triangularis and the pars opecularis of the third frontal convolution (Broca's area), the association cortex in the opercular area of the pre- and post- central gyri, the supramarginal and angular gyri of the parietal lobe, the first temporal gyrus from the supramarginal gyrus to a point lateral to Heschl's gyrus (Wernicke's area), and possibly a portion of the adjacent second temporal gyrus -are responsible for language processing (Caplan, 1994, p 1029). As these areas were not specifically rated when scans were studied by medical personnel for this study, subjects were defined as possibly having lesions in these areas if the three relevant lobes were involved (i.e. left frontal, left temporal and left parietal).

Table A.2. (Cont.)

Predicted Deficits and Actual Deficits among Brain-injured Subjects (N=25)

Skill Area	Test of Skill Area	Lesions associated with poor perform.	Ss with those lesions showing deficit perform.	Lesion side of all Ss with this deficit
Voluntary movements, motor speed (cont.)	WAIS-R Digit Symbol	Any Brain Injury *(Lezak, 1995)*	8/25	Left: 4 Right: 3 Both: 1
	Computer Tracking Task	*Unknown*		Left: 2 Right: 3 Both: 1
	Rey Figure Copy	General Right hemisphere *(Lezak, 1995)*	5/15	Left: 3 Right: 3 Both: 1
Verbal recall	Paragraph recall, immediate	General Left hemisphere lesions *(Lezak, 1995)*	4/13	Left: 3 Right: 0 Both: 1
	Paragraph recall, delayed	as above	5/13	Left: 4 Right: 3 Both: 1
Verbal Expression	WAIS-R Similarities	Left frontal *(Lezak, 1995)*	1/5	Left: 2 Right: 1 Both: 2
	HLLST Antonyms	Language Areas *(Caplan, 1994)* (LAs)	5/7	Left: 4 Right: 4 Both: 4
	HLLST Synonyms	LAs	6/7	Left: 5 Right: 3 Both: 4

Table A.2. (Cont.)

Predicted Deficits and Actual Deficits among Brain-injured Subjects (N=25)

Skill Area	Test of Skill Area	Lesions associated with poor perform.	Ss with those lesions showing deficit perform.	Lesion side of all Ss with this deficit
Verbal Expression	HLLST Give Defns	LAs	2/7	Left: 3 Right: 2 Both: 2
	HLLST Prov a Word	LAs	4/7	Left: 6 Right: 4 Both: 3
	HLLST Differences	LAs	2/7	Left: 5 Right: 0
	HLLST Categories	LAs	2/7	Left: 5 Right: 1 Both: 1
	HLLST Sent Formul	Language Areas *(Caplan, 1994)* (LAs)	4/7	Left: 8 Right: 8 Both: 2
	HLLST Analogies	LAs	3/7	Left: 3 Right: 0 Both: 1
	HLLST Homonyms	LAs	1/7	Left: 2 Right: 1
	HLLST Absurdities	LAs	3/7	Left: 4 Right: 3 Both: 2
	HLLST Assoc Name	Left frontal *(Lezak, 1995)*	2/5	Left: 8 Right: 4 Both: 3
	HLLST Sequencing	LAs	2/7	Left: 4 Right: 3 Both: 2

Table A.2. (Cont.)

Predicted Deficits and Actual Deficits among Brain-injured Subjects (N=25)

Skill Area	Test of Skill Area	Lesions associated with poor performance	Ss with those lesions showing deficit performance	Lesion side of all Ss with this deficit
Executive Functions, visual	WCST Conceptualization	Frontal lesions *(Lezak, 1995)*	1/8	Left: 0 Right: 0 Both: 1
	Porteus Mazes (yrs)	Right frontal lesions *(Lezak, 1995)*	3/8	Left: 3 Right: 4 Both: 2
Selection of targets from competing inputs	WCST Persev Errors	Frontal lesions *(Lezak, 1995)*	3/8	Left: 4 Right: 5 Both: 1
	WCST Categories	Frontal lesions *(Lezak, 1995)*	2/8	Left: 3 Right: 2 Both: 1
Visual Recall	Rey Figure Recall	Right hemisphere *(Lezak, 1995)*	5/15	Left: 5 Right: 4 Both: 1
	Picture Recognition	Right hemisphere *(Lezak, 1995)*	3/13	Left: 2 Right: 3 Both: 1

Table A.3.

Relationship between Deficit Prediction and Interval between Imaging & Testing

For each measure, the subjects showing lesions suggested by previous research to cause deficits on that measure have been identified. These were then divided into two subgroups (i.e. those with predicted deficits on that measure and those without). Average Imaging-Testing intervals for each of the pair of subgroups were calculated. The lesser of the two is shaded grey in the table below. This was to facilitate drawing conclusions about the effect of this interval on detection of deficits.

Skill Area	Test of Skill Area	Imaging-Testing Interval (yrs) Mean (SD)	
		Ss with Predicted Deficits [N]	*Ss without predicted deficits [N]*
Orienting to a verbal stimulus	*HLLST Yes/No Questions*	.01 [1]	2.37 (5.22) [6]
	HLLST Vocabulary	.36 (.43) [3]	3.28 (6.48) [4]
	HLLST Grammar	2.03 (4.85) [7]	-
	HLLST B Aud/Vis Comprehension	.36 (.43) [3]	3.28 (6.48) [4]
Orienting to a visual stimulus	*HLLST C Reading Comprehension*	2.03 (4.85) [7]	-
Voluntary movements, motor speed	*Trail Making Test, Part A*	2.88 (4.87) [7]	3.84 (6.47) [18]
	Trail Making Test, Part B	4.55 (7.71) [10]	2.85 (4.53) [15]
	WAIS-R Digit Symbol	2.79 (4.52) [8]	3.94 (6.67) [17]
	Computer Tracking Task		
	Rey Figure Copy	3.95 (5.53) [5]	3.99 (5.27) [10]

Table A.3. (Cont.)

Relationship between Deficit Prediction and Interval between Imaging & Testing

Skill Area	Test of Skill Area	Imaging-Testing Interval (yrs) Mean (SD)	
		Ss with Predicted Deficits [N]	*Ss without predicted deficits [N]*
Verbal recall	*Paragraph recall, immediate*	3.64 (5.61) [4]	4.47 (8.22) [9]
	Paragraph recall, delayed	7.50 (10.03) [5]	2.16 (4.57) [8]
Verbal Expression	*WAIS-R Similarities*	.04 [1]	9.29 (10.96) [4]
	HLLST Antonyms	.25 (.34) [5]	6.46 (9.24) [2]
	HLLST Synonyms	.20 (.33) [6]	13.00 [1]
	HLLST Give Defns	.12 (.11) [2]	2.79 (5.72) [5]
	HLLST Prov a Word	.27 (.39) [4]	4.37 (7.47) [3]
	HLLST Differences	.39 (.65) [2]	2.68 (5.77) [5]
	HLLST Categories	.10 (.14) [2]	2.80 (5.71) [5]
	HLLST Sent Formul	.05 (.11) [4]	4.67 (7.22) [3]
	HLLST Analogies	.06 (.14) [3]	3.51 (6.34) [4]
	HLLST Homonyms	-.07 [1]	2.39 (5.21) [6]
	HLLST Absurdities	.08 (.11) [3]	3.49 (6.35) [4]
	HLLST Assoc Name	.11 (.09) [2]	12.33 (11.17) [3]
	HLLST Sequencing	.02 (.03) [2]	2.83 (5.69) [5]

Table A.3. (Cont.)

Relationship between Deficit Prediction and Interval between Imaging & Testing

Skill Area	**Test of Skill Area**	**Imaging-Testing Interval (yrs) Mean (SD)**	
		Ss with Predicted Deficits [N]	***Ss without predicted deficits [N]***
Executive Functions, visual	***WCST Conceptualiz-ation***	.85 [1]	4.71 (6.07) [7]
	Porteus Mazes (yrs)	2.59 (4.34) [3]	5.24 (6.74) [5]
Selection of targets from competing inputs	***WCST Persev Errors***	4.05 (7.07) [3]	4.33 (5.78) [5]
	WCST Categories	-.03 (.05) [2]	5.64 (6.09) [6]
Visual Recall	***Rey Figure Recall***	3.94 (5.54) [5]	4.00 (5.26) [10]
	Picture Recognition	7.48 (6.11) [5]	2.58 (4.27) [10]

Table A.4.

Results for Subjects with lesions in the LEFT Dorsolateral Prefrontal Circuit

(Standard Scores shaded are at least 1.65 in the direction of deficit, i.e. -1.65 in most instances.)

Skill Area	Test of Skill Area	Subjects (N=6)						
	Subject ID No.s	***5***	***20***	***36***	***40***	***45***	***48***	***Proportion of Other BD Ss with deficit ****
Language Expression	HLLST Give Definitions	-2.53	-1.47	-2.00	-3.58	-3.05	-.42	**3/19 (16%)**
Performance of Complex Programs of Motor Activity	**Trail Making Test, Part B**	4.99	2.16	2.16	0.18	4.96	1.84	**5/19 (26%)**
Language Comprehension	HLLST Auditory Visual Comprehension	-1.80	-3.80	-1.80	-3.80	-7.80	.20	**5/19 (26%)**
Language Expression	HLLST Antonyms	.56	-1.67	-2.78	-3.89	-2.78	-.56	**5/19 (26%)**
" "	HLLST Absurdities	.33	-6.33	-3.00	-6.33	.33	-3.00	**5/19 (26%)**
" "	HLLST Synonyms	-3.13	.63	-4.38	-4.38	-4.38	-.63	9/19 (47%)
Complex Motor Activity	WAIS-R Digit Symbol	-2.67	-1.33	-2.67	-1.67	-2.33	-1.67	9/19 (47%)
Executive Functions	HLLST Association Naming	-2.30	-1.67	-3.41	-2.78	-4.05	-2.30	9/19 (47%)
Language Expression	HLLST Provide a Word	-6.33	.33	-3.00	-16.33	-13.00	-3.00	9/19 (47%)
" "	HLLST Sentence Formulation	-3.18	-4.09	-2.27	-4.09	-4.09	.45	13/19 (68%)

Explanation of Abbreviations: HLLST (Higher Level Language Screening Test), WAIS-R (Wechsler Adult Intelligence Scale -Revised) BD (Brain Damaged)

These are the other brain-injured subjects with verified lesions that did not include this circuit. Where the proportion of the others was well 50%, it is highlighted in **bold, as this is required for a deficit on this test to be tentatively ascribed to a circuit-lesion.*

Table A.5.

% of Structures Showing Damage among LEFT Dorsolateral Prefrontal Subjects

Brain areas involved in the circuit are shown in **bold**. *Larger brain regions incorporating those involved areas, typically more discernible in brain scans, are shown in italics. Key: ?= unknown, 0 = none, 1 = <20%, 2 = 20-50%, 3 = >50%.*

	Subjects					
Subject ID No.s	***5***	***20***	***36***	***40***	***45***	***48***
Cortex, Left						
Dorsolateral Prefrontal Cortex	0	0	0	?	0	0
General frontal lobes	0	0	0	2	0	0
Striatum, Left						
Dorsolateral head of the Caudate Nucleus	?	0	?	0	?	0
General Caudate Nucleus	3	0	3	0	3	0
Pallidum & Substantia Nigra, Left						
Lateral dorsomedial, internal segment of the Globus Pallidus	0	0	0	0	1	3
General Globus Pallidus	2	0	0	0	1	3
Rostrolateral Substantial Nigra	0	0	?	0	?	?
General Substantia Nigra	0	0	?	0	?	?
Thalamus, Left						
Thalamic Nuclei (ventralis anterior pars parvocellularis & medialis dorsalis pars parvocellularis)	0	?	0	?	0	0
General Thalamus	0	2	0	?	0	0
Brain Areas Involved Other than this circuit						
Left Cortex (other than above)	-	-	+	+	-	-
Left Subcortex (other than above)	+	+	+	-	+	+
Left Lateral Orbital Cirtcuit	+	+	+	+	+	+
Left Anterior Cingulate Circuit	+	+	+	-	+	+
Right Cortex	-	-	-	+	-	-
Right Subcortex	-	-	-	-	-	-
Right Dorsolateral Circuit	-	-	-	-	-	-
Right Lateral Orbital Circuit	-	-	-	+	-	-
Right Anterior Cingulate circuit	-	-	-	-	-	-

Table A.5. (Cont.)

