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Dissociation of

Declarative and Nondeclarative Memory Systems

in Alzheimer's Disease, Parkinson's Disease,

and Ischaemic Vascular Dementia

by

Heather Lynn Gitlin

A dissertation submitted to the Graduate Faculty in Psychology
in partial fulfillment of the requirements for the degree of Doctor of Philosophy,
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Chair of Examining Committee

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Abstract

DISSOCIATION OF DECLARATIVE AND NONDECLARATIVE MEMORY SYSTEMS IN ALZHEIMER'S DISEASE, PARKINSON'S DISEASE, AND SUBCORTICAL ISCHAEMIC VASCULAR DEMENTIA

by

HEATHER LYNN GITLIN

Adviser: Professor Doreen Berman

The goals of this study were to: (1) investigate diagnostic similarities and differences between Alzheimer's disease patients (AD), Parkinson's disease patients with dementia (PD), and ischaemic vascular dementia patients (IVD); (2) compare memory test performance between these groups; and (3) study the relationship between neuropsychological performance and compromise to the white matter of the basal ganglia thalamo-cortical motor loop, as shown on MRI, in IVD and AD. The basis for this investigation was that patients with subcortical dementia (such as IVD and PD) exhibit impaired retrieval on declarative tests, impaired motor learning, and spared priming, while patients with cortical dementia (such as AD) exhibit impaired encoding on declarative tests, impaired priming, and spared motor learning. This was the first investigation of nondeclarative memory in IVD.

15 AD, 15 IVD, 14 PD, and 15 elderly control subjects (EC), similar in age, educational status, and dementia level (for AD, IVD, and PD), were administered three memory tests, the California Verbal Learning Test (CVLT), the Rotary Pursuit Test, and priming, as well as executive, language, and visuospatial tasks.

In a descriptive canonical discriminant function analysis, 81% of the patients were correctly classified, with most errors involving overlap between the IVD and PD groups, suggesting that IVD and PD are neuropsychologically similar.

According to a repeated measures MANOVA, performance of all demented groups on the CVLT recognition was below that of EC, but IVD and PD outperformed AD. On the rotary pursuit test, AD outperformed both IVD and PD and did not differ from EC. There were no differences between groups in priming. Thus a double dissociation in performance on declarative memory and motor learning was found between subcortical and cortical dementia patients.

According to a multiple regression analysis, rotary pursuit performance was the strongest predictor of subcortical white matter compromise, while the CVLT and priming did not even enter the multiple regression equation. These results, along with those of the MANOVA, suggest a role for the basal ganglia thalamo-cortical motor circuit in a nondeclarative memory task, motor learning.

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In Honor of . . .

My beloved grandfather, George Goldberg

. . . who at the age of 84 still does not understand why I am so interested in "old people." Surely it is because of his good example. Grandpa demonstrated the vitality possible in the later years by beginning a new and successful career just a few years ago. His love and humor have inspired me for over thirty years.

My darling cousin, Anastasia 'Sula' Baruchin

I have yet to meet anyone with the brilliance, talent, and grace she once exhibited. Alzheimer's disease stole these qualities from Sula at a very young age. While it is too late for her, I hope that someday we will know enough about memory to help others like Sula.

In Memory of . . .

My father, Sheldon Gitlin

November 9, 1937 - July 20, 1997

Though he lived long enough to know this dissertation was defended, he did not survive to celebrate my graduation. It would have meant a lot to him.

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INTRODUCTION

The study of the neuropsychology of human memory has relied on data provided by patients with either acquired or naturally occurring lesions interfering with memory performance. The study of memory function in amnesics elucidated the role of the hippocampus in declarative memory, and allowed investigation of the phenomenon of preserved nondeclarative memory. These two types of memory are now being investigated in various dementias because these disorders provide the opportunity to analyze the contributions of areas not damaged by amnesic syndromes. In particular, investigators have focused on the patterns of impairment and sparing of various types of memory in the cortical versus subcortical dementias.

In Huntington's disease (HD), which results from striatal dysfunction and is usually regarded as the prototypical subcortical dementia, there is a pattern of impaired retrieval of declarative information, but generally spared recognition. This is typically accompanied by a deficit in nondeclarative motor learning, with relatively spared priming. In Alzheimer's disease (AD), which is usually considered the prototypical cortical dementia, investigators have found a different pattern. Impaired retrieval of declarative information on recall is attributed to an encoding deficit, as recognition is not spared. Further, motor learning is spared, but impairment of priming is usually found. Studies of patients with Parkinson's disease (PD), a subcortical dementia resulting from dysfunction of the substantia nigra, show features of both, with a pattern similar to HD, except for a frequent finding of impaired priming. Although preliminary study of ischaemic vascular dementia (IVD), a subcortical dementia affecting periventricular white matter pathways in the extrapyramidal and pyramidal systems, has shown a pattern of declarative memory performance similar to that seen in HD and PD; nondeclarative memory has not yet been investigated in these patients.

In this study, declarative memory and two types of nondeclarative memory (verbal

priming and motor skill learning) will be compared in three patient samples: Alzheimer's disease, Parkinson's disease, and subcortical ischaemic vascular dementia. The first goal is to determine whether cortical and subcortical dementias impair different aspects of nondeclarative memory, priming (i.e. AD) and skill learning (i.e. PD and IVD). A second goal is to examine the relationship between two types of subcortical dementia, PD and IVD, in order to determine if the syndromes are characterized by distinct patterns or by overlapping patterns of effects on declarative and nondeclarative memory. The information gained in the study of these first two objectives will be used to draw conclusions about the relationship of impaired and spared processes in these disorders and their underlying neuroanatomy. Finally, the relationship between the declarative and nondeclarative memory patterns in the three dementias of interest and the overall pattern of neuropsychological functioning will be examined. Information gained from this analysis will provide evidence regarding the neuropsychological correlates of nondeclarative memory function.

The Cognitive Neuropsychology of Memory

The declarative/nondeclarative distinction in memory is based on the findings that: 1) there is a dissociation between performance on priming and declarative memory tasks in normal subjects, 2) there is a dissociation between the effect of levels of processing on performance on declarative and nondeclarative tasks in normal subjects, 3) nondeclarative memory is spared in amnesia, 4) declarative and nondeclarative processes can be differentiated ontogenetically and, perhaps, phylogenetically, 5) nondeclarative tasks tend to rely on automatic processes while declarative tasks tend to rely on effortful processes, and 6) nondeclarative memory is modality-specific while declarative memory is not. However, there are alternative explanations other than the postulation of separate memory systems (Crowder, 1989; Hirst, 1989; Roediger, Weldon, & Challis, 1989) to

explain the data.

Preserved Memory in Amnesia

Current study of declarative (or explicit) and nondeclarative (or implicit) memory derives from almost forty years of research, including investigations of memory patterns in amnesics (e.g., Brooks & Baddeley, 1976; Cermak, Lewis, Butters, & Goodglass, 1973; Cohen, 1984; Cohen & Corkin, 1981; Cohen & Squire, 1980; Corkin, 1965, 1968, 1984; Diamond & Rozin, 1984; Drachman & Arbit, 1966; Graf, Shimamura, & Squire, 1985; Graf, Squire, & Mandler, 1984; Jacoby & Witherspoon, 1982; Milner, 1965, 1966, 1968, 1972; Milner, Corkin, & Teuber, 1968; Nissen, Cohen, & Corkin, 1981; Ogden & Corkin, 1991; Scoville & Milner, 1957; Shimamura, 1986; Shimamura & Squire, 1984; Warrington & Weiskrantz, 1968, 1970) and normal subjects (e.g., Graf & Schacter, 1985, 1987; Grober, Gitlin, Bang, & Buschke, 1992; Hashtroudi, Chrosniak, & Schwartz, 1991; Hultsch, Masson, & Small, 1991; Schwartz & Hashtroudi, 1991). It has become clear that there are at least two memory systems (Nadel, 1994; Nissen, 1992; Schacter & Tulving, 1994), a declarative and a nondeclarative system, and investigators have turned their efforts toward dissociating different subsystems or processes among these major systems.

Weiskrantz (1989) pointed out that "the rare single case, if well chosen, show[s] what is possible . . . its importance in neuropsychology always lies in the disentanglement, that is, the dissociation, of a striking disorder from a background of otherwise intact performance" (p. 108). The dissociation of declarative and nondeclarative memory in amnesia was revealed by the intensive study of a single case, H.M., studied over a number of years by Brenda Milner, Suzanne Corkin, and their colleagues (Corkin, 1965, 1968, 1984; Milner, 1962, 1966, 1968, 1972; Milner et al., 1968; Nissen et al., 1981; Ogden & Corkin, 1991; Scoville, 1954; Scoville, 1968; Scoville & Milner, 1957). This patient was one of a series of patients with intractable

epilepsy who were treated with bilateral resections of the medial temporal area. One of the largest of these resections was performed on the patient H.M. in 1953, when he was 27 years old; the surgery included removal of two-thirds of the hippocampus and parahippocampal gyrus, prepyriform gyrus, amygdala, and uncus (Corkin, 1984; Milner, 1972; Ogden & Corkin, 1991; Scoville, 1968). This lesion resulted in an improvement in the seizure condition, but also a severe anterograde and partial retrograde amnesia, which persist to the present time (Ogden & Corkin, 1991).

As Ogden & Corkin (1991) point out, H.M. is probably the most studied case in neurological or psychological history; his deficits are thus well documented. Consistent with his amnesia, H.M. cannot recognize or recall testing stimuli, regardless of modality of input (Corkin, 1965; Drachman & Arbit, 1966; Jones, 1974; Milner, 1965; Scoville & Milner, 1957). However, he can learn a mirror-tracing task (Milner, 1962, cited in Milner, 1972), a mirror-reading task (Nissen et al., 1981), a short maze task (Corkin, 1965), a rotary pursuit task (Corkin, 1968), a bimanual tracking task (Corkin, 1968), a variant of the Tower of Hanoi puzzle (Cohen & Corkin, 1981), and how to do a mental rotation task (though he does not always show learning on the task itself; Ogden & Corkin, 1991). In addition, he shows savings on a short maze task 1 week and 2 years after training (Milner, 1972). H.M.'s disabilities and abilities have been summarized as impairment of long term memory, anterograde memory, and declarative memory; with sparing of immediate memory and remote memory, except for the period of retrograde amnesia (Ogden & Corkin, 1991).

Findings in this case have been replicated in patients with amnesia resulting from a variety of etiologies. In the past three decades, investigators have repeatedly demonstrated preserved memory in amnesics on many tasks, including jigsaw-puzzle construction (Brooks & Baddeley, 1976), mirror-reading (Cohen & Squire, 1980), verbal and perceptual priming (Graf et al., 1984; Shimamura, 1986; Warrington & Weiskrantz,

1968, 1972), rule-learning (Wood et al., 1982), rotary pursuit learning (Cermak et al., 1973), and the Tower of Hanoi puzzle (Cohen, 1984). In addition, amnesics can be successfully verbally primed on a variety of tasks, including word completion after exposure to homophones (Jacoby & Witherspoon, 1982); learning of real words, though not pseudowords (Diamond & Rozin, 1984; Cermak et al., 1985); and word association by paired associates (Shimamura & Squire, 1984) and category exemplars (Gardner et al., 1973; Graf et al., 1985). Such preserved nondeclarative memory occurs despite declarative memory deficits, as measured by free recall and recognition (Cohen, 1984; Graf et al., 1984; Warrington and Weiskrantz, 1970; Delis, Massman, Butters, Salmon, Cermak, & Kramer, 1991).

Defining Memory Systems

Memory systems have been described in a number of different ways. Most describe the aspects of long-term memory lost and preserved in amnesia as two opposite processes (cf. Weiskrantz, 1989), but few agree on the terms to be used. As Lockhart (1989) humorously points out, "current memory theory would seem to be suffering from a taxonomic crisis, if not a full-blown case of terminological chaos. The ubiquitous symptom is the dichotomy; the terms proceed two-by-two across the theoretical landscape like animals in search of an ark" (p. 3). The two dichotomous distinctions accepted most frequently in the current literature, declarative and nondeclarative, will be used here for the sake of clarity and to maximize comparability between studies. Thus the memory lost in amnesia will be defined as declarative memory, and that retained as nondeclarative memory.

The declarative/nondeclarative distinction is based on the nature of the information to be remembered (Hirst, 1989; Squire, 1987). The systems organization which will be used here is that advanced by Squire and his colleagues (Cohen, 1981, 1984; Squire, 1982, 1987, 1994; Squire & Cohen, 1984; Squire & Zola-Morgan, 1991) and influenced

by Tulving (1972, 1983). Squire's (1994) definitions, shown in Figure 1, fit into a framework in which memory is divided into declarative and procedural elements, and then further separated such that declarative memory is divided into episodic and semantic memory and procedural memory is divided into skill-learning, priming, and simple classical conditioning, as well as other possible processes.

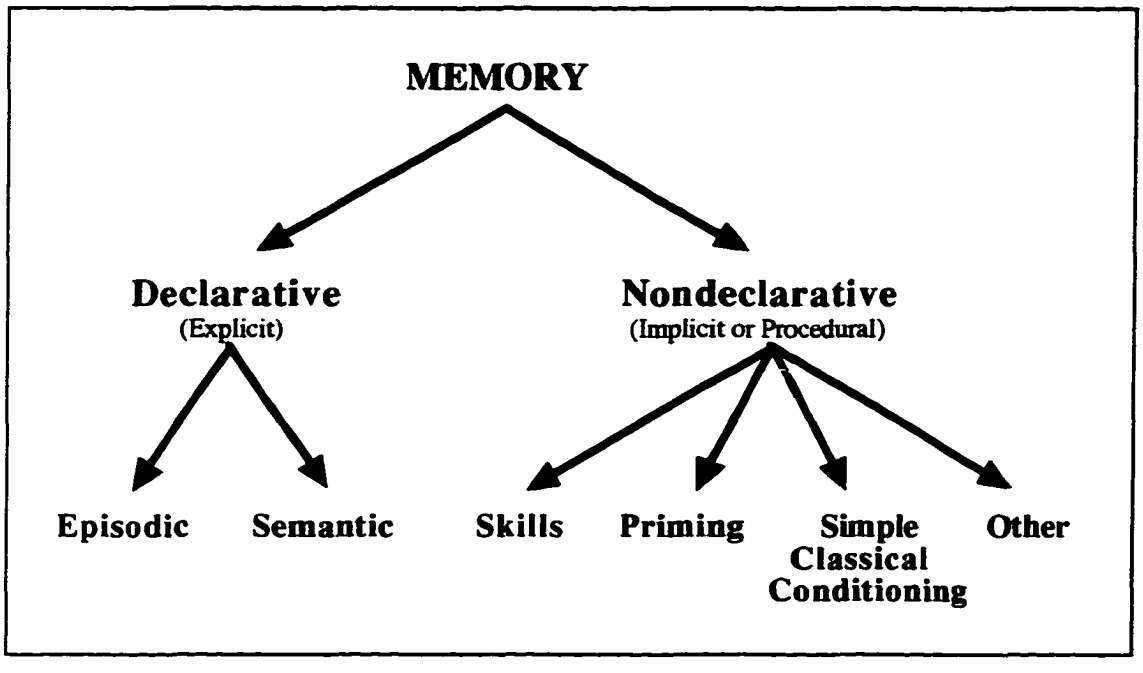

Figure 1. Squire's taxonomy of memory. (Adapted from Squire, 1987, Figure 44, p. 170).

Squire (1987) defines *declarative memory* as memory which is directly accessible to conscious recollection. Declarative memory is acquired via conscious learning and recollection and includes facts and data which "can be brought to mind as a proposition or an image" (Squire, 1987, p. 158). This type of memory is impaired in amnesia and is time-tagged (Thompson, 1988). Squire (1987) originally used the term *procedural memory* to indicate the memory underlying skills or modifiable cognitive operations, in which the learned information is embedded in procedures or is exhibited as changes in how pre-existing cognitive operations are accomplished, and there is no conscious access

to the knowledge base. He (Squire, 1994; Squire & Zola-Morgan, 1991) now uses the more inclusive term *nondeclarative memory.*

Another set of terms, explicit and implicit, are still in common use. The implicit/explicit distinction classifies memory according to whether or not recall is a conscious[1] process (Hirst, 1989). Explicit memory is consciously recalled; implicit memory is that recalled without conscious effort. Further, implicit memory, and occasionally procedural memory, is often referred to via one of the phenomena by which it is demonstrated, that is, priming. *Priming* is facilitation of performance resulting from prior exposure to the material for which memory is being measured (Salmon & Heindel, 1992; Shimamura, 1986); it occurs when a pre-existing declarative representation is activated (Squire, 1987), without conscious awareness.

The Declarative - Nondeclarative Distinction

The dissociation between declarative and nondeclarative memory has led investigators to try to characterize their differences and similarities, in the hope that such information might provide cues to their neuroanatomical substrate or substrates.

According to Squire (1987), nondeclarative learning is slower than declarative learning. One trial learning is more likely in declarative learning situations than nondeclarative ones (with the exception of classical conditioning). Nondeclarative memory is usually more of a slow, automatic, but incremental process. However, priming effects may last longer than those of declarative learning (Jacoby & Dallas,

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[1] *Consciousness*, in this review, will refer to the subject's awareness of his/her cognitive processing; likewise, unconsciousness will refer to a lack of awareness of cognitive operations on the part of the subject. As Hirst (1989) points out, it is difficult to interpret 'consciousness'. He argues that it cannot refer to intentionality; explicit memory can be unintentional, such as when a stimulus acts as an overpowering cue. It cannot refer to process, as explicit memories can be retrieved without the use of effortful strategy. In addition, amnesics can apply strategies, and they do not suffer a uniform retrograde amnesia, which would suggest a lack of use of strategy.

1981; Scarborough, Cortese, & Scarborough, 1977; Scarborough, Gerard, & Cortese, 1979; Tulving, Schacter, & Stark, 1982). For example, Tulving and his colleagues (Tulving et al., 1982) found nondeclarative word fragment completion to remain stable from a period of one hour to one week past study, while recognition performance declined. However, Squire and his colleagues (Squire, Shimamura, & Graf, 1987) found priming effects on a word-fragment completion task in amnesics to be rather short-lived.

Squire (1987, 1994) also points out that nondeclarative memory tends to be modality-specific and is rarely accessible to information processing systems other than those involved in the original learning. Declarative memory is, on the other hand, considered to be readily available to multiple processing and response systems. For example, when Graf and colleagues (Graf et al., 1985) primed amnesics and controls with aurally or visually presented words, subjects performed better on the priming task when tested in the same modality as learning took place; this was not true for the recall task.

Priming and declarative memory are differentially affected by encoding and retrieval characteristics such as level of processing (Graf, Mandler, & Haden, 1982; Jacoby & Dallas, 1981), similarity between encoding and retrieval conditions (Roediger et al., 1989), and semantic relatedness of stimuli (Carroll & Kirsner, 1982; Graf & Schacter, 1985). For example, both semantic and nonsemantic orienting processes (e.g. rating likability or counting number of vowels, respectively) equally improve both word stem completion priming (Graf et al., 1982) and perceptual word identification priming (Jacoby & Dallas, 1981), but not free recall (Graf et al., 1982) or recognition (Jacoby & Dallas, 1981).

The two processes are also differentially affected by certain experimental manipulations. Retroactive and proactive interference do not appear to impair nondeclarative memory as they do declarative memory (Graf & Schacter,1987). Graf and Schacter believe this is because declarative memory for an item pair depends on the

distinctiveness of the representation of the item and how it is distinguished from other items in the list, while nondeclarative memory depends on the components of the representation that relate the words within a pair together; interference only affects item distinctiveness. In support, they cite prior evidence of the importance of distinctiveness in explicit memory (Jacoby, 1974; Moscovitch & Craik, 1976; Watkins & Watkins, 1975).

Finally, there may be both ontogenetic and phylogenetic differences in declarative and nondeclarative memory. Preliminary evidence (Parkin, 1989; Parkin & Streete, 1988) suggests the emergence of two separate memory systems in infancy, first (in early infancy) one underlying novelty preference (or habituation) and classical conditioning, and fitting within Squire's (1987) conception of nondeclarative memory, and second (at about one year of age) a system underlying recording of experiences that is identified as explicit memory. Systems which develop earlier and later in the human infant appear to parallel those preserved and lost, respectively, in amnesia (Schacter, 1984). Similarly, research in elderly subjects shows that while declarative memory decreases with age (Hultsch, Masson, & Small, 1991), certain aspects of nondeclarative memory, particularly priming, may not (Hashtroudi, Chrosniak, & Schwartz, 1991; Laver & Burke, 1993; cf. Hultsch et al., 1991). Similarly, as Rozin (1976) describes, nondeclarative processes, such as classical conditioning, are available to phylogenetically more primitive species. Rozin proposes the theory that declarative memory evolved as a recent adaptation and advance over the inflexible, modality-specific procedural memory.

Problems with and Alternatives to Memory Systems

A number of authors have pointed out the difficulty in inferring memory systems from the presence of performance dissociations. Roediger and his colleagues (Roediger et al., 1989) point out that most researchers choose only one task to represent declarative memory and one to represent nondeclarative memory. The result is that "any form of interaction can be interpreted as reflecting operation of the systems" (p. 18). They

propose that dissociations on priming and declarative memory tasks can be explained by the encoding specificity principle (Tulving, 1983), which states that recall improves as the similarity between retrieval and encoding conditions is maximized. Roediger and colleagues (Roediger et al., 1989) acknowledge that declarative and nondeclarative tests require different retrieval operations or the retrieval of different forms of information, and thus each benefit from different encoding processes. However, they propose that most priming tests, which are affected by surface features, are data driven, and most declarative tests are conceptually driven. Thus results may better be explained by the type (Roediger & Weldon, 1987) or modality (Blaxton, 1985, cited in Roediger et al., 1989) of processing required than by separate memory systems.

Dissociations can be found within a single independent variable when different testing procedures are used (Crowder, 1989). Thus one has to postulate additional memory systems to explain each dissociation (Roediger et al., 1989). In Crowder's (1989) opinion, nondeclarative memory differs from declarative only in that there is no coding of temporal context. He also argues against explaining dissociations by positing the presence of multiple memory systems (such as declarative and nondeclarative memory), because it is possible to demonstrate dissociations within them. As he states, "This does not sound to me like a distinction between procedural and declarative memory as two systems, as such. It sounds like one element of normal memory--the knowledge that *that* processing occurred in *that* context--is compromised" (Crowder, 1989, p. 290, italics in original).

Perhaps the problem lies not in the type of processing, but the particular memory systems postulated. Roediger and colleagues (Roediger et al., 1989) acknowledge that their theory does not account for amnesics' ability to perform conceptually-driven priming tasks. Further, the declarative versus nondeclarative distinction itself does not account for the finding that some recognition may be spared in amnesia (Hirst, 1989).

Could another categorization of memory systems explain the data? Some investigators have described the pattern found in amnesia as an impairment of episodic memory with a sparing of semantic memory (Kinsbourne & Wood, 1975; Wood et al., 1982; Parkin, 1982). However, Squire (1987) argues against this, citing work demonstrating semantic memory impairment in amnesia (Cohen & Squire, 1981; Shimamura & Squire, 1987; Zola-Morgan et al., 1983). Squire (1987) agrees that semantic memory, especially for recently acquired information, is impaired, but points out that amnesics retain some episodic memories, from before the period of retrograde amnesia (Zola-Morgan, Cohen, & Squire, 1983).