% of Structures Showing Damage among LEFT Dorsolateral Prefrontal Subjects

Other Information

Subject ID No.s	***5***	***20***	***36***	***40***	***45***	***4***
Medical Diagnosis (T=Traumatic Basal Ganglia Hematoma, AVM=Arterio-Venus Malformation, CHI=Closed Head Injury, CVA=Cardio-Vascular Accident)	T	AVM	CVA	CHI	CVA	C
Estimated Premorbid IQ 1. (NART-R*)	90	99	73	83	93	1
Estimated Premorbid IQ 2. (Porteus Mazes, z score) only given if >NART-R IQ (IQ scale)		0.80 (112)		-.70 (90)		
Gender	M	F	M	M	M	I
Age at Diagnosis/Injury (completed years)	24	29	30	19	65	
Years since diagnosis/injury at assessment	1.7	20	0.6	8.0	0.1	
Years since Scanning at assessment	2.2	23	0.2	.04	0.2	.
Scan type (C= CT, M=MRI)	M	C	C	M	C	(
Left sided motor signs	0	0	0	2	2	(
Right sided motor signs	13	11	4	0	15	(

** NART-R (National Adult Reading Test -Revised, see Method section for full description.)*

Table A.6.

Results for Subjects with lesions in the RIGHT Dorsolateral Prefrontal Circuit

(Standard Scores shaded are at least 1.65 in the direction of deficit, i.e. -1.65.)

Skill Area	**Tests of Skill Area**	**Subjects (N=9)**						
	Subject ID No.s	*1*	*3*	*4*	*6*	*13*	*25*	*41*
Executive Functions	WCST Perseverative Errors	.47	-2.37	-5.84	.47	-4.26	-3.84	.47
Performance of Complex programs of motor activity	WAIS-R Digit Symbol	-1.67	.00	-1.33	-1.67	-2.67	-2.33	-2.33
	HLLST Sentence Formulation	-2.27	-2.27	-3.18	-3.18	-4.09	-3.18	-3.18

Explanation of Abbreviations: HLLST (Higher Level Language Screening Test), WAIS-R (Wechsler Adult Intelligence Scale -Revised) WCST (Wisconsin Card Sorting Test - Revised). See Method section for full description of testing tasks.

These are the other brain-injured subjects with verified lesions that did not include this circuit. Where the proportion of the others was well below 50%, it is highlighted in **bold, as this is required for a deficit on this test to be tentatively ascribed to a circuit-lesion.*

Table A.7.

% of Structure Showing Damage among RIGHT Dorsolateral Prefrontal Subjects

Brain areas involved in the circuit are shown in **bold**. *Larger brain regions incorporating those involved areas, typically more discernible in brain scans, are shown in italics.*
Key: ?= unknown, 0 = none, 1 = <20%, 2 = 20-50%, 3 = >50%.

Brain Area	**Subjects**								
Subject ID No.s	**1**	**3**	**4**	**6**	**13**	**25**	**41**	**53**	**56**
Cortex, Right									
Dorsolateral Prefrontal Cortex	0	0	0	0	0	0	3	0	0
General frontal lobes	0	3	0	0	0	1	3	0	0
Striatum, Right									
Dorsolateral head of the Caudate Nucleus	0	0	?	?	0	?	3	1	2
General Caudate Nucleus	3	3	3	3	0	1	3	1	2
Pallidum & Substantia Nigra, Right									
Lateral dorsomedial, internal segment of the Globus Pallidus	0	0	?	0	0	?	3	0	1
General Globus Pallidus	2	0	3	0	0	3	3	0	1
ostrolateral Substantial Nigra	0	0	0	0	0	0	?	?	0
General Substantia Nigra	0	0	0	0	0	0	3	?	0
Thalamus, Right									
Thalamic Nuclei (ventralis ant. pars parvocellularis & medialis dorsalis pars parvocellularis)	0	0	0	0	?	0	3	0	0
General Thalamus	0	0	0	0	2	0	3	0	0

Table A.7. (Cont.)

% of Structure Showing Damage among RIGHT Dorsolateral Prefrontal Subjects

Brain areas involved in the circuit are shown in **bold**. *Larger brain regions incorporating those involved areas, typically more discernible in brain scans, are shown in italics.*

Key: ?= unknown, 0 = none, 1 = <20%, 2 = 20-50%, 3 = >50%.

Brain Area	**Subjects**								
Subject ID No.s	**1**	**3**	**4**	**6**	**13**	**25**	**41**	**53**	**56**
Brain Areas Involved Other than this circuit									
Right Cortex (other than above)	-	-	-	-	-	-	+	+	-
Right Subcortex (other than above)	-	+	+	+	-	+	+	+	+
Right Lateral Orbital Circuit	+	+	+	+	+	+	+	+	+
Right Anterior Cingulate circuit	+	+	+	+	+	+	+	+	+
Left Cortex	-	-	-	-	-	-	-	-	-
Left Subcortex	-	-	+	-	-	+	-	-	-
Left Dorsolateral Circuit	-	-	-	-	-	-	-	-	-
Left Lateral Orbital Cirtcuit	-	-	-	-	-	-	-	-	-
Left Anterior Cingulate Circuit	-	-	-	-	-	-	-	-	-

Table A.7. (Cont.)

% of Structure Showing Damage among RIGHT Dorsolateral Prefrontal Subjects

Other Information

Subject ID No.s	***1***	***3***	***4***	***6***	***13***	***25***	***41***	***53***	***56***
Medical Diagnosis *	T	T	T	T	ABS	T	H	CVA	CVA
Est premorbid IQ 1. (NART-R**)	115	107	112	98	93	94	110	122	103
Est premorbid IQ 2. (Porteus Mazes, z score) *only given if >NART-R IQ (IQ Scale)*				1.3 *120*		.30 *105*			
Gender	M	F	M	M	M	M	M	M	M
Age at Diagnosis/Injury	31	30	35	20	63	18	23	63	51
Years since diag/inj at assessment	4.8	12	12	4.9	1.8	6.6	6.2	0.7	1.7
Years since Scanning at assessment	4.7	12	0	4.9	0.1	0.1	7.6	.01	.04
Scan type ***	M	M	C	M	C	C	C	C	C
Left sided motor signs	3	4	6	2	0	11	15	12	0
Right sided motor signs	0	0	0	0	0	0	2	0	0

** T=Traumatic Basal Ganglia Hematoma, ABS=Brain Absess, H=Closed Head Injury, CVA=Cardiovascular Accident*

***NART-R=National Adult Reading Test -Revised*

**** M=MRI, C=CT*

Table A.8.

Results for Subjects with lesions in the LEFT Anterior Cingulate Circuit (z-cores)

(Standard Scores shaded are at least 1.65 in the direction of deficit, i.e. -1.65,or +1.65 for Trail Making Test only.)

Skill Area linked to Circuit	Test of Skill Area	Subjects (N=7)							
	Subject ID No.s	*5*	*20*	*36*	*45*	*46*	*47*	*48*	*Other BD Ss with deficit **
Complex Programs of Motor Activity	Computer Tracking Task	1.03	-2.04	-1.07	-1.13	-1.81	-2.30	-3.85	**2/18**
	Trail Making Test Part B	4.99	2.16	2.16	4.96	.25	-.58	1.84	**5/18**
Auditory/Visual Comprehension	HLLST Auditory/Visual Comprehension	-1.80	-3.80	-1.80	-7.80	-1.80	.20	.20	**5/18**
Verbal Expression	HLLST Antonyms	.56	-1.67	-2.78	-2.78	-2.78	.56	.56	8/16
	HLLST Synonyms	-3.13	.63	-4.38	-4.38	-3.13	.63	-.63	9/18
	HLLST Prov a Word	-6.33	.33	-3.00	-13.00	-3.00	.33	-3.00	9/18
	HLLST Association Naming	-2.30	-1.67	-3.41	-4.05	-.40	1.67	-2.30	10/18
Complex programs of motor activity	WAIS-R Digit Symbol	-2.67	-1.33	-2.67	-2.33	-.67	.67	-1.67	10/18
	HLLST Sen Formultn	-3.18	-4.09	-2.27	-4.09	-1.36	.45	.45	14/18

Explanation of Abbreviations: HLLST (Higher Level Language Screening Test). See Method section for full description of testing tasks. WAIS-R (Wechsler Adut Intelligence Scale -Revised) and WCST (Wisconsin Card Sorting Test -Revised).

Table A.9.

Percentage of Structure Showing Damage among LEFT Anterior Cingulate Circuit Subjects

Brain areas involved in the circuit are shown in **bold**. *Larger brain regions incorporating those involved areas, typically more discernible in brain scans, are shown in italics.*
Key: ?= unknown, 0 = none, 1 = <20%, 2 = 20-50%, 3 = >50%.

Brain Area	**Subjects (N=7)**						
Subject ID Nos	***5***	***20***	***36***	***45***	***46***	***47***	***48***
Cortex, Left							
Anterior Cingulate Cortex	0	0	0	0	1	1	0
General frontal lobes	0	0	0	0	1	1	0
Striatum, Left							
Ventromedial head of the Caudate Nucleus	?	1	3	3	0	0	0
General Caudate Nucleus	3	1	3	3	0	0	0
Ventral Striatum	0	0	?	?	0	0	0
Globus Pallidus & Substantia Nigra, etc, Left							
Rostrolateral internal segment of the Globus Pallidus	?	1	0	1	0	0	3
General Globus Pallidus	2	1	0	1	0	0	3
Ventral Pallidum	?	?	?	?	?	?	?
Rostrodorsal Substantia Nigra	0	0	?	?	0	0	?
General Substantia Nigra	0	0	?	?	0	0	?]
Thalamus, Left							
Thalamic Nuclei (posteromedial medialis dorsalis)	0	?	0	0	0	0	0
General Thalamus	0	2	0	0	0	0	0

Table A.9. (Cont.)

Percentage of Structure Showing Damage among LEFT Anterior Cingulate Circuit Subjects

Brain areas involved in the circuit are shown in **bold**. *Larger brain regions incorporating those involved areas, typically more discernible in brain scans, are shown in italics.*

Key: ?= unknown, 0 = none, 1 = <20%, 2 = 20-50%, 3 = >50%.

Brain Area	**Subjects (N=7)**						
Subject ID Nos	***5***	***20***	***36***	***45***	***46***	***47***	***48***
Brain Areas involved other than this circuit							
Left Cortex (other than above)	-	-	+	-	-	-	-
L Subcortex (other than above)	+	+	+	+	-	-	+
Left Dorsolateral Circuit	+	+	+	+	-	-	+
Left Lateral Orbital Circuit	+	+	+	+	-	+	+
Right Cortex	-	-	-	-	+	+	-
Right Subcortex	-	-	-	-	+	-	-
Right Dorsolateral Circuit	-	-	-	-	-	-	-
Right Lateral Orbital Circuit	-	-	-	-	-	+	-
Right Anterior Cingulate Circuit	-	-	-	-	+	+	-

Table A.9. (Cont.)

Percentage of Structure Showing Damage among LEFT Anterior Cingulate Circuit Subjects

Other Information

Subject ID Nos	***5***	***20***	***36***	***45***	***46***	***47***	***48***
Medical Diagnosis *	T	AVM	CVA	CVA	H	H	CVA
Est Premorbid IQ 1. (NART-R**)	90	99	73	93	108	121	108
Est Premorbid IQ 2. Porteus Mazes, z score only given if >NART-R IQ IQ Scale		0.8 112			0.8 112		
Gender	M	F	M	M	F	F	F
Age at Diagnosis/Injury	24	29	30	65	21	38	36
Years since diagnosis/	1.8	20.6	0.6	0.1	4.3	11.8	1.1
Years since Scanning at assessment	2.2	23.2	0.2	0.2	0.9	13.0	0.01
Scan type ***	M	C	C	C	M	C	C
Left sided motor signs	0	0	0	2	3	0	0
Right sided motor signs	13	11	4	15	0	0	6

** T=Traumatic Basal Ganglia Hematoma, ABS=Brain Absess, H=Closed Head Injury, CVA=Cardiovascular Accident, AVM=Arterio-Venous Malformation.*

***NART-R=National Adult Reading Test -Revised*

**** M=MRI, C=CT*

Table A.10.

Results for Subjects with lesions in the RIGHT Anterior Cingulate Circuit (z-scores)

(Standard Scores shaded are at least 1.65 in the direction of deficit, i.e. -1.65.)

Skill Area linked to Circuit	Test of Skill Area	Subjects (N=10)										
	Subject ID No.s	*1*	*3*	*4*	*6*	*13*	*25*	*41*	*46*	*47*	*53*	***Proportion of other BD Ss with deficit ****
Complex programs of motor activity	WAIS-R Digit Symbol	-1.67	.00	-1.33	-1.67	-2.67	-2.33	-2.33	-.67	.67	-2.0	8/15
Verbal Expression	HLLST Synonyms	.63	-1.88	.63	-.63	-3.13	-4.38	-4.38	-3.13	.63	.63	8/15
	HLLST Sent Formultn	-2.27	-2.27	-3.18	-3.18	-4.09	-3.18	-3.18	-1.36	.45	.45	11/15

Explanation of Abbreviations: HLLST (Higher Level Language Screening Test). See Method section for full description of testing tasks. WAIS-R (Wechsler Adut Intelligence Scale -Revised)

These are the other brain-injured subjects with verified lesions that did not include this circuit. **None of these proportions were well 50%, which is required for a deficit on this test to be tentatively ascribed to a circuit-lesion.*

Table A.11.

Percentage of Structure Showing Damage among RIGHT Anterior Cingulate Circuit Subjects (z-scores)

Brain areas involved in the circuit are shown in **bold**. *Larger brain regions incorporating those involved areas, typically more discernible in brain scans, are shown in italics.*

Key: ?= unknown, 0 = none, 1 = <20%, 2 = 20-50%, 3 = >50%.

Brain Area	**Subjects (N=10)**									
Subject ID No.s	***1***	***3***	***4***	***6***	***13***	***25***	***41***	***46***	***47***	***53***
Cortex, Right										
Anterior Cingulate Cortex	0	0	0	0	0	0	3	1	2	0
General frontal lobes	0	3	0	0	0	0	3	1	2	0
Striatum, Right										
Ventromedial head of the Caudate Nucleus	?	?	?	?	0	?	3	0	0	2
General Caudate Nucleus	3	3	3	3	0	1	3	0	0	2
Ventral Striatum	0	0	0	0	?	?	3	0	0	?
Globus Pallidus & Substantia Nigra etc, Right										
	1	***3***	***4***	***6***	***13***	***25***	***41***	***46***	***47***	***53***
Rostrolateral internal segment of the Globus Pallidus	?	?	?	?	0	?	3	0	0	1
General Globus Pallidus	2	3	3	2	0	3	3	0	0	1
Ventral Pallidum	?	?	?	?	0	0	3	0	0	?
Rostrodorsal Substantia Nigra	0	0	0	0	0	0	3	0	0	0
General Substantia Nigra	0	0	0	0	0	0	3	0	0	0
Thalamus, Right										
Thalamic Nuclei (posteromedial medialis dorsalis)	0	0	0	0	?	0	3	0	0	0
General Thalamus	0	0	0	0	2	0	3	0	0	0

Table A.11. (Cont.)

Percentage of Structure Showing Damage among RIGHT Anterior Cingulate Circuit Subjects (z-scores)

Brain areas involved in the circuit are shown in **bold**. *Larger brain regions incorporating those involved areas, typically more discernible in brain scans, are shown in italics.*

Key: ?= unknown, 0 = none, 1 = <20%, 2 = 20-50%, 3 = >50%.

Brain Area	**Subjects (N=10)**									
Subject ID No.s	***1***	***3***	***4***	***6***	***13***	***25***	***41***	***46***	***47***	***53***
Noncircuit Brain Areas Involved										
R Cortex (other than above)	-	-	-	-	-	-	+	-	-	+
R Subctx (other than above)	+	+	+	+	-	+	+	-	+	+
R Dorsolateral Circuit	+	+	+	+	+	+	+	-	-	+
R Lateral Orbital Circuit	+	+	+	+	+	-	+	+	-	+
Left Cortex	-	-	-	-	-	-	-	+	+	-
Left Subcortex	-	-	-	-	-	-	-	-	-	-
L Dorsolateral Circuit	-	-	-	-	-	-	-	-	-	-
L Lateral Orbital Circuit	-	-	-	-	-	-	-	-	+	-
L Anterior Cingulate circuit	-	-	-	-	-	-	+	-	+	-

Table A.11. (Cont.)

Percentage of Structure Showing Damage among RIGHT Anterior Circuit Subjects

Other Information

Subject ID Nos.	***1***	***3***	***4***	***6***	***13***	***25***	***41***	***46***	***47***	***53***
Medical Diagnosis *	T	T	T	T	ABS	T	H	H	H	CVA
Est premorbid IQ 1. (NART-R**)	115	107	112	98	93	94	110	121	108	122
Est premorbid IQ 2. Porteus Mazes, z sc only given if >NART-R IQ IQ Scale				1.3 120		0.3 105			0.8 112	
Gender	M	F	M	M	M	M	M	F	F	M
Age at Diagnosis/Injury	31	30	35	20	63	18	23	38	21	63
Years since diagnosis/	4.8	12.3	12.8	4.9	1.8	6.6	6.2	11.8	4.3	0.7
Years since Scanning at assessment	4.7	12.2	0	4.9	0.1	0.1	7.6	13.0	0.9	.01
Scan type ***	M	M	C	M	C	C	C	C	M	C
Left sided motor signs	3	4	6	2	0	11	15	3	0	12
Right sided motor signs	0	0	0	0	0	0	2	0	0	0

** T=Traumatic Basal Ganglia Hematoma, ABS=Brain Abscess, H=Closed Head Injury, CVA=Cardiovascular Accident*
*** NART-R=National Adult Reading Test -Revised*
**** M=MRI, C=CT*

Table A.12.

Results for Subjects with lesions in LEFT Language-Related Circuitry (z-scores)

(Standard Scores shaded are at least 1.65 in the direction of deficit, i.e. -1.65.)

Skill Area linked to Circuit	Test of Skill Area	Subjects (N=10)									
	Subject ID No.s	***5***	***21***	***26***	***31***	***36***	***40***	***45***	***47***	***48***	***Proportion of other BD Ss with deficit ****
Complex programs of motor activity	Trail Making Test, Part B	4.99	.53	7.89	1.11	2.16	.18	4.96	-.58	1.84	**5/16**
Verbal Expression	HLLST Synonyms	-3.13	-4.38	-1.88	-1.88	-4.38	-4.38	-4.38	.63	-.63	**6/16**
	HLLST Antonyms	.56	-.56	-3.89	-1.67	-2.78	-3.89	-2.78	.56	-.56	7/16
	HLLST Assoc Naming	-2.30	-2.30	-3.73	-1.98	-3.41	-2.78	-4.05	1.67	-2.30	7/16
	HLLST Prov a Word	-6.33	.33	-9.67	.33	-3.00	-16.3	-13.00	.33	-3.00	8/16
	HLLST Sent Formultn	-3.18	-4.09	-3.18	-1.36	-2.27	-4.09	-4.09	.45	.45	12/16

Explanation of Abbreviations: HLLST (Higher Level Language Screening Test). See Method section for full description of testing tasks. WAIS-R (Wechsler Adut Intelligence Scale -Revised)

These are the other brain-injured subjects with verified lesions that did not include this circuit. Where the proportion of the others was well below 50%, it is highlighted in **bold, as this is required for a deficit on this test to be tentatively ascribed to a circuit-lesion.*

Table A.13.

Percentage of Structure Showing Damage among Subjects with lesions in LEFT Language-Related Circuitry

Brain areas involved in the circuit are shown in **bold**. *Larger brain regions incorporating those involved areas, typically more discernible in brain scans, are shown in italics.*
Key: ?= unknown, 0 = none, 1 = <20%, 2 = 20-50%, 3 = >50%.

Brain Area	**Subjects (N=10)**								
Subject ID No.s	***5***	***21***	***26***	***31***	***36***	***40***	***45***	***47***	***48***
Cortex, Left									
Anterior Language Area	0	3	0	2	0	2	0	1	0
Posterior Language Area	0	0	2	0	0	3	0	0	0
Striatum, Left									
Head of the Caudate Nucleus	0	0	0	0	3	0	3	0	0
General Caudate Nucleus	3	0	0	0	3	0	3	0	0
Globus Pallidus									
Medial Globus Pallidus	0	0	0	0	0	0	1	0	3
General Globus Pallidus	2	0	0	0	0	0	1	0	3
Thalamus, Left									
Ventral Anterior Thalamus	0	0	0	0	0	?	0	0	0
General Thalamus	0	0	0	0	0	?	0	0	0

Table A.13. (Cont.)

Percentage of Structure Showing Damage among LEFT, Other Language-Related Circuitry Subjects (z-scores)

Brain areas involved in the circuit are shown in **bold**. *Larger brain regions incorporating those involved areas, typically more discernible in brain scans, are shown in italics.*

Key: ?= unknown, 0 = none, 1 = <20%, 2 = 20-50%, 3 = >50%.

Brain Area	**Subjects (N=10)**								
Subject ID No.s	***5***	***21***	***26***	***31***	***36***	***40***	***45***	***47***	***48***
Noncircuit Brain Areas Involved									
L Cortex (other than above)	-	+	-	-	-	+	-	+	+
L Subcortex (other than above)	+	-	-	+	+	-	+	-	+
L Dorsolateral Circuit	+	-	-	-	+	+	+	-	+
L Lateral Orbital Circuit	+	+	-	+	+	+	+	+	+
L Anterior Cingulate Circuit	+	-	-	-	+	-	+	+	+
Right Cortex	-	-	+	+	-	+	-	+	-
Right Subcortex	-	-	-	+	-	+	+	-	+
R Dorsolateral Circuit	-	-	-	-	-	-	-	-	-
R Lateral Orbital Circuit	-	-	-	+	-	+	-	+	-
R Anterior Cingulate circuit	-	-	-	-	-	-	-	+	-

Table A.13. (Cont.)

Background Information for subjects with lesions of other Left Language-Related Circuitry

Other Information

Subject ID Nos.	***5***	***21***	***26***	***31***	***36***	***40***	***45***	***47***	***48***
Medical Diagnosis *	H	Ast	Ast	H	CVA	H	CVA	H	CVA
Est premorbid IQ 1. (NART-R**)	90	106	106	106	73	83	93	121	108
Est premorbid IQ 2. Porteus Mazes, z sc only given if >NART-R IQ IQ Scale						90			
Gender	M	M	M	M	M	M	M	F	F
Age at Diagnosis/Injury	23	53	20	16	30	12	58	26	36
Years since diagnosis/	1.8	8.8	6.9	1.8	.6	8.0	.05	11.8	1.1
Years since Scanning at assessment	2.2	-.1	.01	.18	.2	.04	.2	13.0	.01
Scan type ***	MRI	CT	CT	CT	CT	MRI	CT	CT	CT
Left sided motor signs	0	4	12	2	0	2	2	0	0
Right sided motor signs	13	0	6	0	4	0	15	0	6

** T=Traumatic Basal Ganglia Hematoma, ABS=Brain Abscess, H=Closed Head Injury, CVA=Cardiovascular Accident*
Ast= Astrocytoma
*** NART-R=National Adult Reading Test -Revised*

Table A.14.

Studies Providing Age-Related Normative Data

Skill Area	Test	Type of Standard Score *Mean & SD (PD Subjects only)*	Study
Orienting to a Verbal Stimulus (Circuits	HLLST Yes/No Questions	z-score based on age-norms *(Mean: 0.43, SD: 0.54)*	Clarke et al (1998)
	HLLST Vocabulary	z-score based on age-norms *(Mean: 0.31, SD:0.75)*	Clarke et al (1998)
	HLLST Grammar	z-score based on age-norms *(Mean: 0.33, SD: 0.90)*	Clarke et al (1998)
	HLLST B Aud/Vis Comprehension	z-score based on age-norms *(Mean: 0.25, SD: 0.87)*	Clarke et al (1998)
	HLLST C Reading Comprehension	z-score based on age-norms *(Mean: 0.22, SD: 1.07)*	Clarke et al (1998)
Orienting to a visual stimulus	HLLST B Aud/Vis Comprehension	z-score based on age-norms *(Mean: 0.25, SD: 0.87)*	Clarke et al (1998)

Table A.14. (Cont.)