Finally, as Squire (1987) points out, the finding of a double dissociation in one direction does not necessarily indicate that declarative and nondeclarative learning are always dependent on different systems. The example he uses is that of word priming and word recall. Word priming can be impaired while word recall is intact. However, is it possible that the opposite could occur, that word priming could be impaired with word recall remaining intact? If not, then we cannot say for sure that these systems are functionally and anatomically independent. A single system might contribute to both processes, perhaps to a different extent or at different times.

The Neuroanatomy of Memory Systems

With the advent of advanced neuroimaging techniques, there has been a recent focus on memory systems as anatomical entities. Thus Willingham (1992, p. 167) defines a *memory system* as "a set of processes and representations, instantiated in particular neural structures, that together serve a memory function. A particular process or representation may participate in more than one system, but there is little if any flexibility in the way they are used to solve memory tasks; they always operate the same way, but may be used in conjunction with different processes and representations as part

of another memory system". Further, he provides three criteria which a separate system must meet. It must 1) operate independently, 2) serve a unique function, and 3) have a unique neural substrate. This view has greatly expanded upon earlier work which focused only on the hippocampus and diencephalon, seen as the areas involved in declarative memory, and has encouraged researchers to search for the substrate of nondeclarative learning. There has been less work involving the neuroanatomical basis of priming than procedural learning; this may be a result of the disagreement of the theoretical relationship of priming to declarative memory.

The Hippocampus, Diencephalon, and Declarative Memory

Squire and colleagues (1987; Squire, Cohen, & Nadel, 1984) believe that medial temporal structures are involved in the consolidation of memory that results in long-term declarative memory (as opposed to short-term declarative or long-term procedural memory). These structures perform some type of time-limited function during the period of consolidation, in order that memory storage and retrieval may take place in other sites, especially the neocortex. Following consolidation, medial temporal structures are involved either less, or not at all, in memory storage.

In this regard, Mishkin (1978) proposed that damage to both the hippocampus and amygdala is required for amnesia. Hippocampal lesions in monkeys result in some memory impairment, but this lesion combined with a lesion of the amygdala produces a more severe impairment (Mishkin, 1978; Murray & Mishkin, 1986; Squire & Zola-Morgan, 1985). The amygdala appears to mediate cross-modal associations (Murray & Mishkin, 1986), while the hippocampus does not.

Diencephalic amnesia has become a standard term used to refer to the amnesia caused by damage to the medial thalamus, mammillary bodies, or contained fiber tracts (Markowisch, 1991). Etiology varies, but the most common cause of diencephalic amnesia is Korsakoff's syndrome and the severe thiamine deficiency resulting from

alcoholism. Other causes include infarcts, degenerative disorders, viruses, trauma, tumors, and associated neurosurgery.

The mediodorsal nucleus (MD) is the area of the thalamus most frequently associated with memory, though there is not total agreement (Markowitsch, 1991). Victor (Victor, Adams, & Collins, 1971) reported that, in a series of cases involving either MD and the mammillary bodies or the mammillary bodies alone, only those patients with damage to both structures evidenced amnesia. However, Brion and Mikol (1978, cited in Squire, 1987), reported an opposite finding, that in a series of amnesic patients, some had damage to both areas and some had damage only to the mammillary bodies. The main limitation to implicating MD is that the cases with the most severe memory impairment involve lesions to more extensive areas than just this nucleus (Markowitsch, 1991). An example is Squire's amnesic patient N.A. (Squire et al., 1987), who was originally thought to have a circumscribed MD lesion. MRI showed that he also had damage to the internal medullary lamina, most likely affecting MD, ventral anterior (VA), ventral lateral (VL), and midline nuclei as well as the mammillothalamic tract; the left anterior hypothalamus and left and right posterior hypothalamus; and the right anterior temporal lobe.

The Basal Ganglia Thalamocortical Motor Circuit

The extrapyramidal motor system has been implicated in skill learning, and parallel circuits between the thalamus, striatum, and the frontal cortex are beginning to be studied as components of procedural memory systems.

Alexander, DeLong, and Strick (1986) describe five parallel basal ganglia thalamocortical circuits: motor, oculomotor, dorsolateral prefrontal, lateral orbitofrontal, and anterior cingulate. The motor circuit appears to be involved in PD, and both the motor and oculomotor circuits in HD. (Other circuits are likely involved to some extent but their function is not yet well understood.) The motor circuit is shown in Figure 2. It

appears to be involved in motor programming and movement control, including the control of the direction and velocity scaling of the movement. Damage to these areas likely underlies deficits in the predictable tracking required in many motor learning tasks, such as the rotary pursuit test.

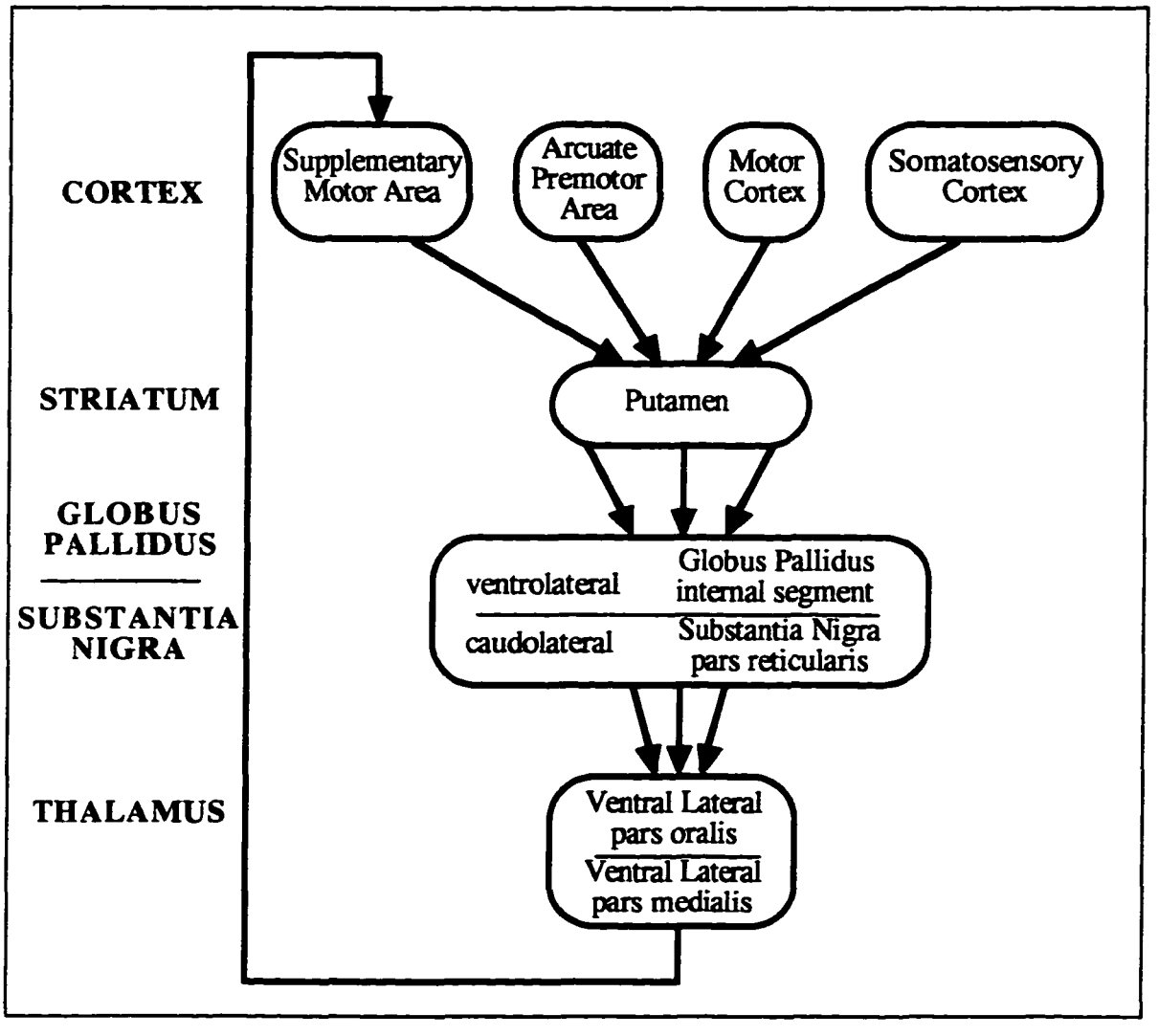

Figure 2. Basal ganglia thalamocortical motor circuit. The striatum receives projections, in an open loop, from the primary motor cortex, supplementary motor area, arcuate premotor area, and somatosensory cortex. This information is progressively funneled through the globus pallidus and substantia nigra, to the ventral lateral nucleus of thalamus, in a parallel, segregrated, somatotopic fashion. The thalamus then projects back to the supplementary motor area in a closed loop. (Adapted from Alexander, DeLong, & Strick, 1986, Figure 2, p. 360 & Figure 3, p. 364).

The motor circuit appears to satisfy Willingham's (1992) criteria for a memory system. He proposes that one of the motor skill systems subserved by Alexander and colleagues' (1986) circuits is responsible for making movements spatially and temporally invariable and underlies performance on the rotary pursuit task (Willingham, 1992). It deals with the sequencing of motor information (but not general sequencing, Willingham, 1992) and is impaired in HD and PD. This is supported by evidence that HD and PD subjects are impaired on repetitive but not random tracking tasks (Flowers, 1978; Harrington, Haaland, Yeo, & Marder, 1990; Heindel, Butters, & Salmon, 1988; Heindel, Salmon, Shults, Walicke, & Butters, 1989; Knopman & Nissen, 1991; Willingham, 1992; Willingham & Koroshetz, 1990; Willingham, Koroshetz, & Peterson, 1996).

The motor circuit is dependent upon a high-level planning loop between the basal ganglia, thalamus, and supplemental motor area, which is responsible for sequencing movements on the basis of visual feedback. Primary motor cortex neurons are associated with movement onset, while supplementary motor area neurons are associated with preparatory set activity before the movement onset (Watts & Mandir, 1992). In PD, disruption of SMA neuronal activity results from defective input from the internal segment of the globus pallidus via the ventrolateral thalamus. This, in turn, causes poor preparation of the motor cortex neurons for efficient initiation and execution of movement; the result is bradykinesia.

Until recently, the role of fiber tracts was underestimated in the study of memory (Markowitsch, 1988). However, the nuclei involved in the motor circuit are interdependent and rely on fiber tracts for intact input and output in order to function properly. It is these fiber tracts that are damaged in IVD, raising the question of the relationship between the memory disorders in PD and IVD.

Clinical Profiles of Dementia Syndromes

It is difficult, if not impossible, to appreciate the sparing of an isolated neuropsychological function, such as implicit memory, in the dementias, without a consideration of the full neuropsychological and clinical profile of these disorders. As Weiskrantz (1989) points out, no one neuropsychological ability can be considered in a vacuum. The significance of a particular function is assigned in a relative sense, in consideration of the myriad other functions which may or may not be available to the subject.

Describing dementia as an individual entity has limited its utility both clinically and scientifically. It is much more fruitful for research to concentrate on the differences between the various types of dementia (Adams, Craig, & Parsons, 1986). DSM-IV labels fail to separate out these differences, thus in the present paper the various types of dementia are referred to not by their DSM-IV labels, but by the most descriptive labels currently in use.

Alzheimer's Disease

AD is a cortical dementia characterized by an insidious onset and progressive course. Severe memory impairment is the primary and usually the presenting symptom. Other cortical dysfunctions may be evident at presentation or appear as the disease progresses. These include deficits in attention, language, visuospatial and perceptual skills, praxis, and executive skills. Personality often changes as the disease progresses. Neurologically, the patient may appear normal in the early stages of the disease or there may be some of the abnormal signs also found in normal elderly persons (e.g. snout reflex, grasp reflex, jaw jerk, rigidity, myoclonus). Paranoid ideation may also be present. In later stages the patient may be apathetic or irritable, agitated, incontinent, and have sleep abnormalities. Many patients eventually become incommunicative and vegetative.

General Clinical Profile

A few different sets of diagnostic criteria for AD have been used, but they all share two basic requirements: 1) gradual onset and progressive course, and 2) the exclusion of other neurologic, psychiatric and medical disorders which could impair cognition (Morris & Rubin, 1991).

The most highly accepted criteria are those established by a combined task force from the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) (McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984). The criteria for *probable AD* are: 1) dementia, as demonstrated by a mental status examination and confirmed by neuropsychological evaluation, 2) deficits in two or more areas of cognition, 3) insidious onset and progressive deterioration of memory and cognitive functions, 4) an absence of disturbance of consciousness, 5) onset between ages 40 and 90, and 6) an absence of neurological or systemic disorders which could account for a progressive decline in memory and cognition. *Possible AD* is diagnosed when: 1) there is some variation in the onset, presentation, and course of the dementia but the other criteria described above have been met, 2) there is a second neurological or systemic disorder which may be sufficient to cause dementia, but is not believed to be the cause in the targeted case, or 3) a single progressively deteriorating cognitive deficit is noted in the absence of another identifiable cause. *Definite AD* can only be diagnosed in the presence of all the criteria for probable AD along with histopathologic evidence from autopsy or biopsy.

AD currently appears to be a syndrome which does not have a single etiology (Blass, 1993; Blass, Ko, & Wisniewski, 1991; Trèves, 1991). Some cases are clearly familial, transmitted in an autosomal dominant fashion with incomplete penetrance or by multigene inheritance. However, in the majority of cases etiology is unclear and may

involve both environmental and hereditary factors. While the disease is more commonly seen in females (Trèves, 1991), this may simply be a function of longer lifespan.

Neuropathology and Neurochemistry

The primary neurochemical lesion in AD consists of decreased cholinergic activity, associated with degeneration of acetylcholinergic cell bodies, especially in the nucleus basalis of Meynert of the basal forebrain, the major source of neocortical acetylcholine. The degeneration of neurons in the nucleus basalis of Meynert results in a reduction in choline acetyltransferase, the enzyme which synthesizes acetylcholine in both the neocortex and hippocampus (McDonald & Nemeroff, 1991).

A variety of other neurotransmitter changes are also noted. There is a loss of nerve growth factor receptors in the nucleus basalis of Meynert, and a reduction of norepinephrine and serotonin associated with degeneration of the locus coeruleus and dorsal raphe nucleus, respectively (for a review, see Blass et al., 1991). In addition, levels of gamma-aminobutyric acid, somatostatin, and corticotropin releasing factor have been found to be reduced in various areas. As Arnold and his colleagues (Arnold, Hyman, Flory, Damasio, & Van Hoesen, 1991, p. 112) state, "The severe and consistent changes we and others have found in the hippocampus-entorhinal cortex amygdala system in AD, as well as the isolation of interconnected laminae of neocortical regions, are likely to play a major role in the learning impairment of AD patients."

A variety of anatomic features are characteristic of AD (Blass, 1993; Blass et al., 1991; McKhann et al., 1984; Moss & Albert, 1988; Perl & Pendlebury, 1986). Grossly, there is cortical atrophy and enlargement of the lateral and third ventricles. Neuritic plaques, or damaged terminal buttons containing amyloid protein are present in the cortex, especially the inferior frontal and parietal regions, but also in the hippocampus, claustrum, nucleus basalis of Meynert, hypothalamus, and dorsorostral brain stem. Neurofibrillary tangles, or abnormal protein fibers derived from the cytoskeleton, are also

widespread in AD, but are not specific to the condition. They are most prominent in the limbic cortices of the ventromedial temporal lobe and the neocortical areas of the lateral temporal lobe. The entorhinal cortex (area 28) and hippocampal subiculum/CA1 zone are the most severely affected (Arnold et al., 1991). Granulovacuolar degeneration of pyramidal cells is found in the hippocampus and Hirano bodies (structures containing actin, actin-related proteins, and tau protein) are found in some cells (Blass et al., 1991).

AD presents on CT and MRI with cortical atrophy and enlarged ventricles, though there is significant overlap between patients with AD and normal elderly subjects (Albert & Lafleche, 1991; Benson, 1986). Because of this overlap, as well as the numerous causes of cortical atrophy, the diagnosis of AD must also be based on clinical neurological and neuropsychological features (McKhann et al., 1984). The presence of periventricular lucencies is controversial, due to varying diagnostic criteria in different laboratories, although white matter abnormalities do appear to be more common in severe AD than in normal aging (Albert & Lafleche, 1991). Studies of cerebral metabolism, as measured by positron emission tomography, and cerebral blood flow, as measured by single photon emission computerized tomography, show decreased metabolic activity in the association cortices, especially in the temporal and parietal lobes (Albert & Lafleche, 1991; Benson, 1986). The pattern is usually symmetric, with primary motor, somatosensory, and occipital cortices relatively spared. Electroencephalography reveals increased generalized slow-wave activity in some AD patients (McKhann et al., 1984).

Neuropsychological Profile

AD is associated with a variety of changes in neuropsychological and psychiatric status. These include a primary disturbance in memory, as well as loss of orientation and attentional capacity, deterioration of linguistic, visuospatial, and executive functions, mood and personality changes, psychotic behavior, and psychomotor disturbances. (For a more comprehensive review see Moss & Albert, 1988). Abstraction ability tends to

decline early in the course of AD but is not as severe as in other cortical dementias such as Pick's disease (Moss & Albert, 1988) and IVD (Libon, Swenson, Malamut, Scanlon, Coslett, & Sands, 1993). Attention is often relatively intact in the early phases but deteriorates with progression of the disease. Word-finding deficits are common early in the disease and are evident in conversation as well as on tests of confrontation naming and verbal fluency. These deficits progress to a fluent aphasia with severe comprehension deficits. Spatial impairments are usually mild at first but increase in severity as the disease progresses. However, deficits interfere with performance on visuospatial tasks, and Alzheimer's patients tend to be perseverative and stimulus-bound (Moss & Albert, 1988).

Deficits in immediate and delayed explicit recall, both in the verbal (Kramer, Delis, Blusewicz, Brandt, Ober, & Strauss, 1988; Massman, Delis, & Butters, 1993) and visual domains have been well documented. Visual and verbal memory deficits tend to be of similar severity in AD, as opposed to the situation in vascular dementias where more focal signs are found (Moss & Albert, 1988). Recognition memory is also impaired (Kramer et al., 1988; Massman, Delis, & Butters, 1993).

Personality changes, especially involving apathy and disinterest, are common in AD. A reactive depression following memory loss is common in the early stages of the disease (Moss & Albert, 1988).

Parkinson's Disease

Motor symptoms of PD include bradykinesia, progressing to akinesia, difficulty in the initiation and cessation of movements, festinating gait, cogwheel rigidity, resting tremor, a characteristic facial mask deplete of expression, dysarthria, micrographia, stooped posture, and decreased postural reflexes. Affectively, depression is a frequent finding. Cognitive symptoms include bradyphrenia, a slowing of thought processes with decreased concentration and attention span.

General Clinical Profile

The course of PD is usually described in terms of the stages suggested by Hoehn and Yahr (Hoehn, 1992; Hoehn & Yahr, 1967), as follows. Stage I is associated with unilateral involvement (tremor, rigidity, akinesia, or postural disturbance) and minimal or no functional impairment. In Stage II, there is bilateral or midline involvement, with or without axial signs, but balance is normal. By Stage III, balance and general level of functioning begin to show impairment, but the patient is still independent. Stage IV is associated with a disabled state in which the patient is able to stand and walk but is highly impaired in level of functioning and dependent for at least some activities of daily living. Finally, in Stage V, the patient is confined to a wheelchair or bed, unless assisted. The duration of the illness varies, but Hoehn and Yahr (1967) reported that two-thirds of their sample, which had a mean age of 55.3 at onset of the disease, died within 9 years, and four-fifths within 14 years. In general, duration is probably underestimated because of the insidious nature of the onset (Hoehn, 1992). Most patients do not seek medical care until symptomatology interferes with functioning, since many of the early symptoms are erroneously interpreted as a result of normal aging. Levodopa therapy improves quality of life and slows the progression of the illness (Hoehn, 1992).

Neuropathology and Neurochemistry

PD results from degeneration of the nigrostriatal bundle, a dopaminergic pathway from the substantia nigra to the caudate and putamen. In idiopathic PD, there is degeneration of the pars compacta of the substantia nigra. Lewy bodies (cytoplasmic inclusions) are found in the substantia nigra, locus coeruleus, dorsal vagal nucleus, and reticular formation (Lishman, 1987). Sometimes neurofibrillary tangles and plaques are also found and there has been some controversy regarding whether the dementia in PD is a result of PD or AD pathology (i.e. Lewy bodies vs. neurofibrillary tangles and plaques). Recent evidence supports the independence of dementia in PD from AD type pathology

(Xuereb, Tomlinson, Irving, Perry, Blessed, & Perry, 1990).

Upon gross neuropathological examination, there is enlargement of the lateral and third ventricles. There is a loss of pigment from the substantia nigra pars compacta, with moderate to severe nerve cell loss; degeneration is more frequent in the ventral tier, relatively sparing the dorsal tier (Gibb, 1992). Lewy bodies are found in many of the remaining cells. Degeneration and Lewy bodies also occur in the locus coeruleus, ventral tegmental area, nucleus basalis of Meynert, raphe nuclei, thalamus, cerebral cortex, and the autonomic nervous system. Demented patients frequently exhibit neurofibrillary tangles and neuritic plaques in the neocortex and hippocampus. There is a large cell loss in the nucleus basalis of Meynert and Lewy bodies are present.

The primary neurochemical lesion is a selective depletion of striatal and nigral dopamine (Graybiel, Hirsch, & Agid, 1990); PD results after a depletion of about 66% (Birkmayer & Riederer, 1986). Decreased dopamine is also found in the limbic system and this may account for the affective and personality changes occurring in the disorder. Acetylcholine deficiency in the globus pallidus, putamen, and frontal cortex is present, but cholinergic findings in the striatum are normal. Loss of cholinergic cell bodies in the nucleus basalis of Meynert is present to a varying extent; such cell loss usually correlates with level of dementia. Nigrostriatal, limbic system, and hypothalamic noradrenergic systems are also affected to some degree, as may be serotonin, neuropeptide, and gamma-aminobutyric acid (GABA) levels.

Imaging studies are indicative of cell loss and extrapyramidal dysfunction. MRI reveals signal attenuation in the substantia nigra of patients with idiopathic PD (Olanow, 1992). Hypermetabolism in the basal ganglia and thalamus, correlated with disease severity, is found with PET scans (Eidelberg, 1992). Variations of this technique, using F-fluoro-L-dopa (F-dopa), show decreased dopamine uptake.

Neuropsychological Profile

Conceptual ability and set maintenance and shift are diminished in PD. Patients with PD achieve fewer categories than controls, and frequently have higher rates of perseverative or nonperseverative errors on the Wisconsin Card Sorting Test (Lichter, Corbett, Fitzgibbon, Davidson, Hope, Goddard, Sharples, & Pollock, 1988). Further, PD patients are deficient in performance on tests of prefrontal cortical function. Executive deficits may permeate performance and thus contaminate studies of other tasks. Cools and colleagues (Cools, Van Der Bercken, Horstink, Van Spaendonck, & Berger, 1984) describe the deficiency in PD as a deficit in 'central programming,' particularly in 'shifting aptitude.'

The majority of PD patients suffer from motoric speech difficulties (Cummings, Darkins, Mendez, et al., 1988) characterized by monotonous pitch and volume, short phrases, and impaired prosody. Nonverbal communication is inhibited by the masked facies (Levin, Tomer, & Rey, 1992). Deficits in cognitive aspects of language in PD, though the focus of much investigation, are less clear, mainly because of difficulties in separating language from other neuropsychological functions. Complex syntactical functions of expressive and receptive language are impaired. Vocabulary is preserved. Naming has been found to be deficient in some studies and preserved in others. Investigations of word retrieval using a verbal fluency paradigm are also inconclusive, with mild deficits of retrieval to letter and semantic category shown in some studies.

Studies of visual analysis and synthesis in PD have shown deficits in visual perception, visual discrimination (Lichter et al., 1988), pattern completion (Huber, Shuttleworth, Paulson, Bellchambers, & Clapp, 1986), embedded figures, and contrast sensitivity. In fact, according to Levin and her colleagues (Levin et al., 1992), visuospatial impairments are the type of deficit most frequently reported in PD. However, like language abilities, these are difficult to tease out from other

neuropsychological functions. A deficit in facial recognition has been found, but measures of this function may be unduly affected by task requirements (Levin, 1992). A deficit in the ability to recognize faces from pictures may be secondary to other visuoperceptual anomalies. An impairment in judgment of orientation (Lichter et al., 1988) has generally been found; but not when the investigators controlled for motor requirements of the task. Performance of subjects with PD is also deficient on tests of constructional praxis (Lichter et al., 1988), even when timing and motor demands are minimized; performance on graphoconstructive tasks is reported as impaired in some studies, with normal performance noted in others.

Numerous studies have shown subjects with PD to be impaired on measures of explicit recall, in both the verbal and visual domains (Huber et al., 1986; Massman, Delis, Butters, Levin, & Salmon, 1990). In addition, subjects with PD are hypersensitive to proactive interference on recall tasks. Recognition appears to be relatively spared, though there may be a higher tendency toward false positive responses in PD. With regard to implicit memory, PD, at least when accompanied by dementia, is associated with an impairment in procedural motor learning (Saint-Cyr, Taylor, & Lang, 1988; Heindel et al., 1989) and semantic priming (Heindel et al., 1989).

Depression is frequently found in subjects with PD (Huber, Shuttleworth, Paulson, Bellchambers et al., 1986; Lichter et al., 1988). There is some controversy regarding whether this depression is reactive or part of the entire clinical picture.

The clinical features of PD are consistent with those of a subcortical dementia. As noted by Freedman (1990), most studies addressing the subcortical-cortical differentiation in dementia have used PD as the prototypical subcortical model and AD as the prototypical cortical model. Such work has been the focus of Huber and his colleagues (Huber, Shuttleworth, & Freidenberg, 1989; Huber, Shuttleworth, Paulson, Bellchambers et al., 1986), who have found two distinct syndromes to be evident. In

their study, subjects with PD were shown to exhibit mild declarative memory and visuospatial impairments and depression, while those with AD showed severe impairment of overall mental, visuospatial, and memory functions, language and praxis deficits, and depression (Huber, Shuttleworth, Paulson, Amaducci et al., 1986), even when equated for level of dementia (Huber et al., 1989). AD subjects were impaired on tests of orientation; recent, immediate, and remote memory; constructional ability; praxis; and naming. PD subjects were impaired in recent memory but showed normal immediate memory and only slight remote memory difficulties. Visuospatial reasoning, only mildly impaired in the AD group, was more impaired in the PD group. PD patients were also more impaired than AD subjects on a test of verbal fluency and they showed depression, which was not seen in the AD group. The authors conclude that these performance patterns support the traditional cortical-subcortical separation of dementia syndromes. However, others (Korczyn, 1991) disagree that the distinction is so simple, due to frequent coexistence of symptoms of PD and AD.

Ischaemic Vascular Dementia

Vascular dementias are the second most common cause of dementia (Lishman, 1987); the most common is AD. A variety of vascular dementias have been described, with most attention given to multi-infarct dementia. However, there is now substantial evidence indicating that the subcortical vascular dementias (IVD) are not covered within the scope of the multi-infarct dementia diagnosis. Multi-infarct dementia is associated with large cerebral artery infarction, while IVD is associated with subcortical small vessel involvement (Wallin & Blennow, 1993).

Wallin and Blennow (1993), in a comprehensive review of vascular dementias, describe three subcortical types associated with hyalinosis, or endothelial swelling related to vessel wall transformation. These are lacunar dementia, Binswanger's disease (BD; Alzheimer, 1902, cited in Román, 1987), and subcortical white-matter dementia. In these

conditions, small periventricular arterioles are damaged. In lacunar dementia this leads to damage to the deep gray nuclei, such as the basal ganglia and thalamus (Cummings, 1992). In BD and subcortical white-matter dementia, this leads to destruction of the periventricular white matter. The effects are also frequently referred to as periventricular white matter alterations, PWMA. The focus here is on these latter processes, collectively described as IVD.

General Clinical Profile

IVD is a progressive dementing condition usually presenting at midlife with insidious onset, focal neurological and neuropsychological signs, cognitive decline, personality and mood changes (apathy), pyramidal and extrapyramidal dysfunction, pseudobulbar signs, cerebellar signs, elevated systolic blood pressure, and periventricular white matter hypodensity seen on MRI and CT (Funkenstein, 1988; Lishman, 1987; Stuss & Cummings, 1990).

The diagnostic criteria for ischaemic vascular dementia (IVD) have been specified by Chui and colleagues (Chui et al., 1992). For *probable IVD*, the criteria include all of the following: 1) the presence of dementia; 2) evidence of two or more ischaemic strokes by a) history, b) neurologic signs, c) CT or MRI, or the occurrence of a single stroke with a documented temporal relationship to the dementia onset; and 3) evidence by CT or T1 weighted MRI scan of at least one infarct outside the cerebellum. The criteria for *possible IVD* are the presence of dementia and one or more of the following: 1) history of a single stroke (but not multiple strokes) without a clearly documented temporal relationship to the onset of dementia, 2) the presence of extensive white matter changes on imaging, or 3) Binswanger's syndrome (without multiple strokes). The diagnostic criteria for Binswanger's syndrome are all of the following: a) urinary incontinence not explained by urologic disease, b) gait disturbance not explained by peripheral causes, and c) the presence of vascular risk factors. The criteria for the diagnosis of *definite IVD* are:

1) clinical evidence of dementia, 2) histopathologic confirmation of multiple infarcts, some outside of the cerebellum, and 3) the absence of AD or any other pathologic disorder that may have contributed to the dementia. If the third criterion cannot by met, the dementia is diagnosed as mixed.

Neuropathology

With the availability of advanced imaging technology such as CT and MRI, there has been a renewed interest in Binswanger's disease, also called Senile Dementia of the Binswanger Type (Román, 1987), or occasionally subcortical arteriosclerotic encephalopathy (Olszewski, 1962), which formerly could only be diagnosed neuropathologically. The neuropathology of IVD is associated with lesions of the subcortical white matter and enlarged ventricles, but a relatively spared cortex (Binswanger, 1894, cited in Román, 1987, and Nichols, 1988). There are multiple minute infarctions in the subcortical areas irrigated by arterioles of the medullary arteries (Nichols, 1988). Damage occurs primarily to white matter, with diffuse demyelination occurring secondary to Wallerian degeneration (Toole, 1984). Arcuate fibers are spared because they are perfused by cortical arteries (Román, 1987). CT or MRI reveal multiple white matter lucencies, symmetrically distributed, in the periventricular centra semiovalia, and usually ventricular enlargement (Román, 1987; Toole, 1984). This damage to the periventricular white matter may result in a disconnection of the cortex, leading to a truly subcortical dementia (Román, 1987). Etiology has been attributed to diffuse ischaemia resulting from hypertension (Caplan & Schoene, 1978) and chronic hypoperfusion of the watershed areas (Loizou, Kendall, & Marshall, 1981).

Related to the rekindled interest in BD is a current focus on periventricular white matter alterations (PWMA), or leukoaraiosis. According to Wallin and Blennow (1993), this condition is characterized more by generalized white matter changes, indicating vessel wall disturbance, than by actual infarcts. The blood-brain barrier is broken,

allowing cerebrospinal fluid to seep into the periventricular white matter. On MRI this is evidenced by generalized lucency.

Neuropsychological Profile

Specification of the neuropsychological profile in persons with PWMA has been hampered by a variety of methodological problems (Libon et al., 1993). Most prominent has been the exclusion of subjects with hypertension, a risk factor for stroke. PWMA is frequently found in subjects with hypertension; thus this exclusion may result in a subject sample with only a minimal extent of PWMA symptomatology, resulting in a lack of any detectable relationship between PWMA and neuropsychological impairment. This problem is further confounded by the tendency of most previous studies to rely on mental status screening instruments or limited neuropsychological batteries to delineate the pattern of functioning associated with PWMA (e.g., Steingart, Hachinski, Lau, Fox, Fox, Lee, Inzitari, & Merskey, 1987). However, in general, it appears that the pattern of dementia in persons with PWMA is very similar to that found in other subcortical dementias.

PWMA is associated with reduced performance on executive tests, unlike AD, where executive functioning is usually preserved in early stages. Clinically, the severity of executive deficits is often out of proportion to other deficits. Subjects with PWMA perform more poorly on the Attention subtest (but not the Conceptualization subtest) of the DRS (Kertesz, Polk, & Carr, 1990); the Stroop Test (Junqué, Pujol, Vendrell, Bruna, Jódar, Ribas, Viñas, Capdevila, & Marti-Vilalta, 1990), and serial sevens (Gupta, Naheedy, Young, Ghobrial, Rubino, & Hindo, 1988[2]). In comparison with AD subjects, subjects with PWMA perform more poorly on an abbreviated Trail Making Test

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[2]It should be noted that there were methodological problems in this study, such as a lack of clear quantification of radiological findings and the inclusion of patients hospitalized for neurological disorder in the control group.

and Luria's (1980) competing programs and go-no-go tests (Libon et al., 1993).

PWMA is correlated with poor performance on the Luria Motor Test (fist-edge-palm) and the appearance of three primitive reflexes (glabellar, snout, and jaw jerk) (Junqué et al., 1990). WAIS Digit Symbol performance has also been found to be reduced (Gupta et al., 1988).

Language may be impaired to the same extent with PWMA as in other cortical dementias. Gupta and colleagues (Gupta et al., 1988) found that subjects with PWMA exhibited poor performance on Benton's Verbal Fluency Test. Kertesz and colleagues (Kertesz et al., 1990) found that the Western Aphasia Battery did not discriminate demented subjects with and without PWMA. These authors suggested that periventricular lesions might erode the language network, resulting in language comprehension difficulties. Early comprehension difficulties, then, might even become a marker for these disorders and a distinguishing feature from PD.

Subjects with PWMA perform poorly on the Rey-Osterrieth Complex Figure Test (Gupta et al., 1988); however, there is no current evidence to suggest that subjects with PWMA differ in visuospatial abilities from subjects with cortical dementias (Bernard, Wilson, Gilley, Bennett, & Fox, 1992).

Bernard and colleagues (Bernard et al., 1992) compared episodic and semantic memory in BD and AD. On recognition memory, controls performed better than both diagnostic groups, and BD and AD were similarly insensitive to manipulations of frequency of presentations within a semantic category. They concluded that in BD episodic memory is relatively spared, while semantic memory is affected to the same degree as in AD. They suggested that the cortical-subcortical hypothesis is not sufficient to explain these results and suggested that this may be due to nucleus basalis of Meynert damage in AD and cortical-cortical and cortical-subcortical interruptions in BD.

Subjects with PWMA exhibit reduced spontaneity and creativity and show blunted

affect (Gupta et al., 1988). Junqué and his colleagues (Junqué et al., 1990) found the degree of PWMA to be correlated with behavioral difficulties on the Behavioral Measurement of Disturbance.

Neuropsychological Profile in Related Conditions

A variety of studies have examined the neuropsychological characteristics of PWMA in otherwise healthy subjects. Occasional relationships between PWMA and neuropsychological status have been found on tests of general mental status (Steingart et al., 1987). Libon and his colleagues (Libon, Scanlon, Swenson, & Coslet, 1990) found nondemented subjects with PWMA to perform more poorly than those without PWMA on measures of immediate and delayed recall of a prose passage; however, subjects with PWMA do not perform as poorly on declarative verbal memory tests as do subjects with AD (Libon et al., 1993). Subjects with PWMA also perform more poorly on other serial learning tests (Gupta et al., 1988) and the WMS (Gupta et al., 1988; Kertesz et al., 1990), except perhaps the Visual Reproduction subtest (Kertesz et al., 1990). Overall, relatively preserved performance of subjects with IVD/PWMA on recognition tasks indicate the disease affects retrieval rather than encoding (Bernard et al., 1992; Junqué et al., 1990). Other studies have shown little or no relationship between PWMA and cognition in otherwise healthy persons (Harrell, Duvall, Folks, et al. 1991; Hendrie, Farlow, Austrom, Edwards, & Williams, 1989; Hunt, Orrison, Yeo, 1989; Mirsen, Lee, Wong, Diaz, Fox, & Hachinski, 1991; Schmidt, Fazekas, Offenbacher, Lytwyn, Blematl, Niederkorn, Horner, Payer, & Friedl, 1991; Rao, Mittenberg, Bernardin, Haughton, & Leo, 1989; Tupler, Coffey, Logue, Djang, & Fagan, 1992).

Because hypertension is a risk factor for PWMA and IVD, the researcher must consider the neuropsychological characteristics of hypertension itself. Schmidt and his colleagues (Schmidt et al., 1991) compared asymptomatic hypertensive subjects with normotensive controls on tests of memory and learning, attention, vigilance and reaction

time, and mood, as well as on MRI scans. Verbal and total memory scores were lower in the hypertensive group, but there was no relationship between test scores and number of white matter lesions in this group. Thus the authors concluded that the lesions could not be implicated as a cause of the cognitive impairment. It is important to note that anti-hypertensive medications may also affect cognitive abilities (Light, 1978).

Cortical versus Subcortical Dementia and Memory

Subcortical dementia is a term first used by Albert and his colleagues (Albert, Feldman, & Willis, 1974) and by McHugh and Folstein (1975) to describe progressive supranuclear palsy and HD, respectively. These two groups independently described subcortical dementia in a very similar manner. Albert's group noted four major characteristics: forgetfulness, slowed thought processes, altered personality (including apathy or depression), and difficulty manipulating knowledge. McHugh and Folstein described inefficient thought and memory processes and low initiative, as well as the absence of signs of cortical pathology (e.g., aphasia, alexia, apraxia, agnosia, and amnesia). The clinical picture is still described in the same manner (Cummings & Benson, 1984). Recognized subcortical dementias include, in addition to progressive supranuclear palsy and HD, PD, Wilson's disease, spinocerebellar degenerations, basal ganglia calcification, multiple sclerosis, and AIDS-related dementia. While most investigators support the distinction between cortical and subcortical dementia (Albert, 1978; Cummings, 1986, 1988; Cummings & Benson, 1983, 1984; Mandell & Albert, 1990; Massman et al., 1990), there are a few who disagree (Brown & Marsden, 1988; Friedland, 1993; Whitehouse, 1986).

Cummings and Benson (1984) define as subcortical those dementias which involve primarily the deep gray-matter structures (the thalamus, basal ganglia, and brain-stem nuclei). They point out that the label has been criticized because damage actually often

extends beyond these areas, but state, "The terminologic shortcomings do not abrogate the basic tenet that diseases involving primarily subcortical structures produce intellectual deficits distinguishable from those associated with the diseases involving predominantly cortical structures. Subcortical dementia is a clinical, not an anatomic, concept" (Cummings & Benson, 1984, p. 875). Albert and Mandell (Albert, 1978; Mandell & Albert, 1990) agree. They feel that though this nomenclature may leave much to be desired, it serves as a first step toward clarifying the underlying neurochemical and neuropsychological profiles of the two types of dementing illness.

Cummings and Benson (Cummings, 1986, 1988a; Cummings & Benson, 1983, 1984) argue that the dementia found in PD is related to subcortical, not cortical degeneration, because: 1) the clinical features include bradyphrenia and poor executive functioning, but not cortical symptoms such as aphasia and agnosia, 2) the severity of dementia correlates with the severity of bradykinesia and rigidity (though notably not tremor), implicating common underpinnings, 3) there is intellectual improvement with levodopa therapy, and 4) recent studies indicate that age can account for Alzheimer's-like pathology in PD. They argue that the case is similar in HD because: 1) the presence of pathological changes in the frontal cortex of HD patients is variable while dementia is universal, 2) cerebral metabolism studies demonstrate normal metabolism in the cortex of HD patients but deficient metabolism in the caudate nuclei, and 3) there is denervation supersensitivity in the globus pallidus and substantia nigra of these patients, but not the cortex. They describe neuropsychological deficits in executive programming, reinforcement and conditioning, mood and motivation, language, and attention. Thalamic lesions are associated with deficits in arousal, attention, mood, memory, language, abstraction, and categorization. Brain-stem lesions affect arousal, attention, mood, and motivation.

Finally, Cummings and Benson argue that AD is a cortical dementia, based on the

evidence that: 1) cognitive deficits in AD result from cortical dysfunction even if this is a result of a chemical deficiency stemming from subcortical structures, 2) cerebral metabolism studies show cortical hypometabolism with relatively preserved subcortical metabolism, 3) cell loss in the nucleus basalis of Meynert is not specific to AD and also occurs in Pick's disease and PD, as well as other syndromes, 4) nucleus basalis of Meynert atrophy does not correlate with dementia in PD, and thus does not appear sufficient to produce dementia, 5) cortical atrophy and cholinergic enzyme reduction in the cortex does not correspond to the pattern of nucleus basalis of Meynert innervation, and 6) cholinergic therapy has not been successful in the treatment of AD, suggesting that cortical factors are producing the deficits (Cummings and Benson, 1984).

On the other hand, as Friedland (1993) points out, there is evidence both for cortical dysfunction in the subcortical dementias and for subcortical dysfunction in the cortical dementias. Levin and colleagues (Levin et al., 1992) and Brown and Marsden (1988) agree that it is premature to separate the dementias into two general categories. Brown and Marsden stress the individual cognitive patterns associated with each syndrome, the similarities between subcortical and cortical dementias, and the difficulty in matching subjects on level of dementia. Whitehouse (1986) takes a more extreme viewpoint, arguing against the use of anatomic terms and making simple associations between anatomy and psychology. He feels that the view of a subcortical dementia in PD, HD, and progressive supranuclear palsy results from the fact that these patients seek medical attention for motor problems early in the course of their illnesses. He speculates that patients with early AD might show the same cognitive pattern if tested.

The utility of the term subcortical dementia to characterize the cognitive pattern in PD depends on three factors (Brown & Marsden, 1988): 1) the extent to which the neuropsychological pattern differs from cortical dementias, such as AD, 2) the extent to which the neuropsychological impairments found in PD resemble those found in other

subcortical dementias, such as HD, and 3) the anatomic and chemical distinctiveness of cortical and subcortical dementias.

Memory in Cortical Dementia

Declarative Memory

Persons with AD exhibit impairment on every measure of declarative memory tested. Impairment of verbal recall in list learning tasks has been repeatedly demonstrated. Not only are there few items recalled (Delis, Massman, Butters, Salmon, Cermak, & Kramer, 1991; Eslinger & Damasio, 1986), but primacy and recency effects are absent (Massman, Delis, & Butters, 1993), even when cues are provided. Intrusion errors are common (Kramer, Delis, Blusewicz, Brandt, Ober, & Strauss, 1988). Recall in a word stem completion paradigm (Heindel et al., 1989; Salmon, Shimamura, Butters, & Smith, 1988), paired associates (Huber, Shuttleworth, Paulson, Bellchambers et al., 1986) and a word span task (Heindel, et al., 1988) are also impaired. A similar deficit is seen in recall of stories, with both poor recall (Butters, Granholm, Salmon, Grant, & Wolfe, 1987; Butters, Salmon, Heindel, & Granholm, 1988) and a high number of intrusive errors.

AD patients do not improve on recognition tasks. Recognition, like recall, is deficient in learning of a list (Delis, Massman, Butters, Salmon, Cermak, & Kramer, 1991; Kramer, et al., 1988), word stem recall (Heindel et al., 1989; Salmon et al., 1988) and completion of a word span task (Heindel et al., 1988). AD patients do not show primacy and recency effects even in recognition tasks (Massman et al., 1993). Further, they exhibit a high number of false positive responses (Kramer et al., 1988). Declarative memory impairment is not limited to the verbal domain, but has also been demonstrated in face recognition (Eslinger & Damasio, 1986).

Nondeclarative Memory

AD results in a distinctive pattern of both spared and impaired nondeclarative

functions. Patients exhibit deficits in lexical priming tasks, including word stem completion priming (Butters, Heindel, & Salmon, 1990; Salmon et al., 1988) skill learning in mirror reading (Grober, Ausubel, Sliwinski, & Gordon, 1992); and tests of semantic priming, including paired associates (Salmon et al., 1988) and category exemplars (Glosser & Friedman, 1991). They additionally show deficits in pictorial fragment-identification priming (Butters et al., 1990; Heindel et al., 1990). However, they do show lexical priming for associatively related word pairs (Glosser & Friedman, 1991).

Against this background of impairment on so many declarative and nondeclarative tasks, there is a striking preservation of procedural learning. This includes motor learning in the rotary pursuit task (Butters et al., 1990; Heindel et al., 1988; Butters et al., 1988; Eslinger & Damasio, 1986; Heindel et al., 1989), adaptation to visually distorting prisms (Paulsen, Butters, Salmon, Heindel, & Swenson, 1993), repetition priming in mirror reading (Grober, Ausubel, et al., 1992), and biasing of weight judgments following exposure to light or heavy weights, a task requiring motor programming and expectation (Butters et al., 1990).

Memory in Subcortical Dementia

Although patients with subcortical dementia also show declarative deficits, these differ in quality from those seen in cortical dementia. In addition, the pattern of nondeclarative performance is generally opposite of that seen in cortical dementia.

Declarative Memory

Patients with HD exhibit impairment on a number of declarative measures, including recall in list learning tasks (Butters, Wolfe, Martone, Granholm, & Cermak, 1985; Delis et al., 1991), word span tasks (Heindel et al., 1988; Butters et al., 1988), word stem completion (Heindel et al., 1989; Salmon et al., 1988), and story recall (Butters et al., 1987; Butters et al., 1988). The pattern of declarative test performance includes

decreased primacy effects in list learning, even when cues are provided (Massman et al., 1993), and the production of more perseverative errors than AD patients in list learning tasks (Delis et al., 1991), but fewer intrusion errors than is found in AD (Butters et al., 1987; Butters et al., 1988).