Studies Providing Age-Related Normative Data

Skill Area	Test	Type of Standard Score *Age-based Mean & SD (PD Subjects only)*	Study
Voluntary Movements, Motor speed	Trail Making Test, Part A *(positive score corresponds to poor performance)*	z-score based on age-norms *(Mean: -0.19, SD: 0.65)*	Ernst, et al (1987)
	Trail Making Test, Part B*(positive score corresponds to poor performance)*	z-score based on age-norms *(Mean: -0.97, SD: 0.44)*	Ernst, et al (1987)
	WAIS-R Digit Symbol	Wechsler Scaled scores based on age norms. *(Mean: 9.0, SD: 2.22)*	Ivnik et al (1992)
Executive Function, visual	WCST Conceptualization	T-scores, based on norms for both age and years of education *(Mean: 54.0, SD: 8.5)*	Heaton, et al (1993)
	WCST Perseverative Errors	T-scores, based on norms for both age and years of education *(Mean: 65.85, SD: 11.9)*	Heaton, et al (1993)

Table A.14. (Cont.)

Studies Providing Age-Related Normative Data

Skill Area	Test	Type of Standard Score *Age-based Mean & SD (PD Subjects only)*	Study
Verbal Recall	Paragraph Recall Immediate	z-score based on age-norms *(Mean: -1.01, SD: 1.03)*	Cockburn & Smith, 1989
	Paragraph Recall, Delayed	z-score based on age-norms *(Mean: -0.99, SD:1.15)*	Cockburn & Smith, 1989
Visual Recall	Picture Recognition	z-score based on age-norms	Cockburn & Smith, 1989
Recallings words in a time limit	HLLST Association Naming	z-score based on age-norms *(Mean: 0.63, SD: 1.19)*	Clarke et al, 1998
Ordering verbal memories into a time sequence	HLLST Sequencing	z-score based on age-norms *(Mean: 0.19, SD: 0.98)*	Clarke et al, 1998
Expressive Syntax	HLLST Sentence Formulation	z-score based on age-norms *(Mean: -1.21; SD: 1.03)*	Clarke et al, 1998
Verbal Expression	WAIS-R Similarities	Wechsler Scaled scores based on age norms. *(Mean: 10.75; SD: 2.4)*	Ivnik et al (1992)

Table A.14. (Cont.)

Studies Providing Age-Related Normative Data

Skill Area	Test	Type of Standard Score *Age-based Mean & SD (PD Subjects only)*	Study
	HLLST Antonyms	z-score based on age-norms *(Mean: 0.10; SD: 1.01)*	Clarke et al (1998)
	HLLST Synonyms	z-score based on age-norms *(Mean: 0.31; SD: 0.87)*	Clarke et al (1998)
	HLLST Give Defns	z-score based on age-norms *(Mean: 0.08; SD: 1.20)*	Clarke et al (1998)
	HLLST Provide a word	z-score based on age-norms *(Mean:0.25; SD: 0.47)*	Clarke et al (1998)
	HLLST Differences	z-score based on age-norms *(Mean: 0.07; SD: 0.69)*	Clarke et al (1998)
	HLLST Categories	z-score based on age-norms *(Mean: 0.59; SD: 0.08)*	Clarke et al (1998)
	HLLST Sent Formultn	z-score based on age-norms *(Mean: -1.21; SD: 1.03)*	Clarke et al (1998)
	HLLST Analogies	z-score based on age-norms *(Mean: 0.36, SD: 0.86)*	Clarke et al (1998)

Table A.14. (Cont.)

Studies Providing Age-Related Normative Data

Skill Area	Test	Type of Standard Score *Mean & SD (PD Subjects only)*	Study
Verbal Expression (Cont.)	HLLST Homonyms	z-score based on age-norms *(Mean: 0.37, SD: 1.02)*	Clarke et al (1998)
	HLLST Absurdities	z-score based on age-norms *(Mean: 0.39, SD: 0.49)*	Clarke et al (1998)
	HLLST Sequencing	z-score based on age-norms *(Mean: 0.19, SD: 0.98)*	Clarke et al (1998)
	HLLST Assoc Naming	z-score based on age-norms *(Mean: 0.63, SD: 1.19)*	Clarke et al (1998)

Table A.15.
Background Information on PD subjects

Subject ID No.	*8*	*9*	*10*	*11*	*14*	*15*	*16*	*17*	*18*	*19*	*35*	*38*	*39*
Gender	F	M	F	F	F	F	M	F	M	M	M	F	F
Age at Diagnosis (complete years)	67	67	61	69	60	56	66	65	62	64	59	64	52
Yrs since Diagnosis at Assessment	0.55	0.17	1.39	3.20	0.19	1.50	1.84	7.38	0.96	5.46	0.69	5.62	0.36
Est Prediag IQ (NART-R)	116	124	111	123	117	111	122	121	117	114	113	101	107
NART-R z-score*	1.06	1.6	0.73	1.53	1.13	0.73	1.47	1.4	1.13	0.93	0.87	0.07	0.47
Hohn & Yahr Stage **	1	1	2	2	1	1	2	2	2	1	1	2	1
No. of Left motor signs	1	1	1	3	2	0	3	0	2	0	2	4	0
No of Right motor signs	0	1	1	4	0	1	3	3	3	2	0	0	1

* These z-scores were calculated using the published standardization data. This was done to facilitate comparison with age-related standard scores, used to report PD test performance in Table 60.

** **Definition of Hohn & Yahr (1967) Stages:**
Stage 1: Unilateral involvement only, usually with minimal or no functional impairment.
Stage 2: Bilateral or midline involvement, without impairment of balance.

Table A.16.

T-test Comparison of PD Subjects' (N=13) Performance on Lesion-sensitive Tests with Pre-morbid Ability Level (NART-R IQ)

(NART-R IQ Mean=115; SD=6.7, corresponding to a mean of 1.01 and SD of 0.44, in z-score units)

Test Revealing Deficit in Study 2 *(Mean & SD, as z-scores, based on age-based norms, where available)*	***Task Involved***	*
WAIS-R Digit Symbol Subtest *Mean=-0.33; SD=0.74*	*Writing as many symbols as possible within a time limit*	p<.05
Trail Making Test, *Part B, Mean=-0.97; SD=0.44*	*Dot-to-dot task, alternating between number and letter sequences*	n.s.
Computer Tracking Task *Mean= -1.92; SD=1.49*	*Using a joystick to keep a 5mm circle inside a 15 mm square randomly moving around a computer screen*	p<.001
WCST-R Perseverative Responses *Mean= -1.32 SD=1.26*	*Persistence at sorting cards according to an incorrect principle*	p<.001
HLLST Auditory/Visual Comprehension Test *Mean= 0.25; SD=0.87*	*Following examiner's instructions in relation to a picture*	p<.05
HLLST Association Naming Test *Mean= 0.63; SD=1.19*	*Naming as many items as possible in a category in 60 seconds*	n.s.
HLLST Antonyms Test *Mean=0.10; SD=1.0*	*Giving the opposite of a given word*	p<.001
HLLST Synonyms Test *Mean=0.31; SD=0.87*	*Giving another word that means the same as a given word*	p<.01
HLLST Give Definitions *Mean=-.66; SD=1.54*	*Explaining word meanings*	p<.01
HLLST Absurdities *Mean= -.44; SD=1.46*	*Explaining the absurdity of a short story*	p<.01
HLLST Sentence Formulation *Mean=-1.21; SD=1.03*	*Construction of a sentence around three set words*	p<.001

Table A.17.

Correlations between Lesion-sensitive Tests and Tests Revealing Deficits for PD Subjects only

Lesion-sensitive Test from Study 5	Tests Revealing Deficits for PD Subjects only			
	Computer Tracking Task	Sentence Formu-lation	Story Recall, Immediate	Story Recall, Delayed
WAIS-R Digit Symbol Subtest	-.03	.38	-.20	.19
Trail Making Test, Part B	.03	-.32	-.09	-.33
Computer Tracking Task	-	-.10	-.11	.03
WCST-R Perseverative Responses	-.37	.41	.06	.18
HLLST Auditory/Visual Comprehension Test	.28	.06	**-.63****	-.45
HLLST Association Naming Test	-.12	.08	.45	**.60****
HLLST Antonyms Test	-.16	-.48	.35	.31
HLLST Synonyms Test	-.44	-.10	**.63****	**.64***
HLLST Give Definitions	.12	.22	.24	**.60****
HLLST Absurdities	-.22	.22	-.10	.01
HLLST Sentence Formulation	-.10	-	.11	.25

* $p<.1$
**$p<.05$

Table A.18.

Tests involving Complex Programmes of Motor Activity & Conscious Attention

	Tests Associated with Lesions			Tests NOT associated with lesions		
Test	**Computer Task**	**Trail Making Test, Pt B**	**WAIS-R Digit Symbol**	Trail Making Test, Pt A	Rey Figure, Copy & Recall	Porteus Mazes
Cognitive Process						
Dynamic allocation of attention between competing inputs	+	+	+			
Visual search/recognition	+	+	+	+	+	+
Visuo-spatial problem solving	+	+			+	+
Several pieces of information have to be kept in working memory and all considered in decision about specific test response		+	+			
Visuo-motor tracking	+	+		+		
Simple pencil-drawing ability		+	+	+	+	+
Controlling a joystick	+					

Table A.18.

Executive Function Tests

	Test Associated with Lesions			Tests NOT Associated with Lesions	
Test	**WCST-R Persev Responses**	**Trail Making Test, Pt B**	**HLLST Association Naming**	Rey Figure, Copy & Recall	Porteus Maz
Cognitive Process					
Visual search/recognition	+	+		+	+
Visuo-motor tracking		+			
Simple pencil-drawing ability		+		+	+
Processing speed included in performance index		+	+		
Dynamic allocation of attention between competing inputs		+			
Several pieces of information have to be kept in working memory and all considered in decision about specific test response	+	+	+		
Visuo-spatial problem solving				+	+
Phonological-based memory search for single words			+		
Category-based memory search for single words			+		
Utterance of series of single words			+		
Brain Area Associated with Deficits					
R Dorsolateral Prefrontal circuit	+				
Combination of globus pallidus & caudate nucleus in either L or R hemisphere (involved in all 3 circuits)		+			
General left Hemisphere			+		
Correlation between Test Performance & Lateralized Motor Signs					
Left sided motor signs	n.s.	n.s.	n.s.	n.s.	n.s.
Right sided motor signs	n.s.	.54**	-.47*	n.s.	n.s.

Table A.20.: Language Tests related to Lesions

	HLLST Auditory/ Visual Comprhnsn	HLLST Antonyms	HLLST Synonyms	HLLST Give Definitions	HLLST Absurdities	HLLST Association Naming	
Visual search/recognition	+						1
Processing speed included in performance index						+	1
Brief verbal sequential memory	+						1
Oral word comprehension	+	+	+	+	+	+	6
Oral Sentence comprehension	+						1
Written sentence comprehension							
Phonological-based memory search for single words						+	1
Category-based memory search for single words						+	1
Memory search for a specific word(s), meaningfully related to orally presented information		+	+	+	+		4
Several pieces of information have to be kept in working memory and all considered in decision about specific test response	+					+	2
Verbal explanation of an idea				+	+		2
Utterance of single words		+	+	+	+	+	3

Brain Area Associated with Deficits

L Dorsolateral prefrontal circuit	+	+		+	+	
R Dorsolateral prefrontal circuit				+	+	
R Frontal lobe		+	+			
L Language-related circuitry			+			
General Left Hemisphere						+

Correlation between Test Performance & Lateralized Motor Signs

Left side motor signs	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Right side motor signs	-.70***	n.s.	n.s.	-.45*	n.s.	-.47*

Table A.21.: Language Tests NOT related to Lesions (1)

	HLLST Yes/No Questions	HLLST Vocabulary	HLLST Grammar	HLLST Reading Comprehension	HLLST Provide a word	HLLST Differences	HLLST Categories	Total
Visual search/recognition		+		+				2
Processing speed included in performance index								-
Brief verbal sequential memory			+	+				2
Single word comprehension	+	+	+	+	+	+	+	7
Oral Sentence comprehension	+		+		+			3
Written sentence comprehension				+				1
Phonological-based memory search for single words							+	1
Category-based memory search for single words								
Memory search for a specific word(s), meaningfully related to orally presented information					+	+		2
Several pieces of information have to be kept in working memory and all considered in decision about specific test response			+	+				2
Verbal explanation of an idea								
Utterance of single words					+	+	+	3
Left side motor signs								
Right side motor signs								

Table A.21.: Language Tests NOT related to Lesions (2)

	HLLST Sentence Formulation	HLLST Analogies	HLLST Homonyms	HLLST Sequencing	WAIS-R Similarities	Total (12)
Visual search/recognition						2
Processing speed included in performance index						-
Brief verbal sequential memory	+					3
Single word comprehension	+	+	+	+	+	12
Oral Sentence comprehension	+					4
Written sentence comprehension						1
Phonological-based memory search for single words						1
Category-based memory search for single words			+		+	2
Memory search for a specific word(s), meaningfully related to orally presented information	+	+	+			5
Several pieces of information have to be kept in working memory and all considered in decision about specific test response	+			+		4
Verbal explanation of an abstract idea						
Utterance of single words	+	+	+	+	+	8
Left side motor signs						
Right side motor signs						

Appendix B.: Comprehensive Data for Individual Subjects

Subjects are identified by identification numbers (ID No.s) which were assigned in order of the subject's engagement for this study. These ID No.s were used consistently throughout. The purpose of this Appendix is to provide full information on each individual subject. Locating background data on an individual subject, identifiec ID No., requires knowledge of the etiology of each subject's neurological impairment. Etiology for each subject i shown in Table B.2. Data are presented, grouped by etiology. Etiological categories used in this way are: spinal injury, Parkinson's Disease, and Acquired Brain Injury. The latter includes all subjects with closed head injury, cardiovascular accidents and other lesions. Then subject ID Numbers, (arranged in numerical order) can be searcl within the corresponding table.