PD patients exhibit the same general performance as HD subjects. They demonstrate impairment in list learning (Saint-Cyr et al., 1988), word stem recall (Heindel et al., 1989), paired associate learning (Huber et al., 1989; although it is better than in AD, Huber, Shuttleworth, Paulson, Bellchambers et al., 1986), and story recall (Saint-Cyr et al., 1988). PD patients are deficient in the achievement of declarative knowledge of a repeating pattern in the motor domain (Pascual-Leone, Grafman, Clark, Stewart, Massaquoi, & Hallett, 1993), but can achieve declarative knowledge of repeating visual pattern.

IVD has received much less attention, but preliminary evidence suggests a similar deficit. Recall of prose passages (Libon et al., 1990) and list learning (Libon et al., 1993) is impaired in IVD, although in one study significance of results in declarative memory disappeared when age was covaried (Junqué et al., 1990).

Unlike patients with cortical dementia, HD and PD patients often exhibit relatively spared recognition. Recognition performance is often adequate in HD (Butters et al., 1985; Delis et al., 1991; Kramer et al., 1988; Martone, Butters, Payne, Becker, & Sax, 1984), including normal primacy and recency effects (Massman et al., 1993; as opposed to decreased primacy in recall). HD patients produce fewer false positive responses (Delis et al., 1991; Kramer et al., 1988) except when the disease is advanced (Kramer et al., 1988). However, recognition is impaired in a word span task (Heindel et al., 1988; Butters et al., 1988) and following word stem recall (Heindel et al., 1989; Salmon et al., 1988).

Recognition in PD is preserved on delayed matching-to-sample of words, images,

and positions (Saint-Cyr et al., 1988) and following word stem recall (Heindel et al., 1989). Recognition in BD, which has received much less attention, also appears to be spared relative to the situation in AD (Bernard et al., 1992; Libon et al., 1993).

Nondeclarative Memory

The pattern of performance of HD subjects on nondeclarative tasks is in many ways opposite that of AD subjects. HD subjects are impaired on the rotary pursuit learning task (Butters et al., 1990; Heindel et al., 1988; Butters et al., 1988; Heindel et al., 1989), learning of maze routes predictable due to repetition (Fedio et al., 1979; cf. Bylsma, Brandt, & Strauss, 1990, in which the authors believe the task may have been too easy), a repetitive tracking task (Willingham, Koroshetz, & Peterson, 1996), skill learning on a mirror reading task (Martone et al., 1984), and the biasing of weight judgments following exposure to light or heavy weights (Butters et al., 1990). HD patients fail to adapt to visually distorting prisms and do not show aftereffects (Paulsen et al., 1993).

Data regarding the Tower of Toronto and Tower of Hanoi tasks is equivocal. Although Saint-Cyr and colleagues (Saint-Cyr et al., 1988) found impaired performance on the Tower of Toronto task, Butters' group (Butters et al., 1985) found spared performance in early HD on the Tower of Hanoi, a more difficult task. Similarly, patients with PD are impaired on rotary pursuit motor learning (Heindel et al., 1989), prism adaptation (Stern, Mayeux, Hermann, & Rosen, 1988), and the Tower of Toronto task (Saint-Cyr et al., 1988). Despite the above, HD patients can learn a random motor sequencing task (Willingham & Koroshetz, 1990), a random tracking task (Willingham et al., 1996), and exhibit repetition priming on a mirror reading task (Martone et al., 1984).

With regard to semantic and lexical priming, they show relatively spared stem-completion priming as compared with AD, though they are impaired relative to controls (Butters et al., 1990; Salmon et al., 1988) and, paired associate priming (Salmon et al., 1988). In addition, pictorial fragment-identification priming (Butters et al., 1990;

Heindel et al., 1989) is spared relative to the pattern found in AD.

PD patients are impaired on the rotary pursuit task (Heindel et al., 1989), tracing and tracking tasks (Hocherman & Aharon-Peretz, 1994). They do show procedural learning on the serial reaction test acquired, though this learning is slower than in controls (Pascual-Leone et al., 1993). However, unlike patients with HD, those with PD are impaired on word stem completion priming (Heindel et al., 1989).

Summary

Patients with either cortical or subcortical dementia show declarative memory deficits. The pattern of declarative memory deficit seen in AD, with little learning, poor response to cues, and poor recognition is interpreted as an encoding deficit. The deficit in declarative memory in subcortical dementia appears to be a dysfunction in the initiation of retrieval strategies (Butters et al., 1988).

With regard to nondeclarative memory, the evidence to date is best summarized by Butters and his colleagues (Butters et al., 1990). "AD and HD patients . . . can be dissociated with implicit memory tasks that involve the priming of semantic memory and the initiation of motor programs. . . . This double dissociation suggests that portions of the association cortex and the basal ganglia mediate quite different forms of implicit memory: the association cortices appear to be vital to tasks that rely upon the integrity of semantic knowledge, the basal ganglia to tasks that involve the generation of motor programs to guide behavior" (Butters et al., 1990, pp. 359-360). Preliminary results of investigations in subjects with PD indicate that both procedural memory and priming are impaired. Overall, these results have been interpreted as evidence of separate neuroanatomical *nondeclarative* memory systems.

Rationale and Design of the Experiment

Investigations of declarative memory in AD, PD, and HD have resulted in two major findings. First, declarative memory is severely impaired in AD, while it is impaired to a lesser extent in HD and PD (Heindel et al., 1989; Martone et al, 1984; Shimamura, Salmon, Squire, & Butters, 1987). Second, the cognitive deficit in AD appears to be mainly in encoding, while in HD and PD evidence indicates a retrieval deficit (Butters, 1984; Butters et. al., 1985; Massman et al., 1990).

Regarding nondeclarative memory, double dissociations of priming and procedural motor learning in AD versus HD and PD suggest an alignment of the two systems along the cortical-subcortical axis, with priming representing a cortical function and procedural motor learning a subcortical one (Bondi & Kaszniak, 1991; Butters et al., 1985, 1990; Heindel et. al., 1989, 1991; Martone et al., 1984; Randolph, 1991). However, frontal lobe involvement in HD and PD, and priming deficits often found in PD, argue against a simple explanation based on a circumscribed anatomical location. Another explanation is that procedural motor learning is dependent upon a motor circuit between the ventrolateral thalamus, the basal ganglia, and the supplementary motor area (Alexander et al., 1986; Saint-Cyr & Taylor, 1992), with very limited cortical involvement, while priming is independent of this motor circuit. Data from previous studies of nondeclarative memory would support such an anatomical distribution. The neuroanatomical circuit could be investigated by a study of IVD and PD, in which it is affected, and AD, in which it is spared.

Evidence to support this theory could be obtained from a demonstration that damage to this circuit affects procedural motor learning, but not priming. Such a demonstration might be found in another diagnostic group, IVD. IVD interferes with the periventricular white matter pathways to and from the prefrontal cortex and supplementary motor area. While investigators have found impairments in declarative

memory retrieval in IVD (Bernard et al., 1992; Gupta et al., 1988; Libon et al., 1990, 1993; Junqué et al, 1990; Kertesz et al., 1990), nondeclarative memory has not yet been investigated in this syndrome. Thus IVD will be compared with PD, which depletes nigrostriatal dopamine, resulting in basal ganglia dysfunction, and AD, which affects primarily the temporo-parietal cortex and hippocampus.

Hypotheses and Predictions

Hypothesis I. Declarative memory is relatively independent of white matter areas.

Prediction 1. Declarative memory will be spared in IVD relative to AD; performance of the IVD group will exceed that of the AD group on the recognition task, and perhaps also on the recall task.

Prediction 2. Patterns of performance in the IVD group will be similar to those found in other subcortical dementias; IVD and PD subjects will show mainly a retrieval deficit, while AD subjects will show an encoding deficit.

Hypothesis II. Procedural motor learning is dependent on a complex striatal-frontal motor circuit while verbal priming is dependent on the cortical association areas.

Prediction 3. Subjects with AD will have verbal priming impairment, but not procedural motor learning impairment.

Prediction 4. Subjects with PD and IVD will have procedural motor learning impairment, but no verbal priming impairment.

Hypothesis III. Verbal priming and procedural motor learning rely on separate neuroanatomical systems; this will be reflected in their relationships with neuropsychological and neuroanatomical measures.

Prediction 5. Procedural motor learning will be positively correlated with

performance on tests of executive function.

Prediction 6. Verbal priming will be positively correlated with performance on language tests.

Prediction 7. Procedural motor learning, but not verbal priming, will be related to PWMA affecting the pathways involved in the basal ganglia thalamo-cortical motor circuit.

Hypothesis IV. To the degree that neuropsychological tests are effective in delineating brain insult, they are valid predictors of dementing syndromes with varying neuroanatomical correlates.

Prediction 8. Neuropsychological data will effectively discriminate not only between normal function and dementia, but also between the three types of dementia.

METHOD

Subjects

Subject groups consisted of: 1) 15 subjects with IVD, 2) 15 subjects with AD, 3) 14 subjects with PD with dementia (PD), 4) 15 normal elderly control subjects (EC), and 5) 5 subjects with PD without dementia (NDPD). This last group was used only for the purpose of determining whether persons with the motor symptomatology of PD could perform the required motor tasks.

Subjects with AD and IVD were selected from patients receiving diagnostic and/or treatment services from 1) the Geriatric Assessment Program (GAP) at the Senior Health System, Alexander Silberman Center, Crozer-Chester Medical Center (CCMC), Upland, Pennsylvania or 2) the Neuropsychology Service, Psychiatry Department, CCMC. All patients referred for neuropsychological assessment were administered the tests used here; those patients meeting specific diagnostic criteria, however, were asked to participate in the study.

Subjects with PD, both with and without dementia, were selected from patients receiving diagnostic and/or treatment services from 1) the Movement Disorders Center at CCMC, 2) the Neuropsychology Service at CCMC, or 3) the Neurology Department, Robert Wood Johnson Hospital, New Brunswick, New Jersey. As above, only those patients meeting specific diagnostic criteria were asked to participate.

Elderly control subjects were solicited from spouses/caretakers of PD subjects and participants in CCMC's Adult Day Care Program at the Senior Health System, as well as CCMC's Volunteer Service. Control subjects were asked to participate only if they were living independently in the community.

Criteria for Inclusion and Exclusion

Subjects with a history of stroke (other than subcortical infarct in the IVD group),

psychotic disorder, major affective disorder, seizure disorder, thyroid disorder, metabolic disorder, head injury, and alcohol abuse were excluded. Subjects taking medications (other than antiparkinsonian or antihypertensive drugs) which could alter cognitive function were excluded.

In order to be included in the control group, subjects were required to achieve a Mini-Mental State Exam (MMSE; Cockrell & Folstein, 1988; Folstein, Folstein, & McHugh, 1975) score of 28 or above (normal performance) and a Geriatric Depression Scale (GDS) score of 12 or less (at most mild depression). Demented subjects were only included in the study if they achieved MMSE scores between 12 and 26, narrowing the range of impairment and assuring that subjects were intact enough to follow instructions and perform the tasks. Subjects who, upon testing, showed focal impairments (e.g. aphasia or rigidity) or behavioral problems too severe to provide valid and reliable data were not included in the study.

Subjects in the AD and IVD groups had a diagnosis of probable AD or IVD, based on neuropsychological and neurological evaluation, consideration of radiological data, and, when necessary, additional medical tests to rule out other causes of cognitive decline specific to the current or historical health status of the individual. The diagnosis of AD met NINCDS-ADRDA criteria (McKhann et al., 1984) for probable AD. Subjects in the IVD group met Chui and colleagues (Chui et al., 1992) criteria for IVD and had not had any major strokes. Subjects in the PD group had been diagnosed by a neurologist, according to history and clinical picture.

Subject Characteristics

Demographic characteristics of subjects are presented in Table 1 and descriptive statistics are provided in Table 2. As there were correlations between some of the independent variables (See Table 3) a MANOVA was used to analyze between group differences; Tukey's Honestly Significant Difference test was used to conduct post-hoc

analyses. The one-way MANOVA indicated in a significant effect of group [Wilk's Λ = .32, F (15, 136) = 4.68, p < .001], and was thus followed up with univariate F tests. As expected, there was a significant difference in MMSE [F (3,53)=21.52, p < .001], such that mental status scores of the EC group exceeded those of each of the demented groups (p < .05). No differences were found between the experimental groups. There was a marginally significant difference in GDS score [F (3, 53) = 2.92, p = .05], such that the EC group was less depressed than the PD group; the actual difference is not likely to be of clinical significance. There was a significant difference in NART raw score [F (3, 53) = 5.38, p < .01)], such that the EC group performed better than the AD and IVD groups. However, evidence published since the design of this protocol suggests the NART may underestimate premorbid intelligence in AD due to a loss of reading ability (Patterson, Graham, & Hodges, 1994). There were no statistically significant differences in age [F (3, 53) = 1.77, p > .05] or education [F (3, 53) = 2.55, p > .05] between groups.

Table 1
Demographic Characteristics of Subjects

	S	Age	Sex	Ed	MMSE	GDS	NART	NARTIQ
AD	1001	77	M	16	26	6	29	113
	1002	85	F	12	23	10	42	123
	1003	76	F	10	22	4	12	95
	1004	84	M	10	24	6	20	102
	1005	65	M	16	24	2	40	123
	1006	82	M	12	23	10	33	115
	1007	76	F	12	20	0	25	108
	1008	69	F	12	20	0	33	115
	1009	73	F	12	12	0	8	93
	1010	71	F	12	23	2	16	100
	1011	86	M	8	21	2	9	91
	1012	81	F	11	25	8	16	99
	1013	77	F	10	15	0	8	92
	1014	81	F	9	23	2	14	96
	1016	76	F	12	22	12	33	115
IVD	2001	81	M	11	24	10	19	102
	2002	73	M	7	24	2	22	102
	2003	73	M	16	17	2	16	102
	2004	80	M	9	14	4	11	94
	2005	77	F	8	19	2	19	100
	2006	90	M	10	22	4	12	95
	2007	74	F	12	26	10	34	116
	2008	89	F	12	26	12	23	106
	2009	78	F	7	20	0	26	106
	2010	83	F	10	17	12	37	117
	2011	69	F	8	25	0	13	95
	2012	85	F	16	18	10	13	99
	2013	82	F	7	22	7	23	103
	2014	75	F	12	22	2	23	106
	2015	79	F	8	19	-	17	98

(Continued on next page.)

Table 1 (continued)
Demographic Characteristics of Subjects

	S	Age	Sex	Ed	MMSE	GDS	NART	NARTIQ
PD	3001	70	F	12	23	10	34	116
	3002	74	F	8	23	4	6	89
	3003	77	F	13	21	8	16	100
	3004	67	F	12	23	6	33	115
	3005	74	F	14	24	0	41	123
	3006	88	M	19	23	4	38	123
	3007	74	M	12	25	2	28	110
	3008	86	M	3	13	2	7	87
	3009	70	M	12	18	12	22	105
	3010	76	M	18	25	8	38	122
	3011	69	M	16	25	12	40	123
	3012	81	M	16	23	2	36	120
	3013	56	M	16	26	12	24	109
	3015	79	M	12	23	2	25	108
EC	8001	67	F	12	30	0	37	118
	8004	85	F	7	30	4	16	97
	8007	65	M	12	29	6	34	116
	8008	72	M	8	29	2	11	93
	8011	69	F	12	30	4	36	117
	8012	67	F	12	30	2	37	118
	8013	74	F	12	29	0	31	113
	8015	68	F	16	30	2	41	124
	8016	69	F	16	30	0	43	126
	8017	87	M	17	29	4	40	124
	8018	85	M	16	28	3	43	126
	8019	78	M	16	29	0	39	122
	8020	75	M	16	30	2	43	126
	8021	72	F	17	30	-	43	126
	8022	72	M	13	29	0	41	122

Note. AD = Alzheimer's disease; IVD = ischaemic vascular dementia; PD = Parkinson's disease; EC = elderly control; Ed = Education; MMSE = Mini Mental State Exam; GDS = Geriatric Depression Scale; NART = Nelson Adult Reading Test (American version), raw score; NARTIQ = Nelson Adult Reading Test estimated premorbid intelligence quotient; S = subject number.

Table 2
Means and Standard Deviations of Demographic Variables

	AD			SIVD			DPD			EC			Total		
	N	*Mean*	*SD*	*N*	*Mean*	*SD*	*N*	*Mean*	*SD*	*N*	*Mean*	*SD*	*N*	*Mean*	*SD*
Age	15	77.67	6.02	15	79.57	6.07	14	74.80	8.14	15	74.25	7.16	59	76.60	7.04
Educ	15	11.60	2.20	15	10.20	2.98	14	13.07	4.10	15	13.47	3.16	59	12.07	3.35
MMSE	15	21.53	3.70	15	21.00	3.65	14	22.50	3.37	15	29.47	0.64	59	23.64	4.60
GDS	15	4.27	4.13	14	5.50	4.49	14	6.07	4.38	14	2.07	4.38	57	4.47	4.08
NART	15	22.53	11.78	15	20.53	7.64	14	27.71	11.66	15	35.67	9.73	59	26.59	11.67

Note. MMSE = Mini-Mental State Exam, Educ = Education, MMSE = Mini-Mental State Exam, GDS = Geriatric Depression Scale, NART = Nelson Adult Reading Test number correct. AD = Alzheimer's disease, IVD = ischaemic vascular dementia, DPD = Parkinson's disease with dementia, EC = elderly control.

Table 3
Correlations Among Demographic Measures

	Age	Education	MMSE	GDS	NART
Age	1.000				
Education	-0.200	1.000			
MMSE	-0.254	0.372**	1.000		
GDS	0.113	0.122	-0.075	1.000	
NART	-0.240	0.655**	0.588**	0.070	1.000

Note. MMSE = Mini Mental State Exam, GDS = Geriatric Depression Scale, NART = Nelson Adult Reading Test.
Two-tailed statistical significance: *p < .05, **p < .01.

Procedure

Informed consent

Informed consent was obtained for all subjects. Those subjects competent to provide their own consent did so; guardians provided consent for the remaining subjects. For patients, failure to consent to participate in this study had absolutely no effect on

treatment, and patients and their guardians were assured of this. A copy of the consent form is provided in Appendix A.

Neuropsychological Testing

Subjects were tested individually by a neuropsychologist, neuropsychology fellow or intern. In the case of AD, IVD, and a couple of PD subjects, this examination was part of a comprehensive diagnostic study; the tests of interest here were given first, to minimize the effects of fatigue. The remaining PD and control subjects were administered only the tests used in this study.

General Assessment of Dementia

General assessment of dementia included 1) an MRI scan, from which the Junqué score was derived; 2) a mental status examination, which was used for study inclusion/exclusion and to provide an assessment of level of dementia; 3) a measure of premorbid intellectual functioning, for the matching of group demographics; 4) a depression screening scale, and 5) for PD patients only, a general assessment of motor ability.

Magnetic Resonance Imaging (MRI). MRIs were obtained for AD and IVD subjects. Quantification of PWMA was achieved via analysis of the MRI, using Junqué and colleagues' (Junqué et al., 1990; see Appendix B) modification of a scale developed by Rezek's group (Rezek et al., 1987). This analysis was provided by John Bonavita, M.D., Department of Radiology, CCMC. White matter hyperintensities (WMH) on T_2-weighted images were measured in five areas of each hemisphere: 1) the centra semiovale of the frontal region (FCS), 2) the centra semiovale of the parietal region (PCS), 3) the area surrounding the frontal horn of the lateral ventricle (FH), 4) the area surrounding the corpus of the lateral ventricle (LV), and 5) the area surrounding the atrium and occipital horn of the lateral ventricle (OH). PWMA was scored on a scale of 0 to 4, as follows: 0) none present, 1) less than 25% WMH, 2) 25 - 50% WMH, 3) 50 -

75% WMH, and 4) greater than 75% WMH. Thus total scores could range from 0 to 40.

Mini-Mental State Exam. General mental status was assessed with the MMSE (Cockrell & Folstein, 1988; Folstein et al., 1975; See Appendix B), which quantifies functioning on a scale of 0-30, with lower scores representing increasing impairment. Points are derived from ten 1-point orientation items (5 for time and 5 for place), two 3-point memory items (one for registration and one for recall), one 5-point attention/concentration item, four 1-point (2 naming, 1 written language, 1 repetition, 1 simple command) and one 3-point (complex command) language items, and one 1-point construction item.

Nelson Adult Reading Test. Premorbid verbal intelligence was estimated with Grober and Sliwinski's (1991) revision of the American version of the Nelson Adult Reading Test (Am-NART; see Appendix B). Subjects read 45 words with atypical spellings (e.g. ache, chassis). The words were presented in order of difficulty and the test was discontinued after 10 consecutive errors. Grober and Sliwinski's model, which considers both the number of NART errors and years of education, was used to estimate premorbid verbal IQ, as follows: $NART\ IQ = 118.56 - .88 * (NART\ Errors) + .56 * (Years\ of\ Education)$.

Geriatric Depression Scale. Subjects were screened for the presence of depression, using the short form of the Geriatric Depression Scale (GDS, Yesavage, 1988). (See Appendix B.) Subjects were read the 15 questions and responded with yes or no answers. Those items endorsed in the manner indicative of depression were summed and the total multiplied by two to yield a score from 0 (no depression) to 30 (severe depression). Subjects who scored higher than 12 (i.e more than mild depression) were not invited to continue the study.

An item analysis was conducted to determine whether certain items on the GDS

might be more sensitive to dementia or motor impairment than others. If so, these items would lead to inflated depression scores in the demented groups. This was particularly a concern for items 8 ("Do you often feel helpless?"), 10 ("Do you feel you have more problems with memory than most people?"), and 14 ("Do you feel that your situation is hopeless?").

Means and standard deviations of item scores are presented in Appendix B, Table B-1. A 4 (Group) X 15 (Item) MANOVA did not reveal a significant multivariate effect [Wilks' $\Lambda = .29$, $F(3, 45) = 1.19$, $p > .05$]. Item 12 was eliminated from the analysis due to an absence of variance.

Unified Parkinson's Disease Rating Scale. The motor section of the Unified Parkinson's Disease Rating Scale (UPDRS, Fahn, Elton, & members of the UPDRS Development Committee, 1987) was administered to PD patients by a registered nurse specializing in the management of PD.

Memory Measures

Memory measures included 1) the California Verbal Learning Test, for the measurement of declarative memory; 2) a word stem completion test, for the measurement of priming; and 3) a rotary pursuit test, for the measurement of procedural motor learning and retention.

California Verbal Learning Test. The dementia version of the California Verbal Learning Test (CVLT-D, Mattson, Libon, Intrieri, & Socha, 1991; Mattson, Libon, Levine, & Socha, 1991; see Appendix D) was used to measure declarative memory retention in the AD, IVD, and PD groups. The standard CVLT (Delis, Kramer, Kaplan, & Ober, 1987) was used to measure explicit memory in the EC group.

The CVLT-D tests memory of a list of nine items chosen from three semantic groups, with three items per group. The standard CVLT tests memory for a list of 16

items chosen from 4 semantic groups, with four items per group. In both tests, memory of the items is assessed over five learning trials, followed by an interference condition with an alternate similarly structured list, short delayed free and cued recall of the original list, 20 minute delayed free and cued recall of the original list, and finally recognition of the original list. Standard administration procedures (Delis et al., 1987) were used.