List of all Tables in Appendix B.

Table B.1.
Description of Scores Reported in all Tables in Appendix A.

Test	Description of Score
ID No.	Unique identification number for each subject
NART-R IQ	Standard score represented on the familiar IQ scale
Beck Depression Inventory	Raw score
Mini Mental State Exam	Raw score
WAIS-R Digit Symbol	Scaled Score (Mean=10; SD=3). In the case of PD subjects, the same kind of scaled score derived from age-based data (Ivnik et al, 1992).
Trail Making Test, Pt A	Time in seconds to task completion. Thus a higher score meant less proficient performance.
Trail Making Test, Pt B	Time in seconds to task completion. Thus a higher score meant less proficient performance.
Rey Figure Copy	Raw score
Rey Figure Recall	Raw score
Computer Task (%)	The average percentage of time-on-target over four trials of the task.
WCST Perseverative Responses	T-scores (Mean=50, SD=10). These were based on separate tables for subjects of different ages and educational levels.
WCST Conceptualization	T-scores (Mean=50, SD=10). These were based on separate tables for subjects of different ages and educational levels.
WCST No of Categories	Raw score
Porteus Mazes (yrs.)	Mental age level (e.g. 16.5=sixteen and a half years)
RBMT Immediate Paragraph recall	Raw score
RBMT Delayed, Paragraph recall	Raw score
RBMT Picture Recognition	Raw score
HLLST Yes/No Questions	Raw score
HLLST Vocabulary	Raw score
HLLST Grammar	Raw score
HLLST Audio/Visual Comprehension	Raw score
HLLST Reading Comprehension	Raw score
HLLST Antonyms	Raw score
HLLST Synonyms	Raw score
HLLST Give Defns	Raw score
HLLST Provide a Word	Raw score
HLLST Differences	Raw score
HLLST Categories	Raw score
HLLST Sent Formulation	Raw score
HLLST Analogies	Raw score
HLLST Homonyms	Raw score
HLLST Absurdities	Raw score
HLLST Association Naming	Raw Score
HLLST Sequencing	Raw score
WAIS-R Similarities	Scaled Score (Mean=10; SD=3). In the case of PD subjects, the same kind of scaled score derived from age-based data (Ivnik et al, 1992).

Table B.2.

List of all subjects by ID No. and diagnostic group.

Abreviations: Spinal Injury (SI), Parkinson's Disease (PD), Acquired Brain Injury, first set (ABI(1)), Acquired Brain Injury, second set (ABI(2)). The specific diagnosis of all acquired brain injury subjects is also given, e.g. [CHI]. Abbreviations used for those are, Closed Head Injury [CHI], Cardiovascular Accident [CVA], Other Brai Injury [OBD].

ID No.	Diagnostic Group	ID No.	Diagnostic Group
1	ABI(1) [CHI]	30	SI
2	ABI(1) [CHI]	31	ABI(2) [CHI]
3	ABI(1) [CHI]	32	SI
4	ABI(1) [CHI]	33	SI
5	ABI(1) [CHI]	34	SI
6	ABI(1) [CHI]	35	PD
7	ABI(1) [CHI]	36	ABI(2) [CVA]
8	PD	37	SI
9	PD	38	PD
10	PD	39	PD
11	PD	40	ABI(2) [CHI]
12	ABI(1) [OBD]	41	ABI(2) [CHI]
13	ABI(1) [OBD]	42	ABI(2) [CVA]
14	PD	43	ABI(2) [CVA]
15	PD	44	SI
16	PD	45	CVA
17	PD	46	ABI(2) [CHI]
18	PD	47	ABI(2) [CHI]
19	PD	48	ABI(2) [CVA]
20	ABI(1) [CVA]	49	SI
21	ABI(1) [OBD]	50	SI
22	SI	51	SI
23	SI	52	SI
24	ABI(1) [CHI]	53	ABI(2) [CVA]
25	ABI(1) [CHI]	54	ABI(2) [CHI]
26	ABI(1) [CHI]	55	ABI(2) [CVA]
27	ABI(2) [CHI]	56	ABI(2) [CVA]
28	SI		
29	SI		

Table B.3.

Spinal Injury (SI) Subjects: Background Demographics (N=14)

ID No.	22	23	28	29	30	32	33	34	37	44	49	50	51	52
Gender	M	M	F	M	M	M	M	M	M	M	M	F	M	M
DOB	12/8/72	2/10/53	5/2/56	8/12/32	20/8/69	11/9/56	4/2/37	30/5/60	20/8/63	25/8/58	4/4/69	16/9/71	22/10/63	20/2/62
Date of Injury	25/1/87	20/4/90	12/6/90	15/1/59	8/8/86	20/5/83	11/5/56	30/11/88	23/9/86	26/12/76	15/6/92	21/7/91	18/7/92	2/7/92
Age at Testing	20	39	36	59	23	35	55	32	29	34	24	22	29	31
Level of Spinal Lesion	C5-C6		C2-C6	T-12	S1	C3-C5	C5-C6	L1	L3-L4	C5-C6	T3	C4-C5	C5	T3-T4 T4-T5
Handed -ness	Right	Right	Left	Right	Right	Right	Left	Left	Right	Right	Right	Right	Right	Right
Preinjury Occupation *	Student	Semi skilled	Prof	Semi skilled	Unskill	Skill Tr Sm Bus	Student	Skill Tr Sm Bus	Semi skilled	Skill Tr Sm Bus	Skill Tr Sm Bus	Unskill	Skill Tr Sm Bus	Manag
Highest Edn Qual *	Not Qual	Basic Voc	Skilled Voc	Not Qual	Not Qual	Skilled Voc	Higher Degree	Skilled Voc	Not Qual	Bachel Degree	Skilled Voc	Not Qual	Not Qual	Not Qual

***Explanation of Abreviations**

Preinjury Occupation	**Abreviation**	**Highest Educational Qualification**	**Abreviation**
Managerial	Manag	Higher Degree	Higher Degree
Professional	Prof	Bachelor's Degree	Bach Degree
Skilled Trade, small business	Skill Tr, Sm Bus	Undergraduate Diploma	Ungrad degree
Semiskilled	Semi Skilled	Skilled Vocational Qualification	Skilled Voc
Unskilled	Unskill	Basic Vocational Qualification	Basic Voc
Home duties/retired	Home D/Ret	Not Qualified	Not Qual
student	student		

Table B.4.

Spinal Injury (SI) Subjects: Test Results

(For each test, there are often several types of scores that could be presented. For example, raw scores, percentiles, z-scores, T-scores etc. The one included is that arrived from regular 'hand-scoring' of the test, prior to data transformations employed in the analysis (e.g. transformation into z-scores). This would either be a standard score (e.g. NART-R IQ), or a raw score (e.g. all the HLLST subtests).

ID No.	22	23	28	29	30	32	33	34	37	44	49	50	51	52
NART-R IQ	112	96	112	105	114	118	120	109	105	116	97	110	103	93
Beck Depression Inventory	7	6	9	6	11	3	0	3	10	1	13	10	2	3
Mini Mental State Exam														
WAIS-R Digit Symbol		5		6	12	7	6	11	7	6	6	12	7	9
Trail Making Test, Pt A	40	62	47	26	48	24	27	27	34	51	34	37	28	20
Trail Making Test, Pt B	79	157	77	73	72	72	42	46	72	120	84	83	55	50
Rey Figure Copy	34	34	35	33	35	34	33	32	36	36	36	36	36	32
Rey Figure Recall	23	23	13	13	27	14	23	22	17	15	23	18	26	29
Computer Task	53	30	40	59	67	51	50	69	79	48	61	47	63	52
WCST Perseverative Responses	80	45	42	80	80	59	62	80	80	80	80	80	80	80
WCST Conceptualization	63	47	43	56	64	49	56	49	67	55	59	53	79	46
WCST No of Categories	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Porteus Mazes	15.5	16.0	15.0	13.5	16.0	16.0	14.5	16.0	16.5	16.0	17.0	16.5	16.5	14.5
RBMT Immediate Paragraph recall	6	6	8	10	10	9	14	6	5	4	11	9	6	7
RBMT Delayed Paragraph recall	4	5	7	8	6	7	17	9	5	3	8	10	7	7
RBMT Picture Recogntn	10	10	10	10	10	10	10	10	10	9	9	10	10	10
HLLST Yes/No Questions	3	3	4	3	3	4	4	4	3	4	3	4	4	3
HLLST Vocabulary	4	2	2	4	4	4	4	4	4	4	2	4	4	4
HLLSTGrammar	3	1	2	2	2	1	3	3	2	2	2	3	3	3

Table B.4. (Cont.)

Spinal Injury (SI) Subjects: Test Results

ID No.	22	23	28	29	30	32	33	34	37	44	49	50	51	52
HLLST Aud/Vis Compreh	5	5	4	5	5	4	5	5	5	6	4	5	5	5
HLLST Reading Compreh	2	4	4	2	2	4	7	3	3	4	2	4	4	3
HLLST Antonyms	4	4	4	4	4	4	4	4	2	3	2	4	4	3
HLLST Synonyms	4	4	3	4	4	4	4	4	4	4	2	3	3	2
HLLST Give Defns	8	6	6	6	8	8	8	8	2	8	4	8	8	6
HLLST Provide a Word	5	5	4	4	5	5	5	5	5	5	5	5	5	5
HLLST Differences	4	4	3	4	4	4	4	4	4	4	2	4	3	3
HLLST Categories	2	3	3	3	3	3	3	3	3	3	3	3	3	1
HLLST Sent Formulation	5	5	5	1	5	5	5	5	5	5	4	5	5	4
HLLST Analogies	3	2	1	4	4	3	3	3	3	4	2	4	4	2
HLLST Homonyms	3	4	2	4	2	4	4	4	4	4	0	4	3	0
HLLST Absurdities	3	3	0	3	3	3	3	3	3	3	4	2	3	3
HLLST Association Naming	22	29	35	36	30	32	43	44	33	37	28	37	37	27
HLLST Sequencing	2	2	0	2	2	2	2	2	2	0	0	2	2	2
WAIS-R Similarities	11	13		9	12	11	14	11	10	12	8	10	8	4

Table B.5.
Parkinson's Disease (PD) Subjects: Background Demographics (N=13)

ID No.	8	9	10	11	14	15	16	17	18	19	35	38	39
Gender	F	M	F	F	F	F	M	F	M	M	M	F	F
DOB	28/5/23	30/8/22	19/1/29	3/10/20	'8/4/31	21/1/35	18/1/25	29/1/26	2/4/29	24/4/27	30/10/33	17/6/27	18/9/40
Date of Diagnosis	15/1/90	25/4/909	15/1/89	1/4/87	15/8/91	19/7/90	15/12/89	30/6/84	15/11/90	24/4/86	22/7/92	15/10/86	5/11/92
Age at Testing	67	67	61	69	60	56	66	65	62	64	59	64	52
Hoehn & Yahr scale	1	1	2	2	1	1	2	2	2	1	1	2	1
Handed -ness	Right	Right	Right	Right	Right	Right	Right	Right	Right	Right	Right	Right	Right
Preinjury Occupation *	Sk Tr Sm Bus	Prof	Unskill	Prof	Unskill	Semi skilled	Unskill	Prof	Sk Tr Sm Bus	Sk Tr Sm Bus	Semi skilled	H dut/ Ret	Semi skilled
Highest Edn Qual *	Not Qual	8	Not Qual	Skilled Voc	Not Qual	Skilled Voc	Not Qual	Ungrad Dip	Skilled Voc	Skilled Voc	Not Qual	Not Qual	Not Qual
Left Motor Signs	1	1	1	3	2	0	3	0	2	0	2	4	0
Right Motor Signs	0	1	1	4	0	1	3	3	3	2	0	0	1

- *Refer to footnote to Table 82 for explanation.*

Table B.6.