The tests yield measures of immediate recall, including a learning curve; of short and long delayed free and cued recall, and of recognition discrimination. Discrimination was calculated using Corwin's (1994) two-high threshold formula, which accounts for the fact that both forms of the CVLT contain more distractors (i.e. opportunity to make false positive errors) than targets (i.e. opportunities for misses) and, additionally, eliminates problems due to zero denominators. First the hit rate (HR) is calculated using the formula HR = (hits + .5) / (targets + 1). Then the false alarm rate (FAR) is calculated using the formula FAR = (false positives + .5) / (distractors +1). Finally, discrimination (Pr) is calculated from the formula Pr = HR - FAR.

Because experimental subjects were administered a shorter, easier form of the CVLT than the control subjects, *z*-scores for all scores except discrimination were used in the analyses. *Z*-scores for the EC group were calculated from the standardized normative sample (Delis et al., 1987), and for the remaining groups were calculated from the norms provided by Mattson and colleagues (Mattson, Libon, Intrieri, et al., 1991) shown in Appendix D, Table D-1.

Priming Test. The priming task consisted of two parts, 1) a rating task (study phase), and 2) a word stem completion task (test phase). Two alternate forms of each part of the task were used for the purpose of obtaining baseline data. Half of the subjects received each form, in a counterbalanced fashion.

Each form of the rating task contained 20 items, as follows: 1) three foils, to help

eliminate primacy effects, 2) fifteen items, and 3) two foils to help eliminate recency effects. Words used as stimuli were similar to those used by Hasker Davis and his colleagues in a computerized battery of nondeclarative memory tests (Davis, personal communication, 1994). The subject was asked to rate each item according to how much he liked or disliked the word, on a scale of one through five, as follows: 1) dislike very much, 2) dislike, 3) neutral, 4) like, or 5) like very much. Instructions and answer sheets are provided in Appendix B.

The word stem completion task was administered directly following the rating task, but no reference was made to the relationship between these two tasks. Each form of the word stem completion task contained thirty items, as follows: fifteen three-letter stems drawn from the items in the rating task randomly interspersed with fifteen foils. The foils were stems of the items used on the alternate form of the rating test; data obtained from the foils was used to calculate baseline rates for the alternate form. For each item the subject was required to indicate the first word he/she could think of that begins with that stem. An item was discontinued if the subject could not provide a response within ten seconds.

To score the test, a baseline rate was calculated for each item, with the baseline rate equal to the proportion of times the item was correct when it was not primed, i.e., it was not on the studied list and was indicated by chance, for the 60 subjects in the four target groups. The score on a particular subject's test consisted of the sum of correct items minus their baseline rates[3].

Scores on the priming test were analyzed in order to determine the equivalence of Forms A and B. Means and standard deviations of items scores for the two forms are presented in Appendix B, Table B-2. Total scores on each form are presented in Table 4. A 2 (form) X 4 (group) ANOVA revealed a significant main effect of test form on

[3]I.e. *score = number correct - sum (baseline rates).*

number of foil items retrieved [$F(1, 53) = 15.97, p < .001$], indicating that the foil items on Form A were retrieved more frequently than the foil items on Form B. Although the foil items on Form A were the test items on Form B, these items were not retrieved more often in this context than Form A test items [$F(1, 53) = 2.07, p > .05$]. Thus, the difference was only in baseline rates. While the ANOVA revealed a main effect of diagnosis [$F(3, 53) = 5.30, p < .01$], Tukey's test revealed no significant differences between groups ($p > .05$).

Table 4
Means and Standard Deviations of Scores on Each Form of the Priming Test

Form	*Mean*	*SD*
A	5.08	3.53
B	3.04	2.19
Total	4.06	3.09

Rotary Pursuit Test. Procedural motor memory was measured with the Rotary Pursuit Test (Lafayette Instruments Photoelectric Rotary Pursuit, Model #30014), with a circular template and sensitivity equal to 3. A sample score sheet is presented in Appendix C.

Each subject was administered three preliminary trials, to determine the speed at which the learning trials would be conducted. These preliminary trials consisted of 20 second trials, one at 15 rpm, one at 30 rpm, and one at 45 rpm, with 20 second intertrial intervals. The speed at which the subject was on target closest to 25% of the time (i.e., closest to 5 seconds of 20) was used for subsequent trials. This was determined by calculating the absolute value of time on target minus 5 seconds for each trial, and choosing the speed at which this value was closest to 0.[4]

There were two blocks of five 20 second learning trials, with 20 second intertrial intervals, and a 20 minute interval between blocks. The score from the preliminary trial at the determined speed served as the first trial of the first block.

During each learning and delayed retention trial, the subject rested a stylus, with his/her preferred hand, on a small target point on the rotary pursuit disc and tried to maintain contact with it as it rotated at the predetermined speed, in a clockwise direction for right-handed subjects, and a counterclockwise direction for left-handed subjects. (This was to equate difficulty by assuring that arm movements were in the same direction relative to the shoulder and body.) This procedure yielded measures of total time on target and number of impulses (i.e. the number of times of loss and regaining of contact between the stylus and the target) for each trial.

Additional Neuropsychological Tests

Seven additional neuropsychological measures were administered, to assess performance in the areas of executive functioning, language, and visuospatial functioning.

Boston Naming Test (BNT). The Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983) measures confrontational naming, which is found to be deficient in dementia, due to both focal and diffuse left hemisphere compromise. The BNT was administered and scored in the standardized fashion. In addition, an error analysis was used to compute the numbers of each of the following errors: semantic, circumlocutions, literal, perceptual, and perseverative.

Clock Drawing. The Clock Drawing Test measures both executive planning and

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[4]For example, if time on target was 8.69 for 15 rpm, 6.24 for 30 rpm, and 4.13 for 45 rpm, the values would be /8.69-5.00/ = 3.69 for 15 rpm, /6.24-5.00/ = 1.24 for 30 rpm, and /3.41-5.00/ = 1.59 for 45 rpm. Since /6.24-5.00/ is closest to zero (i.e. 6.24 is closest to 5.00), a speed of 30 rpm would be used.

visuoperceptual skills. It was administered in the manner used by Kaplan and colleagues (Goodglass & Kaplan, 1983; Kaplan, 1988; Libon et al., 1993). Standard instructions are as follows: "Draw the face of a clock showing the numbers and the hands set to ten after eleven." After completion of this task the subject was required to copy a clock with the hands set for the same time, with the instructions, "Copy this drawing of a clock." The test was scored in the manner used by Sunderland and colleagues (Sunderland, Hill, Mellow, Lawlor, Gundersheimer, Newhouse, & Grafman, 1989). The test form and scoring criteria are presented in Appendix C.

Controlled Oral Word Association Test (COWA). COWA measures flexibility and intactness of the semantic network, as well as executive control. It was administered as described by Spreen and Strauss (1991; also see Lezak, 1983). The subject is required to perform six related tasks. The first three tasks require generation according to a phonemic cue. In each, the subject is instructed to say as many words as he/she can think of in 60 seconds, beginning with the letter **F**; beginning with the letter **A**; and beginning with the letter **S**. The subject is, in addition, instructed to exclude proper nouns and words already given with a different suffix. Instructions (from Spreen & Strauss, 1991, p. 220) are as follows:

> I will say a letter of the alphabet. Then I want you to give me as many words that begin with that letter as quickly as you can. For instance, if I say 'B', you might give me 'bad', 'battle', 'bed' . . . I do not want you to use words that are proper names such as 'Boston', 'Bob', or 'Brylcreem.' Also, do not use the same word again with a different ending such as 'eat' and eating'. Any questions?" {Pause} "Begin when I say the letter. The first letter is 'F'. Go ahead.

The final three tasks in COWA require generation according to a semantic cue. In the first two of these, the time limit is again 60 seconds, and the subject is required to say as many words as he/she can think of belonging to the categories "animals;" and "fruits

and vegetables." The sixth task is actually made up of four smaller tasks. Here the subject is allowed 15 seconds per category and is required to say as many animals as he/she can think of belonging to the following categories: those living in the jungle; those living on the farm; birds; and pets.

For each of the six tasks a raw score, consisting of the number of correct words generated (i.e. excluding words not fitting the rules of the task and perseverations), was calculated. For the final task, correct items for all four categories were added up for the raw score. In addition, two composite scores were calculated: a *phonemic fluency* score, the sum of the raw scores from the first three tasks; and a *semantic fluency* score, the sum of raw scores of the fourth and fifth tasks.

Finger Tapping (FT). FT measures central control of motor function. It was tested, for each hand, in seven 10-second trials. The dominant hand was tested first. A one minute rest break was given at least after every three trials, and more frequently if necessary. The test was administered with the Manual Finger Tapper (Model #7) from the Reitan Neuropsychology Laboratory and the standard instructions from the Halstead Reitan Battery were used (Reitan & Wolfson, 1993). The average score for each hand was computed by dropping the highest and lowest scores and computing the mean of those remaining. Because this measure was added to the battery after the study had begun, not all subjects were given this test.

Graphical Sequences Test (GST). Goldberg's Graphical Sequences test is a measure of executive function which requires rapid alteration of modality of graphic output. Although the test is quite simple for a healthy subject, patients with frontal lobe pathology tend to produce perseverative errors. The short form of the GST was administered and scored according to standard procedures. The total error score was used in analyses.

Boston Revision of the Wechsler Memory Scale Mental Control Subtest (MC). The MC is a measure of executive control. It requires the ability to establish and maintain set in an attentional capacity. It consists of seven items, the first three of which are taken from the WMS Mental Control subtest and administered in standardized fashion (Wechsler, 1987). These items are as follows: 1) counting backward from 20 to 1, 2) saying the alphabet, and 3) counting by threes from 1 to 40. The final four items are administered in similar fashion, with the subject required to say each of the following as quickly as he/she can (Cloud, Swenson, Malamut, Kaplan, Sands, Gitlin, & Libon, 1994): 4) months of the year forwards, 5) months of the year backwards, 6) letters rhyming with the word "key" (B, C, D, E, G, P, T, V, Z), and 7) capital letters containing curved lines (B, C, D, G, J, O, P, Q, R, S, U). These tests are all timed to facilitate speed, although time is not the dependent variable.

Each item was scored by an index which takes into consideration correct hits (H), omissions (Om), false positives (FP), and perseverations (Psv). The index is as follows: *[1 - (Om + FP + Psv)/ Maximal Possible Hits] X 100.* Two summary scores were derived by calculating the mean of scores on automatized tasks (items 1, 2, and 4) and non-automatized tasks (items 3, 5, 6, and 7).

Copy of Wechsler Memory Scale Visual Reproduction Items (VR). Copying the WMS-R Visual Reproduction figures requires the use of visuoperceptual skills. The subject was required to copy each of the four figures from the Wechsler Memory Scale Visual Reproduction subtest (Wechsler, 1945). Each figure was scored according to the criteria presented in the manual and the total was calculated.

Order of Presentation of Tests

Tests were given in the order shown in Table 5. The order was designed to minimize proactive interference. The entire testing protocol required approximately 2 hours to administer.

Table 5
Order of Administration of Tests

1	Demographic Interview
2	Mini-Mental State Exam
3	Geriatric Depression Scale
4	California Verbal Learning Test (FR & CR Trials 1-8)
5	Boston Revision of the Wechsler Memory Scale Mental Control Subtest
6	Clock Drawing
7	Rotary Pursuit (Trials 1-5)
8	California Verbal Learning Test (FR & CR Trials 9 & 10, Recognition)
9	Controlled Oral Word Association
10	Boston Naming Test
11	Rotary Pursuit (Trials 6-10)
12	Nelson Adult Reading Test, American Version
13	Priming Test
14	Goldberg's Graphical Sequences Test
15	Copy of Wechsler Memory Scale Figures
16	Finger Tapping

Note. CR = cued recall, FR = free recall.

Data Analysis

Data were analyzed with SPSS 4.0.4 on a Power Macintosh (7100/80Av). Analyses were planned, programmed, and interpreted by the author, with the guidance of Kathleen Bittner, Ph.D., who served as a statistical consultant.

Hypotheses I and II

Due to the views and data of some previous investigators (Blaxton, 1985, cited in Roediger et al., 1989; Crowder, 1989; Randolph, 1991; Roediger, et al., 1989) suggesting that declarative memory and priming may be different aspects of a single memory system, a multivariate analysis of variance (MANOVA) was used to investigate

hypotheses regarding the independence of declarative memory and verbal priming from the basal ganglia thalamo-cortical motor circuit and the dependence of procedural motor learning on this motor circuit. This method is recommended in order to control the experimentwise alpha level (Norusis, 1988; Pedhazur & Schmelkin, 1991; Weinfurt, 1995). Norusis (1988, page B-104) explains the reasoning behind using this approach in such situations:

> Although ANOVA tests can be computed separately for each of the dependent variables, this approach ignores the interrelation among the dependent variables. . . . substantial information may be lost when correlations between variables are ignored. For example, several bivariate regression analyses cannot substitute for a multiple regression model which considers the independent variables jointly. Only when the independent variables are uncorrelated with each other are the bivariate and multivariate regression results equivalent. Similarly, analyzing multiple two dimensional tables cannot substitute for an analysis that considers the variables simultaneously.

Planned comparisons were used to follow up on the results of the overall MANOVA and to test the four predictions regarding differences in the various scores produced by the three memory tests that: (1) performance of the IVD group would exceed that of the AD group on recognition hits and false positives, and possibly recall, (2) IVD and PD subjects should show mainly a retrieval deficit (i.e. recall less than EC with recognition hits and false positives either similar to EC), while AD subjects should show an encoding deficit (i.e. recall less than EC and recognition hits and false positives worse than EC), (3) EC, and possibly PD and IVD, would exceed AD on the verbal priming task but not the procedural motor learning task, and (4) EC, and possibly AD, would exceed PD and IVD on the procedural motor learning task, but not the verbal priming task. Tukey's Honestly Significant Difference Test (Tukey's HSD) was used for

post-hoc testing.

Hypothesis III

The relationships between the two nondeclarative memory measures and neuropsychological and neuroanatomical measures was analyzed with correlation and regression procedures. Pearson correlations were used to investigate whether (5) procedural motor learning is positively correlated with performance on tests of executive function (i.e. MC, COWA FAS, GST), and (6) whether verbal priming is positively correlated with performance on language tests (i.e. BNT, COWA categories).

Preceding the investigation of the seventh prediction, Junqué scores were examined with respect to hemisphere and localization with a repeated measures MANOVA, to confirm the symmetry of white matter pathology. A major goal of this study was to determine whether procedural motor learning would be related to PWMA affecting the pathways involved in the basal ganglia thalamo-cortical motor circuit, while verbal priming would not. To investigate (7) whether procedural motor learning performance predicts Junqué scale score while verbal priming does not, a multiple regression analysis was used. To determine the multiple R, all variables were entered in a single step. This procedure was followed by a stepwise multiple regression.

Hypothesis IV

Finally, for prediction 8, it was necessary to investigate whether these neuropsychological tests are effective in delineating brain insult and are thus valid predictors of dementing syndromes with varying neuroanatomical correlates. The capacity of the neuropsychological data to effectively discriminate not only between both normal function and dementia, but also between the three types of dementia, was examined with a canonical discriminant function analysis.

RESULTS

Hypotheses 1 and 2

Means and standard deviations of memory test scores are presented in Table 6. The memory variables involved in hypotheses 1 and 2 were analyzed first via MANOVA. Planned comparisons were then used to assess the specific predictions involved. Because a total of 18 comparisons were made, a modified Bonferroni correction was made to yield an alpha level of .008[5] (Keppel, 1982).

Table 6
Means and Standard Deviations of Memory Test Scores

		AD		IVD		DPD		EC		Total	
		Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
CVLT	Total	-4.07	1.10	-3.85	2.10	-3.63	1.87	0.35	1.01	-2.79	2.42
	Discrim	0.37	0.17	0.58	0.16	0.58	0.21	0.85	0.09	0.59	0.24
RP	Mean	7.38	2.31	4.81	1.77	5.67	2.19	6.93	1.84	6.21	2.24
PT	Score	3.11	3.03	3.02	2.87	4.74	3.54	4.83	2.51	3.98	3.06

Note. AD = Alzheimer's disease; IVD = ischaemic vascular disease; PD = Parkinson's disease; EC = elderly control. CVLT = California Verbal Learning Tests; PT = Priming Test; RP = Rotary Pursuit. CVLT Total scores are presented in z-score format, and Discrimination scores are presented as Corwin's *Pr* (desribed in the Procedure section). The Rotary Pursuit score is mean time on target (seconds out of 20) for trials 1-5. The Priming score has a possible range of 0-15.

Hypothesis 1 involved comparisons among the various CVLT indices. A 4 (Group) X 6 (condition) repeated measures MANOVA was conducted with primacy, recency,

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[5]The method presented by Keppel (1982) was used to calculate the modified Bonferroni correction for the a level, as follows (c = number of planned comparisons, Fw = Familywise):

$\alpha_{Fw\ planned} = \alpha * (conditions-1) = .05 * (4-1) = .15.$

$\alpha_{planned} = \alpha_{Fw\ planned} / c = .15 / 18 = .0083.$

slope of the learning curve, cued recall/free recall index, recognition response bias, and recognition false positives as the dependent variables as the dependent variables. There were significant main effects of group [F (3, 51) = 10.21, p < .001, η^2 = .38] and condition [Wilks Λ = .03, F (5, 47) = 333.02, p < .001, η^2 = .97], and a significant group X condition interaction [Wilks Λ = .23, F (15, 130) = 6.22, p < .001, η^2 = .39].

Planned comparisons revealed that EC subjects exhibited a greater recency effect (t (53) = -2.80, p = .008), steeper learning curve (t (53) = 5.23, p < .001), and greater improvement from free to cued recall (t (54) = -3.30, p < .008) on the recall portion of the test, as well as less of a 'yes' bias (t (52) = -11.45, p < .001) on the recognition test, than all the demented groups. However there were no differences on these measures among the demented groups themselves (t (53) = -1.55, p > .05; t (54) = 1.16, p > .05; t (54) = -0.16, p > .05; t (52) = -0.14, p > .05, respectively). All three demented groups produced more false positive responses than EC on the recognition test (t (52) = -6.51, p < .001); in addition, the AD group produced more false positives than the IVD and PD groups (t (52) = -3.28, p < .008). There were no differences between any of the groups on the primacy measure (for EC vs. all demented groups, t (53) = -0.62, p > .05; for AD vs. IVD and PD, t (53) = 0.01, p > .05).

Hypothesis 2 involved comparisons between the CVLT, Rotary Pursuit Test, and Priming Test.[6] A 4 (Group) X 4 (condition) repeated measures MANOVA, with CVLT recall total trials 1 through 5, CVLT discrimination (*Pr*), RP Mean Trials 1 through 5 and Priming Test score as the dependent variables, revealed significant main effects of group [F (3, 49) = 5.59, p = .002, η^2 = .26] and condition [Wilks Λ = .05, F (3,

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[5]Rotary pursuit scores should be considered in light of UPDRS scores for the DPD group. The mean UPDRS motor score for the 11 DPD patients for which it was available was 22.18 (SD = 11.45). The correlation between the Rotary Pursuit mean score of trials 1 through 5 and the UPDRS was -.453, p > .05.

47) = 284.08, $p < .001$, $\eta^2 = .95$]; the group X condition interaction was also significant [Wilks $\Lambda = .33$, F (9, 114) = 7.25, $p < .001$, $\eta^2 = .35$].

According to planned comparisons, EC exceeded all three demented groups on CVLT total recall for trials 1 through 5 (t (54) = 8.86, $p < .001$), but the AD group did not differ from the IVD and PD group (t (54) = 0.56, $p > .05$). EC also outperformed the other groups on the CVLT recognition task (t (53) = 6.97, $p < .001$); in addition, the IVD and PD groups outperformed the AD group (t (53) = 4.12, $p < .001$). On the rotary pursuit mean of trials 1 through 5, the AD and EC groups outperformed the IVD and PD groups (t (55) = 3.60, $p = .001$). The comparison involving the priming test, that EC, IVD and PD would perform better than AD, was not significant (t (49) = 1.16, $p > .05$). Post-hoc testing with Tukey's test showed no additional significant differences.

Hypothesis 3

Correlations between the two nondeclarative tests and the various neuropsychological measures are presented in Table 7. As shown, Rotary Pursuit scores correlated with the Clock Command and Copy conditions, COWA FAS, GST errors, and Visual Reproduction. Priming correlated only with MC automatic.

Means and standard deviations of Junqué scale scores are presented in Table 8. A 2 (diagnosis AD or IVD) X 2 (hemisphere) X 5 (Area) repeated measures MANOVA revealed a significant effect of diagnosis [F (1, 21) = 36.23, $p < .001$, $\eta^2 = .63$], such that the IVD group exhibited more white matter damage than the AD group and a significant effect of area [F (4, 84) = 4.34, $p < .01$ $\eta^2 = .17$)], such that the centra semiovale of the frontal region, the area surrounding the corpus of the lateral ventricle, and the area surrounding the atrium and occipital horn of the lateral ventricle were all more affected than the area surrounding the frontal horn of the lateral ventricle (all $p < .05$). There was

no significant effect of hemisphere [F (1, 21) = 0.82, p > .05 η^2 = .04)]. There were no significant interactions of diagnosis by area [Wilks λ = .61, F (4, 84) = 2.42, p > .05, η^2 = .10)], diagnosis by hemisphere [F (1, 21) = 0.82, p > .05, η^2 = .04)], hemisphere by area [Wilks λ = .82, F (4, 84) = 1.15, p > .05, η^2 = .05)], or diagnosis by hemisphere by area [Wilks λ = .73, F (4, 84) = 1.57, p > .05, η^2 = .07)].

Table 7
Correlations Between Nondeclarative Memory Tests and Neuropsychology Tests

	Rotary Pursuit	Priming
Boston Naming Test	-0.155	-0.121
Clock Command	0.337**	0.118
Clock Copy	0.328**	-0.039
Controlled Oral Word Association/ FAS	0.313**	0.199
Controlled Oral Word Association/ Categories	0.118	0.146
Graphical Sequences Test, Total Errors	-0.224*	-0.171
Mental Control/Automatized	-0.138	0.241*
Mental Control/Non-Automatized	0.148	0.063
Visual Reproduction	0.481***	0.125

Note. One-tailed significance: *p < .05, **p < .01, ***p < .001.

Table 8
Means and Standard Deviations of Junqué Scale Scores

		AD		IVD		Total	
		Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*
Right	FCS	0.57	0.51	1.67	0.87	1.00	0.85
	PCS	0.50	0.52	1.22	0.83	0.78	0.74
	FH	0.21	0.43	1.22	0.67	0.61	0.72
	LV	0.57	0.65	1.67	0.87	1.00	0.90
	OH	0.43	0.51	2.11	0.93	1.09	1.08
	Total	2.29	1.86	7.89	3.18	4.48	3.68
Left	FCS	0.50	0.52	1.44	1.01	0.87	0.87
	PCS	0.36	0.50	1.67	0.87	0.87	0.92
	FH	0.21	0.43	1.44	0.73	0.70	0.82
	LV	0.79	0.70	1.78	0.83	1.17	0.89
	OH	0.43	0.51	2.22	1.20	1.13	1.22
	Total	2.29	1.98	8.56	3.13	4.74	3.96
Junque	Total	4.57	3.74	16.44	5.77	9.22	7.45

Note. AD = Alzheimer's disease; IVD = ischaemic vascular disease. FCS = centra semiovale of the frontal region; PCS = the centra semiovale of the parietal region; FH = the area surrounding the frontal horn of the lateral ventricle; LV = the area surrounding the corpus of the lateral ventricle; OH = the area surrounding the atrium and occipital horn of the lateral ventricle. Each area is scored on a scale of 0-4, for a total possible score of 20 per hemisphere and 40 for both hemispheres. For AD, N = 14; for IVD, N = 9.

Correlations between the Junqué scale and neuropsychological measures are presented in Table 9. As can be seen, significant correlations were found between the Junqué scale score and, in order of size, the Rotary Pursuit, Clock copy condition, Visual Reproduction, and Clock command condition.

Table 9
Correlations Between Junqué Scale Scores and Neuropsychological Measures

	Junqué
Boston Naming Test	-0.037
Clock Command	-0.476*
Clock Copy	0.578**
Controlled Oral Word Association FAS	-0.120
Controlled Oral Word Associaiton Categories	0.124
California Verbal Learning Test Free Recall	0.034
California Verbal Learning Test Discrimination	0.343
Graphical Sequences Test Errors	0.376
Mental Control Automatic	0.225
Mental Control Nonautomatic	0.061
Priming	-0.089
Rotary Pursuit	-0.660**
Visual Reproduction copy	-0.562**

Note. Two tailed significance: $*p < .05$; $**p < .01$.

A multiple regression analysis was conducted to determine which neuropsychological tests best predicted the Junqué score. First, all variables were entered into the regression equation in a single step, providing a multiple R of .75 (adjusted R^2 = .20, $F = 1.57, p > .05$). The following predictors were used: BNT total score, Clock Drawing command and copy conditions, COWA "FAS" and categories, CVLT discrimination, CVLT total of trials 1-5, Graphical Sequences Test total errors, Mental Control automatized and nonautomatized summary scores, Priming Test, Rotary Pursuit mean of trials 1 through 5, and Visual Reproduction total.

Second, a stepwise multiple regression analysis was conducted to determine which variables provided the major contributions to the prediction of the Junqué scale. Using strict criteria (p (in) = .05, p (out) = .10), only the RP mean of Trials 1-5 entered the

equation. Because only a single predictor entered the equation, the criteria were relaxed. The second predictor, Clock command condition, entered the equation with criteria of p (in) = .17 and p (out) = .20). Results are presented in Table 10.

Table 10
Stepwise Multiple Regression Analysis to Predict Junqué Score from Memory and Neuropsychological Test Scores

Step	Predictor	B	F	p	R^2
1	Rotary Pursuit. Mean Trials 1-5	-1.67	17.45	< .001	.384
2	Clock Command	-0.80	10.08	< .001	.428

Note. RP = Rotary Pursuit Test; B = raw partial regression coefficient, R^2 = coefficient of multiple determination (proportion of variance in the criterion shared by the combined predictors). Criteria for entry and exit of predictors: p (in) = .17, p *(out)* = .20.

Hypothesis 4

A descriptive canonical discriminant function analysis was used to determine the diagnostic utility of the memory and other neuropsychological tests. Thus these measures were used as predictors, and group membership as the criterion. Unfortunately, in the analysis portion of the procedure 18 cases were excluded due to missing discriminating data points; however, all cases were considered in the classification phase. As there were four groups, three canonical discriminant functions were revealed, as shown in Table 11). The first function explained 83.91% (p < .001) of the between-groups variance, the second explained 14.20% (p < .05), and the third, 1.89% (p > .05). Correlations between individual tests and the three functions are shown in Table 12. In general, verbal memory and language tests loaded on the first factor, the Graphical Sequences Test loaded on the second factor, and the third factor included larger loadings from visuospatial and motor tasks with smaller loadings from priming and executive tasks.

Table 11
Canonical Discriminant Functions in Prediction of Diagnosis

Function	Eigenvalue	Percent of Variance	Canonical Correlation	After Function	Wilks' λ	χ^2	*p*
				0	0.02	122.14	< .001
1	11.77	83.91	0.960	1	0.26	41.92	< .05
2	1.99	14.20	0.816	2	0.79	7.41	> .05
3	0.27	1.89	0.458				

Table 12
Pooled Within-Group Correlations between Discriminating Variables and Canonical Discriminant Functions

	1	2	3
CVLT Discrimination	0.699*	0.083	-0.191
CVLT Total Free Recall	0.383*	0.038	-0.007
COWA FAS	0.350*	-0.301	0.252
COWA Categories	0.337*	-0.074	0.135
BNT Total	-0.266*	0.009	-0.158
GST Errors	-0.176	0.498*	-0.209
Clock Copy	0.139	-0.373	-0.533*
Rotary Pursuit Mean Trials 1-5	0.015	-0.249	0.301*
Visual Reproduction copy	0.166	-0.208	0.233*
Priming	0.062	-0.087	0.230*
MC Non-Automatized	0.157	-0.094	0.211*
Clock Command	0.156	0.053	0.186*
MC Automatic	0.014	-0.024	0.121*

Note. BNT = Boston Naming Test, COWA = Controlled Oral Word Association, CVLT = California Verbal Learning Test, GST = Graphical Sequences Test; MC = Mental Control, FT = Finger Tapping. Two-tailed significance: $*p < .05$.

Subject classifications are presented in Table 13. The functions correctly classified 13 of 15 (86.7%) AD subjects, 10 of 15 (66.7%) IVD subjects, 10 of 14 PD (71.4%) subjects, and 15 of 15 (100%) EC subjects, for a sum of 49 of 59. Thus, sensitivity was 81.35%. Specificity, the number of control subjects identified as such, was 100.00%.

Table 13
Actual vs. Predicted Group Membership Resulting from Discriminant Function Analysis

			Predicted Group Membership			
		N	AD	IVD	PD	EC
Actual Group Membership	AD	15	13	2	0	0
			86.7%	13.3%	0.0%	0.0%
	IVD	15	0	10	5	0
			0.0%	66.7%	33.3%	0.0%
	PD	14	1	3	10	0
			7.1%	21.4%	71.4%	0.0%
	EC	15	0	0	0	15
			0.0%	0.0%	0.0%	100.0%
	Total	59	14	16	14	15

Note. AD = Alzheimer's disease, IVD = ischaemic vascular dementia, PD = Parkinson's disease, EC = elderly control.

Summary

Following is a summary of the results of the study, with regard to the individual hypotheses and predictions.

Hypothesis I. Declarative memory is relatively independent of white matter areas.

Prediction 1. Declarative memory will be spared in IVD relative to AD; performance of the IVD group will exceed that of the AD group on the recognition task, and perhaps also on the recall task.

Result 1. Data were analyzed via MANOVA, followed by planned comparisons.

On the CVLT recall task, performance of all demented groups was

below that of the control group on a number of measures, but there were no significant differences between the demented groups. On the CVLT recognition task, performance of all demented groups was below that of the control group. In addition, IVD and PD patients outperformed AD patients on the recognition task.

Prediction 2. Patterns of performance in the IVD group will be similar to those found in other subcortical dementias; IVD and PD subjects will show mainly a retrieval deficit, while AD subjects will show an encoding deficit.

Result 2. Data were analyzed via the same MANOVA used in Prediction 1, followed by planned comparisons.

For the IVD and PD patients, spared recognition, in contrast to poor recall, was consistent with a retrieval deficit. For the AD patients, recognition and recall impairment, as well as a higher production of false positives than the PD and IVD groups, was consistent with an encoding deficit. Other tests of encoding and retrieval difficulties were not significant for any group.

Hypothesis II. Procedural motor learning is dependent on a complex striatal-frontal motor circuit while verbal priming is dependent on the cortical association areas.

Prediction 3. Subjects with AD will have verbal priming impairment, but not procedural motor learning impairment.

Result 3. Data were analyzed via MANOVA, followed by planned comparisons.

On the priming test, AD patients' performance was not

significantly different from that of any other patient group, not even EC. On the rotary pursuit test, AD patients' performance did not significantly differ from that of the EC group; further, AD patients outperformed both the IVD and PD groups.

Prediction 4. Subjects with PD and IVD will have procedural motor learning impairment, but no verbal priming impairment.

Result 4. Data were analyzed via the same MANOVA used in Prediction 3, followed by planned comparisons.

On the priming test, PD and IVD patients' performance was not significantly different from that of any other patient group, not even EC. On the rotary pursuit test, both the IVD and PD groups performed more poorly than the AD and EC groups.

Hypothesis III. Verbal priming and procedural motor learning rely on separate neuroanatomical systems; this will be reflected in their relationships with neuropsychological and neuroanatomical measures.

Prediction 5. Procedural motor learning will be positively correlated with performance on tests of executive function.

Result 5. Pearson correlations were used for the analysis.

Scores on the rotary pursuit test were positively correlated with scores on the Clock Drawing command condition, Controlled Oral Word Association FAS, and negatively correlated with error scores on the Graphical Sequences Test, all measures of executive function. Additionally, they were correlated with two perceptual measures, the Clock Drawing copy condition and Visual Reproduction.

Prediction 6. Verbal priming will be positively correlated with performance on language tests.

Result 6. Pearson correlations were used for the analysis.
Scores on the priming test were not correlated with scores on any of the language tests. They were positively correlated with one executive measure, Mental Control automatic.

Prediction 7. Procedural motor learning, but not verbal priming, will be related to PWMA affecting the pathways involved in the basal ganglia thalamo-cortical motor circuit.

Result 7. A multiple regression analysis was used.
Rotary Pursuit scores were the strongest predictor of PWMA in the analysis. Priming scores did not enter the prediction equation.

Hypothesis IV. To the degree that neuropsychological tests are effective in delineating brain insult, they are valid predictors of dementing syndromes with varying neuroanatomical correlates.

Prediction 8. Neuropsychological data will effectively discriminate not only between normal function and dementia, but also between the three types of dementia.

Result 8. A discriminant function analysis was used.
81% of the subjects were correctly classified, with most of the errors involving overlap between the IVD and PD groups.

DISCUSSION

The common goal this study was to elucidate the neuroanatomical substrate of declarative memory and two types of nondeclarative memory, priming and procedural motor learning. A number of different strategies were engaged, each corresponding to a different hypothesis:

1. To determine whether declarative memory is relatively independent of white matter areas by comparing declarative performance in patients with and without damage to the basal ganglia thalamo-cortical motor circuit (Alexander et al., 1986).
2. To determine whether procedural motor learning is likely dependent on the basal ganglia thalamo-cortical motor circuit while verbal priming is not, by comparing performance in patients with and without damage to this pathway.
3. To investigate the association between neuropsychological and neuroanatomical status and performance on priming and procedural motor learning tasks.
4. To examine the predictive diagnostic ability of patterns of neuropsychological performance in subcortical and cortical dementia.

Hypothesis 1: Patterns of Declarative Performance

It was hypothesized that declarative memory is relatively independent of subcortical white matter areas. Demonstration of this would require adequate declarative memory even with damage to the basal ganglia thalamo-cortical loop. The Alzheimer's disease (AD), Parkinson's disease (PD), and ischaemic vascular dementia (IVD) groups did not differ on the CVLT recall, the measure of declarative memory, despite differing on an index of white matter insult. Although, as expected, none of the demented groups performed as well as the control group on the recognition test, both IVD and PD patients outperformed AD patients. This confirms the prediction that declarative memory is

spared in IVD relative to AD. This finding is similar to previous reports of the relative sparing of declarative recognition memory in subcortical dementia, in IVD (Libon et al., 1993; Bernard et al., 1992), PD (Heindel et al., 1989; Massman et al., 1990; Saint-Cyr et al., 1988) and Huntington's disease (HD, Butters et al., 1985, 1986; Delis et al., 1991; Martone et al., 1984; Massman et al., 1990, 1993), although sparing probably occurs only in milder, but not severe, HD (Kramer et al., 1988).

Relative sparing of recognition, when recall is impaired, is an indication of a retrieval deficit (Butters et al., 1985; Delis et al., 1987, 1991; Massman et al., 1990, 1993). Subjects' production of items on either the free recall or the recognition task required that the items were indeed encoded. Nevertheless, the more structured recognition task provided retrieval aids not available in the less structured free recall task. Further manifestations of a retrieval deficit, as well as performance patterns not seen with encoding deficits, would bolster the claim of IVD's similarity to the subcortical dementias of PD and HD. Retrieval deficits are also associated with poor free and cued recall (Butters et al., 1985; Delis et al., 1991; Massman et al., 1990), an increased recency effect (Delis et al., 1991; Massman et al., 1990), flat learning curve (Delis et al., 1991; Massman et al., 1990), and an improvement in retrieval of items on cued recall (Delis et al., 1987) or recognition (Butters et al., 1985; Delis et al., 1987, 1991; Massman et al., 1990, 1993), in comparison with free recall. These patterns of performance were predicted to occur in the IVD and PD groups in the present study. On the other hand, an encoding and storage deficit is demonstrated by decreased primacy effects (Klatzky, 1980), passive recall from the recency portion of the list (Delis et al., 1987, 1991), a flat learning curve (Delis et al., 1991; Luria, 1980), co-occurring decreased free and cued recall (Delis et al., 1987), poor recognition with high false positive rates or intrusive errors (Butters et al., 1988), and a 'yes' response bias (Delis et al., 1991). Such patterns of performance were predicted to occur in the AD group in this study. In the present

study, AD patients did indeed produce higher numbers of false positives than subcortical dementia groups.

All the demented groups demonstrated some signs of encoding and storage impairment in comparison with the EC group: a flattened learning curve and more false positives and a "yes" bias on the recognition test. Patterns often associated with encoding impairments have been reported before in patients with subcortical dementia. Examples in HD include poor free recall (Delis et al., 1991; Heindel et al., 1989; Massman et al., 1993); decreased primacy (Delis et al., 1991; Massman et al., 1993); a flattened verbal learning curve, which may or may not differ from that seen in AD and Korsakoff's amnesia (Butters et al., 1985; Delis et al., 1991); poor recognition (Heindel et al., 1989); and more false positives than controls, sometimes with a "yes" response bias (Butters et al., 1985; Kramer et al., 1988). Examples in PD (Heindel et al., 1989) and IVD (Libon et al., 1990) include poor free recall. While such examples provide quantification of encoding and storage problems, it is the relative differences between the dementias which are of greatest interest here. Most of these deficits are interpreted as mild because the preserved recognition seen in these same patients with subcortical dementia provides evidence that encoding and storage have in fact taken place. Such evidence is not found in AD.

On other measures used to differentiate between encoding and retrieval deficits, slope of the learning curve, primacy, recency, improvement from free to cued recall, and "yes" bias on discrimination, the performance of the demented groups did not differ. A clearer separation of cortical and subcortical dementia with respect to encoding versus retrieval deficits was expected. The N of 14-15 subjects per group may have been a factor. In addition, the MMSE range for demented subjects was 12 to 26, and likely the inclusion of patients with moderately severe levels of dementia was a greater factor. The neuropsychological and clinical profiles (neuropsychological, Kramer et al., 1988; Levin

et al., 1992; Lichter et al., 1988; clinical, Cummings & Benson, 1983) of cortical and subcortical dementia tend to overlap more and more as the severity of dementia increases. This increasing similarity at lower ends of the MMSE scale likely blurred the differences between groups.

Hypothesis 2: Patterns of Nondeclarative Performance

It was hypothesized that procedural motor learning is dependent on a complex subcortical circuit, involving basal ganglia thalamo-cortical motor pathways such as that proposed by Alexander and his colleagues (Alexander et al., 1986), but that verbal priming is independent of this circuit and dependent on cortical association areas. If this were true, one would expect two findings. First, there would be deficits in procedural motor learning in PD and IVD, dementias associated with damage to the basal ganglia thalamo-cortical motor circuit, but spared procedural motor learning in AD, a dementia which does not involve damage to this area. Second, there would be a verbal priming impairment in AD subjects, who have damage to cortical association areas, with spared priming in PD and IVD subjects, who do not.

Procedural Motor Learning

As predicted, AD subjects performed normally on the procedural motor learning test while both subcortical dementia groups were impaired on this measure. It has been known that AD (Eslinger & Damasio, 1986) and KA (Cohen, 1984) patients have demonstrated preserved procedural motor learning. A dissociation in procedural motor learning between cortical and subcortical dementia has been demonstrated with AD and HD patients (Butters et al., 1988; Butters et al., 1990; Heindel et al., 1991), HD and KA patients (Butters et al., 1985), and HD patients and normal controls (Bylsma et al., 1990). Results have been more equivocal with PD patients. PD patients have been found to be impaired on tests of procedural motor learning per se (Heindel et al., 1989; Hocherman &

Aharon-Peretz, 1994). In tasks with the motor component removed procedural learning may be preserved though acquisition is slower than in normal controls (Pascual-Leone et al., 1993). The present results would be consistent with these prior results. The critical finding here is that IVD patients clearly performed more poorly than AD patients on the rotary pursuit task. This relative deficit was similar in extent to that seen in the PD patients. This is the first demonstration of such a deficit in nondeclarative learning in an IVD patient group, and carries implications for the anatomical basis of nondeclarative learning (See below).

Priming

Various authors have had differing results when attempting to determine whether priming is affected or preserved in cortical dementia. AD patients have historically demonstrated deficits on most priming tasks, and HD patients have demonstrated preservation. As demonstrated in Table 14, results are remarkably consistent across tasks in these patient groups. Many studies support a priming deficit in AD (Butters et al., 1990; Heindel et al., 1989; Salmon et al., 1988) and PD (Heindel et al., 1989), but there have been previous studies in which AD patients (Glosser & Friedman, 1991; Grober, Ausubel, et al., 1992) have showed normal priming. Prior studies have consistently found preserved priming in HD patients (Butters et al., 1990; Heindel et al., 1989; Martone et al., 1984; Salmon et al., 1988). In the present study no differences between groups were seen on the priming test, in AD versus PD and IVD, or even between demented and control subjects.

Though prior authors have attributed priming to the cortical association areas, the evidence in the present study does not support such a conclusion. While the preservation of procedural motor learning in AD versus IVD and PD argues for the dependence of this skill on the complex subcortical motor circuit; the evidence would have been more

convincing if there were an impairment of the AD subjects on the priming test, resulting in a double dissociation of the two tasks. In this case procedural motor learning would be shown to be dependent on subcortical white matter and priming on cortical association areas and *not* white matter pathways. It is possible that differences between studies as to whether there is a priming deficit in AD or any another dementia might be due to the particular tests used. It is difficult to determine the status of priming in subjects with PD and IVD, which have been less studied.

Table 14
Status of Priming Ability in Various Dementias

Group	Type	Test	Impaired	Preserved
AD	Lexical	Mirror Reading Skill	Grober et al., 1992	
		Paired Associates		Glosser & Friedman, 1991
		Word Stem Comp.	Salmon et al., 1988	Present Study
	Semantic	Paired Associates	Glosser & Friedman, 1991 Salmon et al., 1988	
		Pictorial Fragment Id.	Heindel et al., 1990	
HD	Lexical	Mirror Reading Rep.		Martone et al., 1984
		Word Stem Comp.	Salmon et al., 1988	
	Semantic	Paired Associates		Salmon et al., 1988
		Pictorial Fragment Id.		Heindel et al., 1989
IVD	Lexical	Word Stem Comp.		Present Study
PD	Lexical	Word Stem Comp.	Heindel et al., 1989	Present Study

Note. AD = Alzheimer's disease; HD = Huntington's disease; IVD = ischaemic vascular dementia; PD = Parkinson's disease; Comp. = Completion; Id. = Identification; Rep. = Repetition. Impairment is shown relative to controls. In the Salmon et al., 1988 study, HD patients outperformed AD patients.

The results of this study agree with those of Glosser and Friedman (1991), who found preserved lexical priming in AD. However, they clearly differ from those of prior

studies: while lexical priming was found to be preserved in this sample, deficits have been found in other samples studied. Aspects of our methodology may have differed from that of the other study which investigated lexical priming via word stem completion in AD (Salmon et al., 1988). Because scores of the demented subjects in the present study did not differ from those of the controls, it may be that the priming test was too easy. However, the Salmon study used the same rating system, and the priming task appears to have been even easier. Similar stems and words were used, only 10 to-be-remembered stimuli were presented (as opposed to 15 in the present study), the rating procedure was conducted twice in succession with the same stimuli (as opposed to only once in the present study), the test procedure directly followed the study presentation (same), and the stimuli were presented among 10 foils (as opposed to 15 here). Yet the AD patients in the Salmon study were impaired on this task while those in the present study were not. A second explanation would be that the controls in the present study performed more poorly than those in the Salmon study, minimizing any differences from one or more of the demented groups. The EC group in this study scored a mean of 4.83, or 32.2%, on the priming test. The control group in Salmon's study scored over 40%, as determined from the published graphs. However, the mean score of the AD group in his study was roughly 15% while it was 20.1% in this study. While the controls in the present study may have performed somewhat worse, the AD group may also have performed somewhat better. The lack of significance found in this study may also result from the extremely high standard deviations (refer to Table 6). A third explanation would be that in the Salmon study priming test performance was contaminated by declarative recognition memory, due to the multiple presentations of study material. It is, then, difficult to draw any conclusions about the preservation or impairment of priming from the present study; further investigation will have to settle this issue.

Hypothesis 3: The Neuroanatomical Substrate of Nondeclarative Memory

It was hypothesized that the reliance of verbal priming and procedural motor learning on separate neuroanatomical systems would be reflected in their relationships with the neuropsychological and neuroanatomical measures. Scores on verbal priming should be positively correlated with performance on language tests: the Boston Naming Test and Controlled Oral Word Association FAS. Procedural motor learning scores should be correlated with performance on tests of executive function: positive correlations would exist between the rotary pursuit and Mental Control, Controlled Oral Word Association FAS and the Clock Command condition, with a negative correlation between Rotary Pursuit and Graphical Sequence Test errors. Finally, procedural motor learning performance, but not verbal priming performance, should be correlated with PWMA affecting the pathways involved in the basal ganglia thalamo-cortical motor circuit.

Priming

There were none of the expected relationships between priming and the language tests, although priming was positively correlated with Mental Control automatic, an executive measure. Most previous investigators have suggested that word stem completion relies on perceptual identification processes (Schacter, 1992; Tulving & Schacter, 1990). However, as pointed out by Winocur and colleagues (Winocur, Moscovitch, and Stuss, 1996), several studies have shown significant correlations between performance on this task and tasks dependent on frontal lobe function (Borkowski, Benton, & Spreen, 1967; Davis, Cohen, Gandey, Colombo, Van Dusseldorp, Simolke, & Romano, 1990; cf. Shimamura, Gershberg, Jurica, Mangels, & Knight, 1992), and the present finding is consistent with this. Winocur's group (Winocur et al., 1996) found a double dissociation in elderly persons in which performance on explicit versions of word stem and word fragment completion tests correlated with performance

on traditional tests of hippocampal-dependent memory, while performance on an implicit version of the word stem completion (but not fragment completion) correlated with performance on frontal tasks. The authors drew a parallel between the generative ability required by both the Controlled Oral Word Association FAS and the implicit word stem completion task, though they did suggest that word fragment completion is a perceptual identification task. While word stem completion was found to be uncompromised in HD and PD patients in previous studies (Bondi & Kaszniak, 1991; Heindel et al., 1989; Huberman, Moscovitch, & Freedman, 1994), Winocur and colleagues (Winocur et al., 1996) believe that, had the data been looked at, a significant correlation between performance on word stem completion and executive tasks would have been found.