PD Subjects' Medications

8 Oroxine, 50 mg, 3/day, Sinamet, 100 mg 3/day	17 Sinamet
9 None	18 Sinamet, 100 mg, 2/day
10 Parlodel/Bromocriptine 10 mg, 3/day, Isoptin, 40 mg, 2/day, Diclofenac, 50 mg, 2/day	19 Madapar, 3 tablets/day
11 Sinamet, 100 mg, 2/day, Amantadine, 100 mg, 2/day	35 Sinamet
14 Sinamet, 100 mg, 2/day	38 Sinamet
15 Sinamet	39 Sinamet
16 None	

Table B.7.

Parkinson's Disease (PD) Subjects: Test Results

ID No.	8	9	10	11	14	15	16	17	18	19	35	38	39
NART-R IQ	116	124	111	123	117	111	122	121	117	114	113	101	107
Beck Depression Inventory	0		4	4	3	0	7	0	0	0	0	1	0
Mini Mental State Exam	25	29	30	30	29		26	30	27	25		22	
WAIS-R Digit Symbol *	10	9	8	11	8	11	11	10	6	7		5	12
Trail Making Test, Pt A	77	77	66	47	54	37	63	37	36	66	48	27	36
Trail Making Test, Pt B	105	105	157	79	145	70	105	75	113	208	94	130	66
Rey Figure Copy	32	32	22	35	32	34	34	35	34	36	33	32	36
Rey Figure Recall	11	11	7	20	17	14	26	18	14	17	23	2	23
Computer Task (%)	9	12	11	38	69	34	32	19	65	28	38	30	33
WCST Perseverative Responses	65	63	80	64	47	80	46	71	61	52	74	47	69
WCST Conceptualization	62	45	45	67	53	59	37	53	58	59	59	46	59
WCST No of Categories	6	4	6	6	6	6	1	6	6	6	6	6	6
Porteus Mazes (yrs)	13.5	17	11	15	13.5	14.5	14.5	15.5	16.5	16.5	16	12.5	16
RBMT Immediate Paragraph recall	4	10	5	13	8	3	3	8	1	6	7	3	4
RBMT Delayed Paragraph recall	0	10	5	10	8	3	4	5	0	0	7	0	5
RBMT Picture Recogntn	10	10	9	10	10	10	10	10	10	10	10	10	10
HLLST Yes/No Questions	4	3	4	4	4	4	4	3	4	3	4	3	4
HLLST Vocabulary	3	3	4	4	4	3	4	4	2	3	3	4	4
HLLSTGrammar	1	2	3	3	3	3	3	3	1	2	3	1	3

Table B.7. (Cont.)

Parkinson's Disease (PD) Subjects: Test Results

ID No.	8	9	10	11	14	15	16	17	18	19	35	38	39
HLLST Aud/Vis Compreh	5	3	5	4	5	5	5	5	5	4	5	5	5
HLLST Reading Compreh	2	3	2	4	4	3	4	4	4	3	4	1	4
HLLST Antonyms	4	4	4	4	4	4	4	4	3	3	4	2	2
HLLST Synonyms	4	4	4	4	4	3	4	4	1	3	4	2	3
HLLST Give Defns	3	8	7	4	8	2	8	8	6	2	8	0	8
HLLST Provide a Word	5	4	5	5	5	5	5	5	4	5	5	4	5
HLLST Differences	2	4	4	4	4	4	3	3	3	3	3	2	4
HLLST Categories	3	3	3	3	3	3	3	3	3	3	3	3	3
HLLST Sent Formulation	2	2	2	2	1	1	0	1	1	1	5	2	5
HLLST Analogies	2	4	4	3	4	4	4	4	3	3	3	1	3
HLLST Homonyms	4	4	4	4	4	3	4	4	4	0	4	0	4
HLLST Absurdities	3	3	3	3	2	3	3	2	3	3	3	2	3
HLLST Association Naming	28	31	41	50	33	44	37	48	24	16	42	27	31
HLLST Sequencing	1	2	2	0	2	2	1	0	2	2	1	2	0
WAIS-R Similarities *	11	14	12	10	13	11	14	12	8	8		7	9

** Age norms used. See Results section, Study 3.*

Table B.8.
Acquired Brain Injury (BI) Subjects (1): Background Demographics

ID No.	1	2	3	4	5	6	7	12	13	20	21	24	25	26
Aetiology of BI	CHI	CHI	CHI	CHI	CHI	CHI	CHI		Brain Absess	CVA	Astrocytoma	CHI	CHI	CHI
Gender	M	M	F	M	M	M	M	Male	Male	Female	Male	M	M	M
DOB	17/4/58	29/2/52	8/10/58	8/2/56	24/9/64	21/2/69	16/10/62	6/7/63	23/6/26	3/4/62	29/11/30	18/9/63	7/4/74	16/12/66
Date of Injury	28/11/84	6/4/81	8/4/77	1/6/78	7/5/87	26/8/84	8/11/85	5/5/79	18/8/88	30/6/71	26/4/83	15/9/82	13/4/86	28/1/86
Age at Testing	31	37	30	35	24	20	26	26	63	29	61	29	18	26
Handed -ness	Right	Left	Right	Right	Right	Right	Right	Right	Right	Right	Right	Right	Right	Right
Preinjury Occupation *	Prof	Sk Tr Sm Bus	Student	Semi skilled	Manag	Student	Sk Tr Sm Bus	Student	Unskill	Student	Sk Tr Sm Bus	Unskill	Student	Unskill
Highest Edn Qual *	Skilled Vooc	Not Qual	Basic Voc	Not Qual	Basic Voc	Basic Voc	Not Qual	Not Qual	Not Qual	Not Qual	Not Qual	Not Qual	Not Qual	Not Qual
Left Motor Signs	3	8	4	6	0	2	0	4	4	0	4	0	11	12
Right Motor Signs	0	0	0	0	13	0	2	1	0	11	0	12	0	6

** Refer to footnote to Table B.1.*

Table B.9.

Acquired Brain Injury (BI) Subjects (1): Test Results

ID No.	1	2	3	4	5	6	7	12	13	20	21	24	25	26
NART-R IQ	115	89	107	112	90	98	113	105	93	99	106	65	94	106
Beck Depression Inventory	3	2		3	0	7		0	0	1	5	7	9	15
Mini Mental State Exam											23			
WAIS-R Digit Symbol	5	4	10	6	2	5	7	6	2	6	6	3	3	2
Trail Making Test, Pt A	38	112	39	40	36	38	35	47	110	40	29	124	138	162
Trail Making Test, Pt B	90	396	68	118	234	90	59	105	348	145	94	287	131	325
Rey Figure Copy	36	29	36	32	34	33	35	32	24	32	30	28	31	36
Rey Figure Recall	28	9	14	16	27	21	22	21	6	0	7	6	5	6
Computer Task (%)	64	74		47	69		75	76	20	31	39	67	65	51
WCST Perseverative Responses	80	29	53	20	80	80	80	80	35	80	37	21	39	37
WCST Conceptualization	37	34	48	25	45	67	61	55	36	60	33	31	42	27
WCST No of Categories	6	5	6	1	6	6	6	6	2	6	1	2	6	1
Porteus Mazes (yrs.)	16.5	13	15.5	14.5	13	17	16	15.5	9	16.5	15	12	16	11
RBMT Immediate Paragraph recall	4	0	9	3	2	6	9	4	8	4	5	1	3	5
RBMT Delayed Paragraph recall	3	0	9	0	1	4	8	5	0	1	4	0	1	0
RBMT Picture Recogntn	10	9	10	9	10	9	10	10	7	10	10	9	10	10
HLLST Yes/No Questions	4	2	3	4	4	3	4	3	3	1	4	3	3	2
HLLST Vocabulary	3	0	4	3	3	4	4	4	2	3	3	1	3	3
HLLSTGrammar	3	1	3	3	0	2	3	3	0	3	3	1	0	1

Table B.9. (Cont.)

Acquired Brain Injury (BI) Subjects (1): Test Results

ID No.	1	2	3	4	5	6	7	12	13	20	21	24	25	26
HLLST Aud/Vis Compreh	5	4	5	5	4	4	5	5	4	3	5	2	4	5
HLLST Reading Compreh	4	4	4	3	1	3	2	2	1	1	4	1	3	3
HLLST Antonyms	4	0	3	3	4	2	4	4	1	2	3	0	0	0
HLLST Synonyms	4	0	2	4	1	3	3	3	1	4	0	1	0	2
HLLST Give Defns	8	0	8	6	2	4	4	4	2	4	4	0	2	8
HLLST Provide a Word	5	1	5	5	3	5	5	3	4	5	5	4	4	2
HLLST Differences	4	0	3	4	0	3	4	1	4	4	1	4	3	4
HLLST Categories	3	0	3	2	2	2	2	0	2	3	2	0	0	1
HLLST Sent Formulation	2	0	2	1	1	1	2	0	0	0	0	0	1	1
HLLST Analogies	2	1	3	2	2	3	3	3	2	3	1	3	2	3
HLLST Homonyms	4	0	4	2	3	3	3	3	1	3	0	2	0	4
HLLST Absurdities	3	2	2	3	3	3	3	3	1	1	3	0	0	1
HLLST Association Naming	44	14	27	20	19	31	24	16	15	23	19	15	17	10
HLLST Sequencing	2	0	1	1	0	1	0	2	0	1	1	0	0	0
WAIS-R Similarities	8	1	11	7	3	8	9	6	3	8	6	5	6	6

Table B.10.

Acquired Brain Injury (BI) Subjects (1): Location of Brain Lesions

Key: ?=unknown, 0=none, 1=<20%, 2=20-50%, 3=>50%.

Left Hemisphere

ID No.	1	2	3	4	5	6	7	12	13	20	21	24	25	26
Type of scan	MRI	MRI	MRI	CT	MRI	MRI	MRI	CT	CT	CT	CT	CT	CT	CT
Any type of basal ganglia involvement	0	0	0	0	2	0	1	3	0	1	0	0	0	0
Caudate Nucleus (CN)	0	0	0	0	3	0	0	?	0	0	0	0	0	0
CN, dorsolateral head	0	0	0	?	0	?	0	?	0	0	0	0	?	0
CN, ventromedial head	0	0	0	?	0	?	0	?	0	0	0	0	?	0
Putamen	0	0	0	0	3	0	1	?	0	1	0	0	0	0
Nucleus Accumbens	0	0	0	0	0	0	0	?	0	0	0	0	?	0
Olfactory Tubercle	0	0	0	0	0	0	0	?	0	?	0	0	?	0
Globus Pallidus (GP)	0	0	0	0	2	0	0	?	0	1	0	0	0	0
GP, lateral dorsomedial internal segment	0	0	0	?	0	?	0	?	0	?	0	0	0	0
GP, medial dorsomedial internal segment	0	0	0	?	0	?	0	?	0	?	0	0	?	0
GP, rostrolateral internal segment	0	0	0	?	?	0	0	?	0	?	0	0	0	0
Ventral Pallidum	0	0	0	?	?	?	0	?	0	?	0	0	0	0
Substantia Nigra (SN)	0	0	0	0	0	0	0	?	0	0	0	0	0	0
SN, rostrodorsal	0	0	0	0	0	0	0	?	0	0	0	0	0	0
SN, rostromedial	0	0	0	0	0	0	0	?	0	0	0	0	0	0
SN, rostrolateral	0	0	0	0	0	0	0	?	0	0	0	0	0	0
Thalamus	0	0	0	0	0	0	0	0	0	2	0	0	0	0
Thalamic nuclei (a)	0	0	0	0	0	0	0	0	0	?	0	0	0	0
Thalamic nuclei (b)	0	0	0	0	0	0	0	0	0	?	0	0	0	0
Thalamic nuclei (c)	0	0	0	0	0	0	0	0	0	?	0	0	0	0
Subthalamic nuclei	0	0	0	0	0	0	0	3	0	0	0	0	0	0

Table B.10. (Cont.)