If priming were related to frontal executive systems, some impairment would be expected with PD and especially with IVD, which causes more diffuse damage than PD. In fact, as was true for the AD patients in this study, the PD and IVD subjects did not exhibit impairment on the priming task. However, given the absence of differences between *any* of the demented groups and the control group, this result should not be interpreted as an absence of such a relationship. Rather, further study in these groups is recommended to confirm the preservation of priming. If preservation were confirmed, this would make the meaningfulness of the correlations between priming and executive tasks questionable. If preservation could not be confirmed, the anatomical underpinnings of priming deficits might be revealed through further comparison of memory test and MRI data.

While motor skill learning dissociated from both declarative memory and verbal priming in the present study, this is not convincing evidence that verbal priming involves a memory system separate from that involved in declarative memory. Roediger (e.g. Roediger et al., 1989) has argued that verbal priming and recall/recognition may be two different manifestations of the same system, phenomena which separate due to test

characteristics and not differences in their neural substrates. According to this view, the spared priming in all groups can be explained by the characteristics of the tests used in the various tasks. Parallel tests with only subtle differences (e.g. Willingham et al., 1996) present more convincing evidence for differences in the systems subserving various functions. Using parallel declarative and verbal priming tests, Grober and colleagues (Grober et al., 1992) showed that declarative retrieval of category exemplars in demented subjects was not due to priming.

Other approaches to distinguishing priming from declarative memory are of interest. Cronin-Golomb and colleagues (Cronin-Golomb, Gabrieli, & Keane, 1996) found interhemispheric transfer of verbal priming (word-stem completion task), but not of recall or recognition (list learning tasks), in two patients with histories of callosotomy; thus priming information was transmitted subcortically while declarative information was not. This suggests that priming is supported subcortically, although the information transferred is probably associative and does not consist of word forms themselves. Cronin-Golomb and colleagues suggested there may be differences in the representation of the information which leads to priming and declarative memory. More study in this area is required to determine whether there are separate neural substrates.

Procedural Motor Learning

As expected, procedural motor learning scores were positively correlated with Clock Command and Controlled Oral Word Association FAS scores, and negatively correlated with Graphical Sequences Test error scores. However, they were also correlated with two visuoperceptual measures, Clock Copy and Visual Reproduction, and were not significantly correlated with either of the Mental Control scores. The failure of the rotary pursuit measure to correlate with the two Mental Control scores may be due to the low number of subjects or simply the differences between the demands of the task. The Mental Control task does have a heavy attentional component which may not be as

crucial to Rotary Pursuit performance. What is more interesting here is the positive correlations between the Rotary Pursuit task and the two perceptual measures. The Rotary Pursuit task likely requires eye-hand coordination also reflected on the perceptual tasks. Despite the simplicity of this interpretation, it is difficult to draw conclusions from the relationship between the rotary pursuit and some of the executive measures given these other results. Replication is needed to bolster the claim that these relationships reflect similar underpinnings and not simply chance.

Stronger support for the relationship between the substrates of executive functions and procedural motor learning is given by the results of the multiple regression analysis. Rotary pursuit performance was the strongest predictor of PWMA, as measured by Junqué scale score, while verbal priming did not even enter the multiple regression equation. Previous studies have repeatedly demonstrated dissociations in the performance of subjects with cortical and subcortical dementia. However, this is the first neuroanatomical measure suggesting the dependence of procedural motor learning on the basal ganglia thalamo-cortical motor circuit. Previous empirical study and theoretical discussion has been focused on implicating this pathway in procedural motor learning by demonstrating single and double dissociations in the performance of procedural motor and priming tasks in subcortical and cortical dementias (e.g. HD and PD versus AD). Such study has focused on the effects of damage to the nuclei shown in Figure 2. MRI data on IVD patients clearly indicates damage to the white matter pathways funneling information from one nucleus to the next, as well as to the reciprocal connections returning to the frontal cortex. The results of this multiple regression analysis not only indicate the importance of white matter in frontal function, but also support the claims, based on studies of gray matter damage, that the basal ganglia thalamocortical circuit underlies procedural motor learning.

Hypothesis 4: Diagnostic Considerations

The final hypothesis involved the degree to which neuropsychological tests discriminate among the different dementias. Credibility of the value of the diagnostic categories would result from their maximal separation according to the neuropsychological data, but important information could also be gained from analysis of patterns of overlap.

81% of the subjects were correctly classified by the neuropsychological tests used, including all of the control subjects. The incorrect placement of two AD subjects in the IVD group draws attention to the possible overlap between cortical and subcortical symptomatology. However, the majority of classification errors occurred as a result of interchanges between the IVD and PD groups, with all five misclassified IVD subjects being placed in the PD group and three of the four misclassified PD subjects being placed in the IVD group. This pattern of classification errors demonstrates the similarity in IVD and PD profiles. In 8 of the 29, or 27.6% of the cases of subcortical dementia, test results could not distinguish between the two disorders. The similarity in neuropsychological profiles might be explained by the similarity of the neuroanatomical profiles of these two disorders.

On the other hand, the fact that most subjects were correctly classified, as either cortical or subcortical dementia, or normal, speaks to the differences between the disorders and illustrates the variability within the category of subcortical dementia. Previous authors (e.g. Massman et al., 1990) have acknowledged such differences between subcortical syndromes.

Conclusions in Perspective

The results indicate a pattern of declarative memory test performance in IVD similar to that seen in other subcortical dementias, such as HD and PD. This pattern is

characterized by impaired retrieval, with relatively spared encoding and storage. Spared declarative processes occur despite damage to the basal ganglia thalamo-cortical circuit in both IVD and PD. This finding lends credence to the hypothesis that declarative learning is independent of the basal ganglia thalamo-cortical circuit.

With regard to nondeclarative processes, the rotary pursuit results clearly indicated a single dissociation between procedural motor learning performance in AD as compared to IVD and PD, and a double dissociation between procedural motor learning performance and declarative memory performance in cortical versus subcortical dementia. Possible dependence of rotary pursuit learning on the basal ganglia thalamo-cortical circuit is suggested by the relationship between performance on the procedural motor learning task and neuroanatomical compromise shown on MRI. The present study supports the view that rotary pursuit performance depends on the basal ganglia thalamo-cortical circuit, both by the patterns of performance seen in the various diagnostic groups and by the effective prediction of subcortical insult by the Rotary Pursuit score. Further evidence must be obtained by attempting to replicate the double dissociation between priming and procedural motor learning found previously (Butters, Heindel, & Salmon, 1990) and by looking at other measures of nondeclarative procedural learning in a similar paradigm. Particularly, it would be useful if additional procedural tasks, in particular nonmotor tasks (e.g. Tower of Hanoi or Nissen's serial reaction time task, Knopman & Nissen, 1991) could be shown to correlate with neuroanatomical data in IVD or another subcortical syndrome; such tasks might affect the parallel basal ganglia thalamo-cortical circuits described by Alexander and colleagues (Alexander et al., 1986).

Despite the clarity of findings involving the other nondeclarative process, the results of this study reveal no clear relationship between priming and either cortical association areas or the frontal thalamo-cortical circuit involved in motor learning. Results of the word stem completion test, a lexical priming test, add to the equivocal

literature regarding dementia and the loss or preservation of priming; in this light it is difficult to interpret IVD performance. IVD and PD need to be compared with HD and AD groups on a larger variety of lexical and semantic priming tests. The neuroanatomical substrate of priming is still in question. Perhaps the solution to this problem lies not only in further study with patient groups, but also in clarification of what exactly is being tested in priming tests, an issue raised by Roediger and his associates (e.g. Roediger et al., 1989). In the long run, an irrefutable demonstration that IVD shows the same nondeclarative memory profile as HD and PD would require evidence gathered from more than one test for each nondeclarative function.

Finally, the discriminant function analysis indicated alignment of IVD with PD and not AD when performance on a variety of neuropsychological measures was considered. Such a demonstration bolsters the other results of this study. More importantly, it provides support for the further use of IVD patients as a representative group for subcortical dementia in further studies of the neuroanatomy of the memory systems.

APPENDICES

Appendix A: Consent Form

Consent Form: Implicit Memory in Dementia

I, _____, willingly agree to participate in this study, which has been explained to me by _____. This research study is being conducted by the Neuropsychology Service at Crozer-Chester Medical Center.

I have been asked if I would volunteer to participate in a study of the neuropsychological characteristics of dementia. The purpose of the study is to help determine which functions are effected by various dementias and how these relate to brain structure.

___ **Control Subject:** The study involves a 2 hour testing session during which I will receive neuropsychological tests of my memory, concentration, language, visual perception, motor skills, and mood.

___ **Clinical Subject:** I have already requested a neuropsychological evaluation as part of a dementia evaluation. I understand that results of tests given during this evaluation, as well as results of other procedures already completed for related purposes (including MRI and CT scan of the brain, EEG, and general medical history) may be used for research purposes.

I understand that participation in the testing session may cause fatigue. I realize that I will receive no personal benefit from my participation in this study. Possible benefits to society include a further understanding of the dementias, which may eventually lead to more effective diagnosis and/or treatment.

Participation in this study is voluntary and no compensation for participation will be given. I understand that I am free to withdraw my consent to participate in this study at any time without prejudice to my subsequent care. Refusing to participate will result in no penalty and will have absolutely no effect on any treatment I receive at Crozer-Chester Medical Center. I understand that a record of my test results will be kept in a confidential file at the Neuropsychology Service. No information by which I can be identified will be released or published.

I understand that I may contact Heather Gitlin, M.A., or David Libon, Ph.D., at (610) 447-6014, if I have any further questions about this study. I have read all of the above, asked questions, received answers concerning areas I did not understand, and willingly give my consent to participate in this study. Upon signing this form, I will receive a copy.

_____ _____

(Subject Signature) (Date)

_____ _____

(Witness Signature) (Date)

Appendix B: Item Analyses

Appendix B-1: Geriatric Depression Scale Item Analysis

Table B-1
Means and Standard Deviations of Geriatric Depression Test Item Scores

Item	AD		IVD		DPD		EC		All	
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
1	.08	.28	.00	.00	.17	.39	.29	.47	.14	.35
2	.54	.52	.20	.42	.50	.52	.14	.36	.35	.48
3	.00	.00	.30	.48	.08	.29	.07	.27	.10	.31
4	.15	.38	.30	.48	.25	.45	.14	.36	.20	.41
5	.00	.00	.00	.00	.08	.29	.00	.00	.02	.14
6	.00	.00	.00	.00	.08	.29	.07	.27	.04	.20
7	.00	.00	.10	.32	.08	.29	.07	.27	.06	.24
8	.08	.28	.30	.48	.17	.39	.14	.36	.16	.37
9	.23	.44	.20	.42	.25	.45	.07	.27	.18	.39
10	.38	.51	.20	.42	.25	.45	.07	.27	.22	.42
11	.00	.00	.00	.00	.08	.29	.00	.00	.02	.14
12	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00
13	.31	.48	.40	.52	.75	.45	.21	.43	.41	.50
14	.00	.00	.20	.42	.08	.29	.00	.00	.06	.24
15	.23	.44	.10	.32	.08	.29	.07	.27	.12	.33
Total	2.00	2.04	2.30	2.21	2.92	2.23	1.36	1.50	2.10	2.01

Note. AD = Alzheimer's disease, IVD = ischaemic vascular dementia, PD = Parkinson's disease, EC = elderly control. All items were scored either 1 (consistent with depression) or 0 (not consistent with depression). See Appendix C for item questions.

Appendix B-2: Priming Test Item Analysis

Table B-2
Analysis of Priming Forms: Means and Standard Deviations of Item Scores for the Two Forms

		Form A		Form B				Form A		Form B	
Item		*Mean*	*SD*	*Mean*	*SD*	*Item*		*Mean*	*SD*	*Mean*	*SD*
1	F	0.00	0.00	0.00	0.00	16	F	0.12	0.33	0.00	0.00
2	F	0.69	0.47	0.04	0.19	17	T	0.46	0.51	0.59	0.50
3	F	0.08	0.27	0.00	0.00	18	T	0.46	0.51	0.07	0.27
4	T	0.12	0.33	0.30	0.47	19	T	0.54	0.51	0.44	0.51
5	F	0.00	0.00	0.00	0.00	20	F	0.23	0.43	0.00	0.00
6	T	0.23	0.43	0.96	0.19	21	F	0.00	0.00	0.04	0.19
7	T	0.12	0.33	0.22	0.42	22	T	0.42	0.50	0.30	0.47
8	F	0.00	0.00	0.15	0.36	23	T	0.58	0.50	0.04	0.19
9	T	0.12	0.33	0.11	0.32	24	F	0.15	0.37	0.11	0.32
10	T	0.69	0.47	0.26	0.25	25	T	0.19	0.40	0.30	0.47
11	T	0.42	0.50	0.00	0.00	26	F	0.00	0.00	0.04	0.19
12	F	0.00	0.00	0.00	0.00	27	F	0.00	0.00	0.11	0.32
13	F	0.08	0.27	0.71	0.27	28	T	0.35	0.49	0.22	0.42
14	T	0.38	0.50	0.48	0.51	29	F	0.04	0.20	0.00	0.00
15	T	0.46	0.51	0.22	0.42	30	F	0.08	0.27	0.03	0.19

Note. T = target, F = foil. Items were scored 1 if correct and 0 if incorrect.

Appendix C: Tests and Measures

Appendix C-1: Demographic Information Form

Name: _____ Subject # ❑❑❑❑
(Name for phone screening records only.
Remove name upon testing of subject.)
❑ Alzheimer's Disease
❑ Parkinson's Disease (❑DPD ❑NDPD)
❑ Subcortical Ischaemic Vascular Dementia
❑ Control Subject

Date: ❑❑/❑❑/❑❑❑❑
Birthdate: ❑❑/❑❑/❑❑❑❑
Age: ❑❑❑
Sex: ❑ Male ❑ Female

Source:
CCMC: ❑ GAP ❑ Private ❑ MDC ❑ Volunteer
RWJMS: ❑ Golbe ❑ Other: _____

Race: ❑ White ❑ African-American ❑ Hispanic ❑ Asian ❑ Other: _____

Marital Status: ❑ Single ❑ Married ❑ Widowed ❑ Divorced/Separated

Education: ___ years (Degrees & Subjects: _____)

Occupation: _____

Geographic Area (current):
❑ Pennsylvania ❑ Urban
❑ New Jersey ❑ Suburban
❑ Other: _____ ❑ Rural

For Patients: Duration of Illness: ❑❑.❑ years (to nearest half year)

Medical History:
❑ HTN ❑ HD/MI ❑ HI ❑ CVA
❑ Seizures ❑ ↓ B12 ❑ Psych. ❑ EtOH
❑ Cancer (_____) ❑ Other: (_____) ❑ Other: (_____)

Notes: _____
_____
_____

Examiner Initials: _____

Appendix C-2: Mini-Mental State Examination

Name: _____ Date: _____ Score: ___ Subject #_____

A. Orientation

1. What is the year? _____ season? _____ ___ (5)
   day? _____ date? _____ month? _____

2. Where are we? state? _____ county? _____ ___ (5)
   town? _____ hospital? _____ building/floor? _____

B. Registration

Can I test your memory? I'll say three words. Just listen and then repeat them for me.

Toothbrush ___ Cigarette ___ Pen ___ (1 second each). ___ (3)
Trials needed for correct recall: ___ (Score = Words recalled on first attempt.)

C. Attention and Calculation (Count 1 or 2 but not both.)

1. I would like you to start at 100 and then subtract. Take away 7, then take away 7 from that, and keep taking away 7 until I say "Stop." Okay? (Demonstrate as needed). Ready? Go!
   100 93 86 79 72 65 ___ (5)
   ___ ___ ___ ___ ___

2. I would like you to spell the word "world" backwards.
   D L R O W
   ___ ___ ___ ___ ___ ___ (5)

D. Recall

Can you tell me the three words I asked you to remember a few minutes ago?
(If no response, cue with "toothbrush.")
Toothbrush ___ Cigarette ___ Pen ___ ___ (3)

E. Language

1. Look here. What is this called? ___ Watch ___ Pencil ___ (2)

2. Now, please listen and repeat after me: "No ifs, ands, or buts." ___ (1)

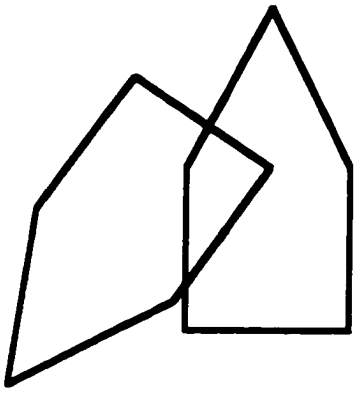
3. Please take this paper in your right hand, fold it in half, and then put it on the floor.
   ___ Right hand ___ In half ___ On floor ___ (3)

4. Please read this and do what it says. (Hold up "Close your eyes" sign.) ___ (1)

5. Please make up a complete sentence and write it out. (Must have noun and verb.) ___ (1)

6. Make a copy of this drawing. (Intersecting hexagons.) ___ (1)
   (Score: All 10 angles and proper intersection of figures are present.)

CLOSE YOUR EYES



Appendix C-3: Geriatric Depression Scale (GDS)

(Short Form)

Name: _____ Date: _____ Subject #_____

Choose the best answer for how you have felt over the past week.

1.	Are you basically satisfied with your life?	yes	no
2.	Have you dropped many of your activities and interests?	yes	no
3.	Do you feel that your life is empty?	yes	no
4.	Do you often get bored?	yes	no
5.	Are you in good spirits most of the time?	yes	no
6.	Are you afraid that something is going to happen to you?	yes	no
7.	Do you feel happy most of the time?	yes	no
8.	Do you often feel helpless?	yes	no
9.	Do you prefer to stay at home rather than going out and doing new things?	yes	no
10.	Do you feel you have more problems with memory than most people?	yes	no
11.	Do you think it is wonderful to be alive now?	yes	no
12.	Do you feel pretty worthless?	yes	no
13.	Do you feel full of energy?	yes	no
14.	Do you feel that your situation is hopeless?	yes	no
15.	Do you think that most people are better off than you are?	yes	no

Total: _____

Score = Total X 2: _____

Administration and Scoring

Administration: The examiner asks questions and records responses.

Scoring: 1 point is given for each of the following responses:

1.	No	6.	Yes	11.	No
2.	Yes	7.	No	12.	Yes
3.	Yes	8.	Yes	13.	No
4.	Yes	9.	Yes	14.	Yes
5.	No	10.	Yes	15.	Yes

Appendix C-4: Nelson Adult Reading Test

(American Version)

Name: _____ Date: _____ Subject #_____

Instructions: I would like you to read some words. These words are a little unusual, in that they do not sound the same way as they look. Just read them one by one and try your best. (*Discontinue after 10 consecutive errors.*)

1.	ache	___	26.	algae	___
2.	aisle	___	27.	superfluous	___
3.	capon	___	28.	chamois	___
4.	debt	___	29.	thyme	___
5.	chord	___	30.	apropos	___
6.	heir	___	31.	virulent	___
7.	deny	___	32.	zealot	___
8.	bouquet	___	33.	facade	___
9.	caprice	___	34.	cabal	___
10.	gauge	___	35.	abstemious	___
11.	worsted	___	36.	detente	___
12.	depot	___	37.	scion	___
13.	nausea	___	38.	papyrus	___
14.	naive	___	39.	quadruped	___
15.	subtle	___	40.	prelate	___
16.	pugilist	___	41.	epitome	___
17.	fetal	___	42.	beatify	___
18.	blatant	___	43.	hyperbole	___
19.	placebo	___	44.	imbroglio	___
20.	hiatus	___	45.	syncope	___
21.	simile	___			
22.	meringue	___			
23.	sieve	___			
24.	chassis	___			
25.	cellist	___			

Scoring

Total Correct (TC): ___
NART Errors (NE): 45 - TC = ___
Years Education (Ed): ___

Estimated Premorbid IQ:
118.56 - .88 (NE) + .56 (Ed)
118.56 - .88 (___) + .56 (___) = _____

(Grober & Sliwinski, 1991)

California Verbal Learning Test (9-item version)

Subject #

Date:

Name:

Trial 1: Let's suppose you were going shopping on Monday. I am going to read a list of things for you to buy. Listen carefully, because when I am through, I want you to tell me as many of the things as you can. You can say them in any order--just say as many as you can. *Trial 2:* I am going to read the Monday shopping list again. Like before, tell me as many of the things as you can, in any order. Be sure to also say the things on the list that you told me the first time. *Trials 3-5:* I am going to read the Monday shopping list again. Like before, tell me as many of the things as you can, in any order, including things on the list that you've said before.

List A Items	Sequence					Learning								
	1	2	3	4	5	Trial 1	T	Trial 2	T	Trial 3	T	Trial 4	T	Trial 5	T
cherries															
sweater															
lettuce															
jacket															
cabbage															
plums															
shorts															
grapes															
spinach															
Sequence															
Primacy			%	S 1-5											
Middle			%												
Recency			%												
Totals 1-5 Correct															
Perseverations															
Intrusions															
Cluster															

Interference: Now, let's suppose you were going shopping again, this time on Tuesday. I am going to read a new list of things for you to buy. When I'm through, I want you to tell me as many of the things from this new list as you can. You can say them in any order.

Short Delay Free Recall: Now I want you to tell me all the things you can from the Monday shopping list. The Monday list was the first list, the one I read to you five times. Don't tell me the things that were on the Tuesday list. Only tell me the things that were on the Monday list.

Short Delay Cued Recall: Tell me all the things from the Monday shopping list that are clothing . . . vegetables . . . fruit.

Subject #

Interference		
List B Items	Recall Trial 6	T
cookies		
peaches		
drill		
bananas		
wrench		
cupcakes		
pliers		
brownies		
strawberries		
Correct		
Perseverations		
Intrusions		
Cluster		

Short Delay Free Recall	
Trial 7	T

Short Delay Cued Recall		
	Trial 8	
clothing	vegetables	fruit

CVLT-9

2

Subject #

Long Delay Free Recall: I read two shopping lists to you before, the Monday list and the Tuesday list. I want you to tell me all the things you can from the Monday list--that was the first list, the one that I read to you five times.

Long Delay Cued Recall: Tell me all the things from the Monday shpping list that are clothing . . . vegetables . . . fruit.

Recognition: Now, I am going to read a bunch of things that people can buy. After I read each one say "yes" if it was on the Monday list, and say "no" if it was not on the Monday list.