Acquired Brain Injury (BI) Subjects (1): Location of Brain Lesions

Key: ?=unknown, 0=none, 1=<20%, 2=20-50%, 3=>50%.

Left Hemisphere

ID No.	1	2	3	4	5	6	7	12	13	20	21	24	25	26
Locus cerulus	0	0	0	?	0	0	0	?	0	0	0	0	0	0
Hypothalamus	0	0	0	?	0	0	0	0	0	0	0	0	0	0
Dorsal motor vagus nucleus	0	0	0	?	0	0	0	0	0	0	0	0	0	0
Internal Capsule	0	0	0	0	3	0	0	3	0	1	0	0	0	0
External Capsule	0	0	0	0	3	0	2	0	0	0	0	0	0	0
Ventral Tegmentum	0	0	0	?	0	0	0	0	0	0	0	0	0	0
White matter adjacent to lateral ventricle	0	0	0	0	0	0	0	0	0	2	2	0	0	0
Parietal Lobe	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Occipital Lobe	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Temporal Lobe	0	0	0	0	0	0	0	0	0	0	0	0	?	2
Prefrontal Lobe	0	0	0	0	0	0	0	0	0	0	?	0	0	0
Prefrontal Lobe, dorsolateral	0	0	0	0	0	0	0	0	0	0	?	0	0	0
Frontal Lobe	0	0	0	0	0	0	0	0	0	0	3	0	0	0
Lateral Orbitofrontal	0	0	0	0	0	0	0	0	0	0	?	0	0	0
Anterior Cingulate	0	0	0	0	0	0	0	0	0	0	?	0	0	0

Table B.11.

Acquired Brain Injury (BI) Subjects (1): Location of Brain Lesions

Key: ?=unknown, 0=none, 1=<20%, 2=20-50%, 3=>50%.

Right Hemisphere

ID No.	1	2	3	4	5	6	7	12	13	20	21	24	25	26
Type of scan	MRI	MRI	MRI	CT	MRI	MRI	MRI	CT	CT	CT	CT	CT	CT	CT
Any basal ganglia involvement	2	3	3	3	0	2	0	0	0	0	0	0	2	0
Caudate Nucleus (CN)	3	3	3	3	0	3	0	0	0	0	0	0	1	0
CN, dorsolateral head	0	0	0	?	0	?	0	0	0	0	0	0	?	0
CN, ventromedial head	0	0	0	?	0	?	0	0	0	0	0	0	?	0
Putamen	3	3	3	3	0	3	0	0	0	0	0	0	3	0
Nucleus Accumbens	0	0	0	0	0	0	0	0	?	0	0	0	?	0
Olfactory Tubercle	0	0	0	0	0	0	0	0	?	0	0	0	?	0
Globus Pallidus (GP)	2	3	3	3	0	2	0	0	0	0	0	0	2	0
GP, lateral dorsomedial internal segment	0	0	0	?	0	?	0	0	0	0	0	0	?	0
GP, medial dorsomedial internal segment	0	0	0	?	0	?	0	0	0	0	0	0	?	0
GP, rostrolateral internal segment	0	0	0	?	0	?	0	0	0	0	0	0	?	0
Ventral Pallidum	0	0	0	?	0	?	0	0	0	0	0	0	?	0
Substantia Nigra (SN)	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SN, rostrodorsal	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SN, rostromedial	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SN, rostrolateral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Thalamus	0	0	0	0	0	0	0	0	2	0	0	0	0	0
Thalamic nuclei (a)	0	0	0	0	0	0	0	0	?	0	0	0	0	0
Thalamic nuclei (b)	0	0	0	0	0	0	0	0	?	0	0	0	0	0
Thalamic nuclei (c)	0	0	0	0	0	0	0	0	?	0	0	0	0	0
Subthalamic nuclei	0	0	0	0	0	0	0	0	?	0	0	0	0	0

Table B.11. (Cont.)

Acquired Brain Injury (BI) Subjects (1): Location of Brain Lesions

Key: ?=unknown, 0=none, 1=<20%, 2=20-50%, 3=>50%.

Right Hemisphere

ID No.	1	2	3	4	5	6	7	12	13	20	21	24	25	26
Locus cerulus	0	0	0	?	0	0	0	0	0	0	0	0	0	0
Hypothalamus	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dorsal motor vagus nucleus	0	0	0	?	0	0	0	0	0	0	0	0	0	0
Internal Capsule	0	3	3	3	0	3	0	0	0	0	0	0	2	0
External Capsule	0	3	3	?	0	2	0	0	0	0	0	0	2	0
Ventral Tegmentum	0	0	0	?	0	0	0	0	0	0	0	0	0	0
White matter adjacent to lateral ventricle	0	3	3	3	0	0	0	0	0	0	0	0	1	0
Parietal Lobe	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Occipital Lobe	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Temporal Lobe	0	3	0	0	0	0	0	0	0	0	0	0	?	0
Prefrontal Lobe	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Prefrontal Lobe, dorsolateral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Frontal Lobe	0	0	3	0	0	0	0	0	0	0	0	0	1	2
Lateral Orbitofrontal	0	0	3	0	0	0	0	0	0	0	0	0	0	?
Anterior Cingulate	0	0	0	0	0	0	0	0	0	0	0	0	0	?

Table B.12.
Brain Injury (BI) Subjects (2): Background Demographics

ID No.	27	31	36	40	41	42	43	45	46	47	48	53	54	55	56
Aetiology of BI	CHI	CHI	CVA	CHI	CHI	CVA	CVA	CVA	CHI	CHI	CVA	CVA	CHI	CVA	CVA
Gender	Female	Male	Male	Male	Male	Male	Male	Male	Female	Female	Female	Male	Female	Female	Male
DOB	13/4/74	24/11/74	24/12/62	18/8/73	26/9/69*	4/4/38	29/3/21	10/3/38	19/6/71	7/6/55	27/12/56	3/5/30	5/9/71	18/2/20	21/9/44
Date of Injury	4/10/86	5/12/90	7/9/92	4/2/85	16/1/87	13/3/93	29/1/93	5/5/93	15/2/89	23/8/81	20/6/92	24/5/93	23/5/92	8/8/94	15/11/93
Age at Testing	18	17	30	19	23	55	72	65	21	38	36	63	22	74	51
Handed-ness	Left	Right	Right	Right	Right	Right	Left	Right	Right	Right	Right	Right	Right	Left	Right
Preinjury Occupation *	Student	Student	Semi skilled	Student	Sk Tr Sm Bus	Sk Tr Sm Bus	Sk Tr Sm Bus	Semi skilled	Sk Tr Sm Bus	Semi skilled	Sk Tr Sm Bus	Sk Tr Sm Bus	Sk Tr Sm Bus	Manag	Sk Tr Sm Bus
Highest Edn Qual *	Skilled Voc	Not Qual	Not Qual	Not Qual	Basic Qual	Not Qual	Not Qual	Not Qual	Not Qual	Bach Degree	Not Qual	Not Qual	Ungrad Dip	Not Qual	Not Qual
Left Motor Signs	7	2	0	2	15	8	5	2	3	0	0	12	0	2	0
Right Motor Signs	2	0	4	0	2	0	0	15	0	0	6	0	0	0	0

** Refer to footnote for Table B.1.*

Table B.13.

Acquired Brain Injury (BI) Subjects (2): Test Results

ID No.	27	31	36	40	41	42	43	45	46	47	48	53	54	55	56
NART-R IQ	106	106	73	83	110	105	101	93	108	121	108	122	109	121	103
Beck Depression Inventory	0	5	10	2	9	3	7	24	10	0	13	4	1	0	1
Mini Mental State Exam							26	25						27	
WAIS-R Digit Symbol	11	11	2	5	3	6	4	3	8	12	5	4	11	2	5
Trail Making Test, Pt A	30	22	70	51	157	32	72	90	55	21	47	44	37	83	38
Trail Making Test, Pt B	59	112	145	83	290	71	185	233	85	59	135	85	78	117	94
Rey Figure Copy	36	34	27	34	11	36	26	30	33	34	36	33	36	25	31
Rey Figure Recall	13	23	9	15	3	28	7	14	16	24	8	11	20	16	15
Computer Task (%)	69	63	43	68	55	43	46	42	34	28	8	16	57	22	37
WCST Perseverative Responses	80	80	41	80	80	80	72	80	80	80	42	80	80	80	47
WCST Conceptualization	49	64	37	57	51	61	43	60	79	55	44	55	57	67	52
WCST No of Categories	6	6	4	6	6	6	2	6	6	6	6	6	6	6	6
Porteus Mazes (yrs.)	15.5	13	13	15	10	14	11.5	14.5	16.5	17	15.5	15.5	14.5	11	13
RBMT Immediate Paragraph recall	6	4	2	6	5	6	2	2	5	7	7	8	7	7	5
RBMT Delayed Paragraph recall	4	4	2	3	3	4	0	1	4	7	5	7	7	1	2
RBMT Picture Recogntn	9	10	7	10	10	10	10	9	10	9	10	10	10	9	10
HLLST Yes/No Questions	4	4	4	3	4	4	3	3	4	3	3	4	4	4	4
HLLST Vocabulary	3	4	1	2	3	4	2	1	2	3	4	3	3	3	3
HLLSTGrammar	3	3	1	1	1	3	3	2	2	2	3	2	1	3	3

Table B.13. (Cont.)

Acquired Brain Injury (BI) Subjects (2): Test Results

ID No.	27	31	36	40	41	42	43	45	46	47	48	53	54	55	56
HLLST Aud/Vis Compreh	5	5	4	3	5	5	5	1	4	5	5	5	5	4	5
HLLST Reading Compreh	4	3	3	4	2	3	1	0	4	4	4	4	4	3	4
HLLST Antonyms	2	2	1	0	1	4	4	1	1	4	3	4	3	3	4
HLLST Synonyms	3	2	0	0	0	4	1	0	1	4	3	4	3	3	4
HLLST Give Defns	6	4	3	0	8	6	2	1	6	8	6	8	6	8	8
HLLST Provide a Word	5	5	4	0	5	4	3	1	4	5	4	5	4	4	4
HLLST Differences	4	4	4	3	4	3	3	1	0	4	3	4	4	3	4
HLLST Categories	3	3	0	2	3	3	2	0	2	3	1	3	3	1	2
HLLST Sent Formulation	1	3	2	0	1	5	0	0	3	5	5	5	5	4	1
HLLST Analogies	3	2	0	1	2	3	1	0	3	4	3	4	3	3	3
HLLST Homonyms	4	3	1	1	3	4	0	0	2	4	2	4	2	4	3
HLLST Absurdities	3	3	2	1	3	3	2	3	3	3	2	3	3	3	3
HLLST Association Naming	35	21	12	16	25	25	23	8	31	44	19	22	28	18	30
HLLST Sequencing	2	2	1	0	0	2	2	0	2	2	2	1	1	2	2
WAIS-R Similarities	9	8	6	5	9	6	1	3	8	13	8	12	11	7	8

Table B.14.

Acquired Brain Injury (BI) Subjects (2): Location of Brain Lesions

Key: ?=unknown, 0=none, 1=<20%, 2=20-50%, 3=>50%.

Left Hemisphere

ID No.	27	31	36	40	41	42	43	45	46	47	48	53	54	55	56
Type of scan	CT	CT	CT	MRI	CT	CT	CT	CT	MRI	CT	CT	CT	CT	CT	CT
Any basal ganglia involvement	0	0	2	0	0	0	2	3	0	0	3	0	0	0	0
Caudate Nucleus (CN)	0	0	3	0	0	?	0	3	0	0	0	0	0	0	0
CN, dorsolateral head	0	0	3	0	0	?	0	3	0	0	0	0	0	0	0
CN, ventromedial head	0	0	3	0	0	?	0	3	0	0	0	0	0	0	0
Putamen	0	0	1	0	0	?	1	3	0	0	3	0	0	0	0
Nucleus Accumbens	0	0	?	?	0	?	0	?	0	0	0	?	0	0	0
Olfactory Tubercle	0	0	?	?	0	?	0	?	0	0	0	?	0	0	0
Globus Pallidus (GP)	0	0	0	0	0	?	2	1	0	0	3	0	0	0	0
GP, lateral dorsomedial internal segment	0	0	0	0	0	?	?	1	0	0	3	0	0	0	0
GP, medial dorsomedial internal segment	0	0	0	0	0	?	?	1	0	0	3	0	0	0	0
GP, rostrolateral internal segment	0	0	0	0	0	?	?	1	0	0	3	0	0	0	0
Ventral Pallidum	0	0	0	0	0	?	?	?	0	0	3	0	0	0	0
Substantia Nigra (SN)	0	0	?	0	0	?	0	?	0	0	?	?	0	0	0
SN, rostrodorsal	0	0	?	0	0	?	0	?	0	0	?	?	0	0	0
SN, rostromedial	0	0	?	0	0	?	0	?	0	0	?	?	0	0	0
SN, rostrolateral	0	0	?	0	0	?	0	?	0	0	?	?	0	0	0
Thalamus	0	0	0	?	0	0	0	0	0	0	0	0	0	0	0
Thalamic nuclei (a)	0	0	0	?	0	0	0	0	0	0	0	0	0	0	0
Thalamic nuclei (b)	0	0	0	?	0	0	0	0	0	0	0	0	0	0	0
Thalamic nuclei (c)	0	0	0	?	0	0	0	0	0	0	0	0	0	0	0
Subthalamic nuclei	0	0	0	?	0	0	0	0	0	0	0	0	0	0	0

Table B.14. (Cont.)

Acquired Brain Injury (BI) Subjects (2): Location of Brain Lesions

Key: ?=unknown, 0=none, 1=<20%, 2=20-50%, 3=>50%.

Left Hemisphere

ID No.	27	31	36	40	41	42	43	45	46	47	48	53	54	55	56
Locus cerulus	0	0	?	?	0	0	0	?	0	0	?	?	0	0	0
Hypothalamus	0	0	0	?	0	0	0	0	0	0	0	0	0	0	0
Dorsal motor vagus nucleus	0	0	?	?	0	0	0	?	0	0	?	?	0	0	0
Internal Capsule	0	0	2	0	0	0	2	3	0	0	2	0	0	2	0
External Capsule	0	0	2	0	0	0	0	?	0	0	2	0	0	0	0
Ventral Tegmentum	0	0	?	0	0	0	0	?	0	0	?	?	0	0	0
White matter adjacent to lateral ventricle	0	3	1	0	0	0	2	2	0	0	2	0	0	1	0
Parietal Lobe	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Occipital Lobe	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Temporal Lobe	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0
Prefrontal Lobe	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
Prefrontal Lobe, dorsolateral	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
Frontal Lobe	0	2	0	2	0	0	0	0	1	1	0	0	0	0	0
Lateral Orbitofrontal	0	2	0	2	0	0	0	0	0	1	0	0	0	0	0
Anterior Cingulate	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0

Table B.15.

Acquired Brain Injury (BI) Subjects (2): Location of Brain Lesions

Key: ?=unknown, 0=none, 1=<20%, 2=20-50%, 3=>50%.

Right Hemisphere

ID No.	27	31	36	40	41	42	43	45	46	47	48	53	54	55	56
Type of scan	CT	CT	CT	MRI	CT	CT	CT	CT	MRI	CT	CT	CT	CT	CT	CT
Any basal ganglia involvement	1	0	0	0	3	1	0	0	0	0	0	3	0	2	1
Caudate Nucleus (CN)	0	0	0	0	3	?	0	0	0	0	0	2	0	3	1
CN, dorsolateral head	0	0	0	0	3	?	0	0	0	0	0	2	0	3	1
CN, ventromedial head	0	0	0	0	3	?	0	0	0	0	0	2	0	3	0
Putamen	1	0	0	0	1	?	0	3	0	0	3	1	0	1	0
Nucleus Accumbens	0	0	?	?	3	?	0	?	0	0	0	?	0	0	0
Olfactory Tubercle	0	0	?	?	3	?	0	?	0	0	0	?	0	0	0
Globus Pallidus (GP)	1	0	0	0	3	?	0	0	0	0	0	1	0	2	0
GP, lateral dorsomedial internal segment	0	0	0	0	3	?	?	0	0	0	0	1	0	?	0
GP, medial dorsomedial internal segment	0	0	0	0	3	?	?	0	0	0	0	1	0	?	0
GP, rostrolateral internal segment	0	0	0	0	3	?	?	0	0	0	0	1	0	?	0
Ventral Pallidum	0	0	0	0	3	?	?	0	0	0	0	1	0	?	0
Substantia Nigra (SN)	0	0	?	0	3	?	0	?	0	0	?	?	0	0	0
SN, rostrodorsal	0	0	?	0	3	?	0	?	0	0	?	?	0	0	0
SN, rostromedial	0	0	?	0	3	?	0	?	0	0	?	?	0	0	0
SN, rostrolateral	0	0	?	0	3	?	0	?	0	0	?	?	0	0	0
Thalamus	1	0	0	?	3	0	0	0	0	0	0	0	0	0	0
Thalamic nuclei (a)	?	0	0	?	3	0	0	0	0	0	0	0	0	0	0
Thalamic nuclei (b)	?	0	0	?	3	0	0	0	0	0	0	0	0	0	0
Thalamic nuclei (c)	?	0	0	?	3	0	0	0	0	0	0	0	0	0	0
Subthalamic nuclei	0	0	?	?	3	?	0	?	0	0	?	?	0	0	0

Table B.15. (Cont.)

Acquired Brain Injury (BI) Subjects (2): Location of Brain Lesions

Key: ?=unknown, 0=none, 1=<20%, 2=20-50%, 3=>50%.

Right Hemisphere

ID No.	27	31	36	40	41	42	43	45	46	47	48	53	54	55	56
Locus cerulus	0	0	?	?	3	0	0	?	0	0	?	?	0	0	0
Hypothalamus	1	0	0	?	3	0	0	0	0	0	0	0	0	0	0
Dorsal motor vagus nucleus	0	0	?	?	3	0	0	?	0	0	?	?	0	0	0
Internal Capsule	1	0	0	0	3	0	0	0	0	0	0	3	0	1	1
External Capsule	1	0	0	0	3	0	0	0	0	0	0	3	0	0	0
Ventral Tegmentum	0	0	?	0	3	0	0	?	0	0	?	?	0	?	0
White matter adjacent to lateral ventricle	3	3	0	1	3	0	0	0	1	0	0	2	0	1	1
Parietal Lobe	0	0	0	0	3	0	0	0	0	0	0	1	0	0	0
Occipital Lobe	0	0	0	0	3	0	0	0	0	0	0	0	0	0	1
Temporal Lobe	3	0	0	1	3	0	0	0	0	0	0	0	0	0	0
Prefrontal Lobe	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0
Prefrontal Lobe, dorsolateral	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0
Frontal Lobe	3	2	0	1	3	0	0	0	2	1	0	0	0	0	0
Lateral Orbitofrontal	3	2	0	1	3	0	0	0		1	0	0	0	0	0
Anterior Cingulate	0	0	0	0	3	0	0	0	2	1	0	0	0	0	0

Appendix C.

Rating Scale for Areas of Brain Injury from Neuroimaging

(Completed by Medical Specialists during examination of scans.)

Study ID No.: _____ Name: _____

Date of Scan: _____ Type: _____ Rater: _____

Code for damage level to any structure:

Code	Definition
3	Major (>50%)
2	Unspecified/moderate (20-50%)
1	Minor (1-20%)
0	None
?	Unknown

Areas of Damage ***(ID No. of Circuit Involved)***

LEFT	RIGHT

Basal Ganglia Overall

Any Basal ganglia involvement	Any Basal ganglia involvement

Striatum

Caudate Nucleus (overall)	Caudate Nucleus (overall)
Caudate Nucleus (head) *(4)*	
Caudate Nucleus, dorsolateral head *(1)*	Caudate Nucleus, dorsolateral head *(1)*
Caudate Nucleus, ventromedial head *(2)*	Caudate Nucleus, ventromedial head *(2)*
Putamen	Putamen

Ventral Striatum

Nucleus Accumbens *(3)*	Nucleus Accumbens *(3)*
Olfactory tubercle *(3)*	Olfactory tubercle *(3)*

Pallidum

Globus Pallidus (overall)	Globus Pallidus (overall)
Globus Pallidus, medial segment *(4)*	
Globus Pallidus, lateral dorsomedial internal segment *(1)*	Globus Pallidus, lateral dorsomedial internal segment *(1)*
Globus Pallidus, medial dorsomedial internal segment *(2)*	Globus Pallidus, medial dorsomedial internal segment *(2)*
Globus Pallidus, rostrolateral internal segment *(3)*	Globus Pallidus, rostrolateral internal segment *(3)*
Ventral Pallidum *(3)*	Ventral Pallidum *(3)*

Substantia Nigra

Substantia Nigra (overall)	Substantia Nigra (overall)
Substantia nigra, rostrodorsal *(3)*	Substantia nigra, rostrodorsal *(3)*
Substantia nigra, rostromedial *(2)*	Substantia nigra, rostromedial *(2)*
Substantia nigra, rostrolateral *(1)*	Substantia nigra, rostrolateral *(1)*

Thalamus

Thalamus (overall)	Thalamus (overall)
Thalamus, ventral anterior *(4)*	
Thalamic Nuclei (a): ventralis anterior pars parvocellularis & medialis dorsalis pars paralamellaris *(1)*	Thalamic Nuclei (a): ventralis anterior pars parvocellularis & medialis dorsalis pars paralamellaris *(1)*
Thalamic Nuclei (b): medial ventralis anterior pars magnocellulariis & medialis dorsalis pars magnocellularis *(2)*	Thalamic Nuclei (b): medial ventralis anterior pars magnocellulariis & medialis dorsalis pars magnocellularis *(2)*
Thalamic Nuclei (c): posteromedial medialis dorsalis) *(3)*	Thalamic Nuclei (c): posteromedial medialis dorsalis) *(3)*

Other Areas of Subcortex

Subthalamic Nuclei	Subthalamic Nuclei
Locus Cerulus	Locus Cerulus
Hypothalamus	Hypothalamus
Dorsal motor vagus nucleus	Dorsal motor vagus nucleus
Internal capsule	Internal capsule
External capsule	External capsule
Ventral Tegmentum	Ventral Tegmentum

Cortex

White matter adjacent to lateral ventricle	White matter adjacent to lateral ventricle
Parietal Lobe	Parietal Lobe
Wernicke's area *(4)*	
Occipital Lobe	Occipital Lobe
Temporal Lobe	Temporal Lobe
Prefrontal Lobe	Prefrontal Lobe
Prefrontal Lobe, dorsolateral *(1)*	Prefrontal Lobe, dorsolateral *(1)*
Frontal Lobe (overall)	Frontal Lobe (overall)
Lateral Orbitofrontal cortex *(2)*	Lateral Orbitofrontal cortex *(2)*
Anterior Cingulate cortex *(3)*	Anterior Cingulate cortex *(3)*
Broca's area *(4)*	

Circuits Involved (and ID No.s)

1. Dorsolateral Prefrontal (1)	*1. Dorsolateral Prefrontal (1)*
2. Lateral Orbitofrontal (2)	*2. Lateral Orbitofrontal (2)*
3. Anterior Cingluate (3)	*3. Anterior Cingluate (3)*
4. Crosson's language-related circuitry (4)	

Any other significant features of brain scan:

Appendix D.

Assessment of Motor Signs

Study ID No.: _____ Name: _____ Rater: _____

Left Side

Body Part	**Level of Impaired Coordination* (Score)**

	Absent (0)	*Slight (1)*	*Moderate, Intermittent (2)*	*Moderate, most of the time (3)*	*Marked(4)*
Hand					
Arm					
Leg					
Foot					
Trunk					
Total *(mutiplied by level score)*					

Total score for Left side: _____

Right Side

Body Part	**Level of Impaired Coordination* (Score)**

	Absent (0)	*Slight (1)*	*Moderate, Intermittent (2)*	*Moderate, most of the time (3)*	*Marked(4)*
Hand					
Arm					
Leg					
Foot					
Trunk					
Total *(mutiplied by level score)*					

Total score for Right side: _____

***Explanation of Levels**

Level	Explanation
Absent	Absent
Slight	Slight and infrequently present
Moderate, intermittent	Moderate in amplitude and intermittently present
Moderate, present most of the time	Moderate and present most of the time
Marked	Marked in amplitude and present most of the time

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