Notes: _____

Recall		
Total	Free	Cued
Perseverations		
Intrusions		
Cluster		

Long Delay Free Recall	
Trial 9	T

Long Delay Cued Recall		
	Trial 10	
clothing	vegetables	fruit

Recognition							
Item	HO	IS	IO	NP	NO	PS	
shorts							
glasses							
soap							
drill							
pants							
mop							
cherries							
lettuce							
brownies							
apples							
racquet							
keys							
grapes							
corn							
rug							
spinach							
oranges							
sweater							
radio							
cookies							
strawberries							
jacket							
peaches							
socks							
roses							
plums							
drapes							
cabbage							
wrench							
pencil							
wallet							
carrots							
baggage							
Hits							
	False Positives						
Discrimination	%						

Correct	
Perseverations	
Intrusions	
Cluster	

HLG/1993

CVLT-9

3

Appendix C-6: Rotary Pursuit Test

Rotary Pursuit Test

Name: _____ Date: _____ Subject #_____

Trial Length: 20 sec

Laterality: ☐ right ↔ ☐ left

Direction: ☐ clockwise ↔ ☐ counterclockwise

Pattern: ☐ circle ☐ triangle ☐ square

Speed: ☐ 15 rpm ☐ 30 rpm ☐ 45 rpm

Preliminary	
15	
30	
45	

Trial	ITI	Time On	Impulses
1			
2	20 sec		
3	20 sec		
4	20 sec		
5	20 sec		
6	20 min		
7	20 sec		
8	20 sec		
9	20 sec		
10	20 sec		

HLG/1994

Appendix C-7: Priming Test

Rating

Subject #

Priming Test / Form A

Name: _____ **Date:** _____

#	Item	Rating				
1	museum	1	2	3	4	5
2	hostile	1	2	3	4	5
3	nurture	1	2	3	4	5
4	compete	1	2	3	4	5
5	adverb	1	2	3	4	5
6	trivial	1	2	3	4	5
7	dismiss	1	2	3	4	5
8	calorie	1	2	3	4	5
9	meager	1	2	3	4	5
10	tennis	1	2	3	4	5
11	retain	1	2	3	4	5
12	passive	1	2	3	4	5
13	absorb	1	2	3	4	5
14	various	1	2	3	4	5
15	burglar	1	2	3	4	5
16	decide	1	2	3	4	5
17	grammar	1	2	3	4	5
18	immense	1	2	3	4	5
19	kettle	1	2	3	4	5
20	ignore	1	2	3	4	5

HLG
1995

Word Stem Completion

Subject #

Priming Test / Form A

Name: _____ Date: _____

#	Item	>10"	A	B	Type N	Type V	Type A
1	inv						
2	eve						
3	sha						
4	com						
5	exp						
6	adv						
7	tri						
8	mar						
9	dis						
10	cal						
11	mea						
12	str						
13	spi						
14	ten						
15	ret						
16	app						
17	pas						
18	abs						
19	var						
20	fra						
21	wit						
22	bur						
23	dec						
24	cen						
25	gra						
26	bla						
27	per						
28	imm						
29	sal						
30	lin						
A - B =	%						

HLG
1995

Word Stem Completion

Subject #

Priming Test / Form A / Master

Name: _____ Date: _____

#	Item	>10"	A	B	Type N	Type V	Type A
1	invade						
2	evening						
3	shallow						
4	compete						
5	expand						
6	adverb						
7	trivial						
8	margin						
9	dismiss						
10	calorie						
11	meager						
12	strict						
13	spider						
14	tennis						
15	retain						
16	approve						
17	passive						
18	absorb						
19	various						
20	fragrant, fragrance						
21	wither						
22	burglar						
23	decide						
24	central						
25	grammar						
26	blanket						
27	perform						
28	immense						
29	salmon						
30	linear						
A - B =	%						

HLG
1995

Rating

Subject #

Priming Test / Form B

Name: _____ Date: _____

#	Item	Rating				
1	museum	1	2	3	4	5
2	hostile	1	2	3	4	5
3	nurture	1	2	3	4	5
4	invade	1	2	3	4	5
5	evening	1	2	3	4	5
6	shallow	1	2	3	4	5
7	expand	1	2	3	4	5
8	margin	1	2	3	4	5
9	strict	1	2	3	4	5
10	spider	1	2	3	4	5
11	approve	1	2	3	4	5
12	fragrant	1	2	3	4	5
13	wither	1	2	3	4	5
14	central	1	2	3	4	5
15	blanket	1	2	3	4	5
16	perform	1	2	3	4	5
17	salmon	1	2	3	4	5
18	linear	1	2	3	4	5
19	kettle	1	2	3	4	5
20	ignore	1	2	3	4	5

HLG
1995

Word Stem Completion

Priming Test / Form B

Subject # | | | | |

Name: _____ Date: _____

#	Item	>10"	B	A	Type N	Type V	Type A
1	com						
2	adv						
3	tri						
4	inv						
5	dis						
6	eve						
7	sha						
8	cal						
9	exp						
10	mar						
11	str						
12	mea						
13	ten						
14	spi						
15	app						
16	ret						
17	fra						
18	wit						
19	cen						
20	pas						
21	abs						
22	bla						
23	per						
24	var						
25	sal						
26	bur						
27	dec						
28	lin						
29	gra						
30	imm						
B - A =	%						

HLG
1995

Word Stem Completion

Priming Test / Form B / Master

Subject # | | | | |

Name: _____ Date: _____

#	Item	>10"	B	A	Type N	Type V	Type A
1	compete						
2	adverb						
3	trivial						
4	invade						
5	dismiss						
6	evening						
7	shallow						
8	calorie						
9	expand						
10	margin						
11	strict						
12	meager						
13	tennis						
14	spider						
15	approve						
16	retain						
17	fragrant, fragrance						
18	wither						
19	central						
20	passive						
21	absorb						
22	blanket						
23	perform						
24	various						
25	salmon						
26	burglar						
27	decide						
28	linear						
29	grammar						
30	immense						
B - A =	%						

HLG
1995

Appendix C-8: Boston Naming Test

Name: _____ Subject #_____

Age: _____ Education: _____ Date: _____

Summary of Scores

1. Number of spontaneously given correct responses.....____
2. Number of stimulus cues given.....____
3. Number of correct responses following a stimulus cue.....____
4. Total correct (1 + 3).....____
5. Number of phonemic cues given.....____
6. Number of correct responses following a phonemic cue.....____
7. Percent of phonemic cues leading to correct response (6/5).....____
8. Errors.....____
   a. Semantic.....____ e. Part/Whole.....____
   b. Circumlocution.....____ f. Perseveration.....____
   c. Literal.....____ g. Don't know.....____
   d. Perceptual.....____ h. Other.....____

	Correct (w/o cue)	Latency (sec)	W/Stimulus Cue Correct	W/Stimulus Cue Incorrect	W/Phonetic Cue Correct	W/Phonetic Cue Incorrect
1. Bed..... (a piece of furniture)	___	___	___	___	___	___
2. Tree..... (something that grows outdoors)	___	___	___	___	___	___
3. Pencil..... (used for writing)	___	___	___	___	___	___
4. House..... (a kind of building)	___	___	___	___	___	___
5. Whistle..... (used for blowing)	___	___	___	___	___	___
6. Scissors..... (used for cutting)	___	___	___	___	___	___
7. Comb..... (used for fixing hair)	___	___	___	___	___	___
8. Flower..... (grows in a garden)	___	___	___	___	___	___
9. Saw..... (used by a carpenter)	___	___	___	___	___	___

10. Toothbrush .....___ ___ ___ ___ ___ ___
(used in the mouth)

11. Helicopter .....___ ___ ___ ___ ___ ___
(used for air travel)

12. Broom .....___ ___ ___ ___ ___ ___
(used for cleaning)

13. Octopus .....___ ___ ___ ___ ___ ___
(an ocean animal)

14. Mushroom .....___ ___ ___ ___ ___ ___
(something to eat)

15. Hanger .....___ ___ ___ ___ ___ ___
(found in a closet)

16. Wheelchair .....___ ___ ___ ___ ___ ___
(found in a hospital)

17. Camel .....___ ___ ___ ___ ___ ___
(an animal)

18. Mask .....___ ___ ___ ___ ___ ___
(part of a costume)

19. Pretzel .....___ ___ ___ ___ ___ ___
(something to eat)

20. Bench .....___ ___ ___ ___ ___ ___
(used for sitting)

21. Racquet .....___ ___ ___ ___ ___ ___
(used for sports)

22. Snail .....___ ___ ___ ___ ___ ___
(an animal)

23. Volcano .....___ ___ ___ ___ ___ ___
(a kind of mountain)

24. Seahorse .....___ ___ ___ ___ ___ ___
(an ocean animal)

25. Dart .....___ ___ ___ ___ ___ ___
(you throw it)

26. Canoe .....___ ___ ___ ___ ___ ___
(used in the water)

27. Globe .....___ ___ ___ ___ ___ ___
(a kind of map)

28. Wreath .....___ ___ ___ ___ ___ ___
(a Christmas decoration)

29. Beaver .....___ ___ ___ ___ ___ ___
(an animal)

30. Harmonica .....___ ___ ___ ___ ___ ___
(a musical instrument)

31. Rhinoceros .....___ ___ ___ ___ ___ ___
(an animal)

32. Acorn .....___ ___ ___ ___ ___ ___
(it comes from a tree)

33. Igloo .....___ ___ ___ ___ ___ ___
(a type of house)

34. Stilts .....___ ___ ___ ___ ___ ___
(used to make you taller)

35. Dominoes .....___ ___ ___ ___ ___ ___
(a game)

36. Cactus .....___ ___ ___ ___ ___ ___
(something that grows)

37. Escalator .....___ ___ ___ ___ ___ ___
(you go up on it)

38. Harp .....___ ___ ___ ___ ___ ___
(a musical instrument)

39. Hammock .....___ ___ ___ ___ ___ ___
(you lie on it)

40. Knocker .....___ ___ ___ ___ ___ ___
(it's on a door)

41. Pelican .....___ ___ ___ ___ ___ ___
(a bird)

42. Stethoscope .....___ ___ ___ ___ ___ ___
(used by doctors and nurses)

43. Pyramid .....___ ___ ___ ___ ___ ___
(found in Egypt)

44. Muzzle.....___ ___ ___ ___ ___ ___
(used on dogs)

45. Unicorn.....___ ___ ___ ___ ___ ___
(a mythical animal)

46. Funnel.....___ ___ ___ ___ ___ ___
(used for pouring)

47. Accordion.....___ ___ ___ ___ ___ ___
(a musical instrument)

48. Noose.....___ ___ ___ ___ ___ ___
(used for hanging)

49. Asparagus.....___ ___ ___ ___ ___ ___
(something to eat)

50. Compass.....___ ___ ___ ___ ___ ___
(for drawing)

51. Latch.....___ ___ ___ ___ ___ ___
(part of a door)

52. Tripod.....___ ___ ___ ___ ___ ___
(photographers or surveyors use it)

53. Scroll.....___ ___ ___ ___ ___ ___
(a document)

54 Tongs.....___ ___ ___ ___ ___ ___
(a utensil)

55. Sphinx.....___ ___ ___ ___ ___ ___
(it's found in Egypt)

56. Yoke.....___ ___ ___ ___ ___ ___
(used on farm animals)

57. Trellis.....___ ___ ___ ___ ___ ___
(used in a garden)

58. Palette.....___ ___ ___ ___ ___ ___
(artists use it)

59. Protractor.....___ ___ ___ ___ ___ ___
(measures angles)

60. Abacus.....___ ___ ___ ___ ___ ___
(it's used for counting)

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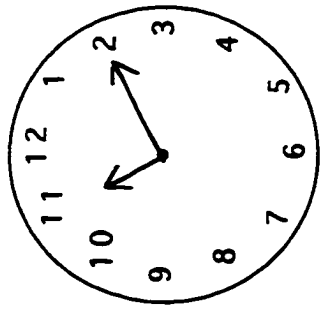
Appendix C-9: Clock Drawing†

Name: _____ Subject # ____ Date: _____



†Size reduced.

Table C-1
Criteria for Evaluating Clock Drawing

Drawing of Clock Face with Circle and Numbers is Generally Intact	10	Hands are in correct position.
	9	Slight error(s) in hand/number placement; hands of equal length; and self-correction.
	8	More noticeable errors in the placement of hour and minute hands.
	7	Placement of hands is significantly off course.
	6	Inappropriate use of clock hands (i.e., use of digital display or circling of numbers despite repeated
Drawing of Clock Face with Circle and Numbers is Not Intact	5	Crowding of numbers at one end of the clock or reversal of numbers. Hands may still be present in some fashion.
	4	Further distortion of number sequence. Integrity of clock face is now gone (i.e., numbers missing or placed at outside of the boundaries of the clock face).
	3	Numbers and clock face no longer obviously connected in the drawing. Hands are not present.
	2	Drawing reveals some evidence of instructions being received but only a vague representation of a clock.
	1	Either no attempt or an uninterpretable effort is made.

Note. After Sunderland et al., 1989.

Appendix C-10. Controlled Oral Word Association

Controlled Oral Word Association
(Verbal Fluency)

Name: _____ Date: _____ Subject #_____

Instructions: Allow 60 seconds each. Separate record into four 15-second segments.

F	A	S	Animals	Fruits & Vegetables	Animals Cued
☐	☐	☐	☐	☐	☐

Total F + A + S Total Categories HLG 1996

Appendix C-11: Finger Tapping

Name: _____ Date: _____ Subject #_____

Instructions: Circle the dominant hand conduct trials with this hand first. Each trial is 10 seconds long. Briefly rest at least once every 3 trials.

Now we are going to do a test to see how fast you can tap. We will use this little key here (demonstrate) *and I want you to tap just as fast as you can, using the forefinger* (point) *of your right/left hand. When you do it, be sure to use a finger movement. Do not move your whole hand or your arm. When you tap this key, you will have to remember to let the key come all the way up and click each time, or else the number on the dial won't change.* (Demonstrate).

Now you move the board to a comfortable position for your hand and try it for practice. Allow brief practice. *Remember to tap as rapidly as you possibly can. All right. Ready! Go!* (Adapted from Reitan & Wolfson, 1993).

L		**R**	
1.	_____	1.	_____
2.	_____	2.	_____
3.	_____	3.	_____
4.	_____	4.	_____
5.	_____	5.	_____
6.	_____	6.	_____
7.	_____	7.	_____
Total:	_____	Total:	_____
Average:	_____	**Average:**	_____

Appendix C-12: Graphical Sequences Test (Goldberg Frontal Lobe Battery)

Graphical Sequences Test

Pre-Test

Directions

Give the patient a black piece of paper and a pencil. Give verbal correction only after the patient has produced a response. If the patient is unable to complete the pre-test given a moderate amount of cuing the GST should not be administered.

1. Draw a square, draw a circle, draw a cross, draw a triangle. (If any item is drawn incorrectly, demonstrate how to draw the figure after the patient produces her/his attempt.)
2. Draw a flower; Draw a small house.
3. Write the number 52.
4. Write the number 52 in words.
5. Draw a square below a circle.
   Draw a triangle to the left of a square.
   Draw a cross to the right of a circle.
   Draw a circle above a triangle.

Graphical Sequences Test
(Goldberg Frontal Lobe Battery)

Name: _____ Date: _____ Subject #_____

Instructions

Every name should rapidly follow completion of the previous figure regardless of whether it is done correctly or not. Do not correct any of the patient's responses. Pause briefly (about 10-15 seconds) after each sequence to see whether the subject will stereotypically continue. Then proceed without interruption to the next item.

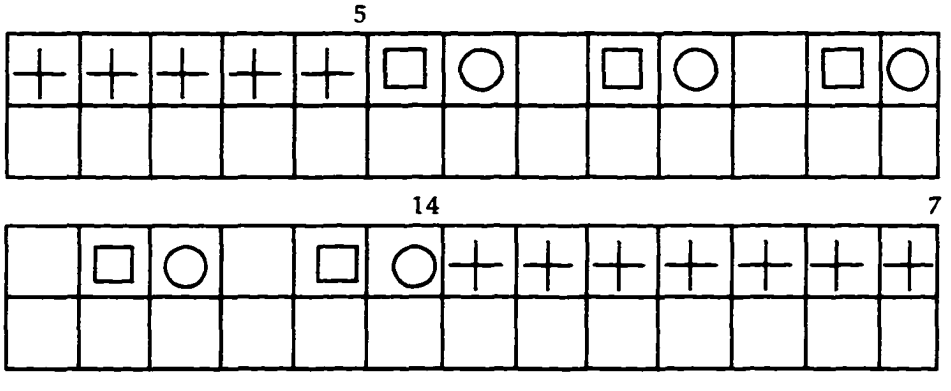
If the subject does not do so spontaneously, explain that the items should be drawn relatively small in size and in a row across the page from left to right. When one row is completed, the subject should begin another row below the previous one. Use legal sized paper (8 1/2" x 14") if available, and nothing smaller than 8 1/2" X 11". The paper should be placed before the subject in a horizontal orientation.

Provide additional sheets of paper as needed. For the purpose of eliciting perseverations, it is often preferable to use the same sheet of paper for several items in order to keep a previous item in the subject's field of vision.

Record responses in the test booklet as well as preserving the subject's response sheets. A check mark is sufficient if no error is detected. Incorrect responses should be drawn in the space provided. Label the response sheets only after they are removed from the subject's field of view.

---

1. Say to the subject, "Draw a cross . . . a crosss . . . a cross . . . cross . . . cross . . . cross . . . cross . . . square . . . circle . . . triangle . . . "



(pause 5-10 seconds without distraction)

2. "Write the following sentence in words: Three squares and two circles."

(pause 5-10 seconds without distraction)

3. A) "Draw four circles."

B) "Draw three crosses and five squares."

C) "Draw three triangles and four circles."

(pause 5-10 seconds without distraction)

4. "Write the following sentence in words: Three big crosses and two small triangles."

(pause 5-10 seconds without distraction)

5. "Draw a small flower to the right of a big house."

(pause 5-10 seconds without distraction)

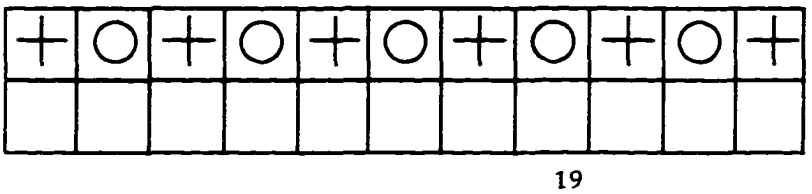
6. Write the following sentence: "A big tree is next to a small car."
(When completed, pause and then say.)

(pause 5-10 seconds without distraction)

7. "Write whatever comes to your mind."

(pause 5-10 seconds without distraction)

8. "Draw a cross . . . a circle . . . a cross . . . a circle . . . cross . . . circle . . . "



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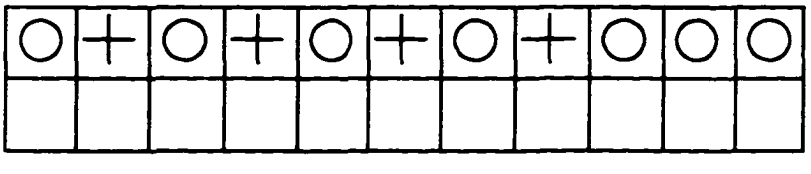

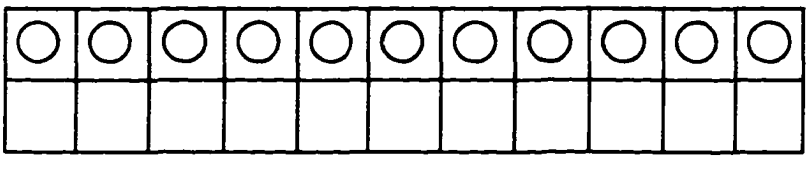

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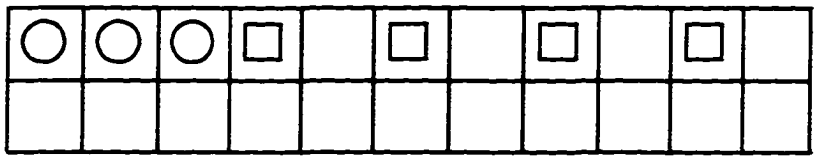

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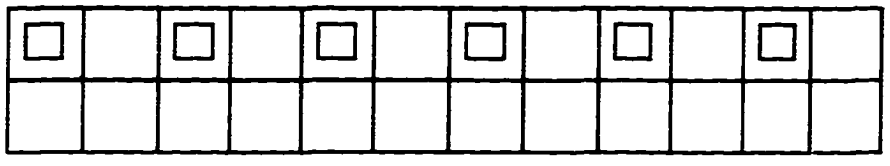

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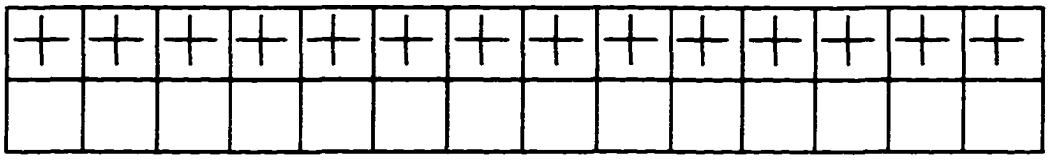


(pause 5-10 seconds without distraction)

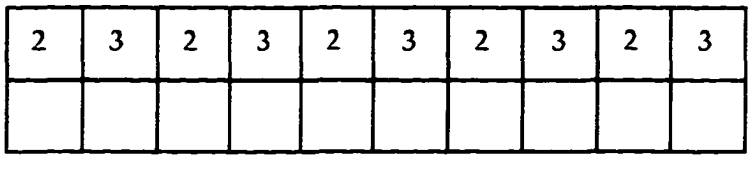
9. A) "Draw two L's, three N's, and an M.

   B) "Draw three K's, two T's, and an F.

(pause 5-10 seconds without distraction)

10. "Draw the number two . . . number three . . . two .. . . three . . . a cross . . . a triangle . . . cross . . . triangle . . . "

10



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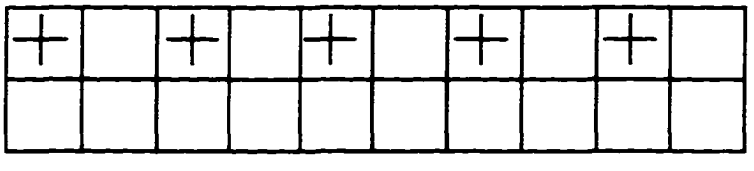

11. (If the subject requests it, a sentence can be repeated. It can be repeated as often as the subject requests, but not if he does not request it.

   A) "Write 23 twice and then 32 three times."

   B) "Write 77 three times and 444 two times."

(pause 5-10 seconds without distraction)

12. "Write whatever comes to your mind."

3

Appendix C-13: Boston Revision of the Wechsler Memory Scale Mental Control *Test*

Name: _____ Date: _____ Subject #_____

1. I want you to count backwards from 20 to 1, like this: 20, 19, 18, ... all the way back to 1. (Allow 30", bonus if w/i 10", 3 max.)

   20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1

   Time: ____" Om: ___ FP: ___ Score: ___/3 (UT: ___/2) Index: ____%

2. I want to see how quickly you can say the alphabet for me: A, B, C--go ahead. (Allow 30", bonus if w/i 10", 3 max.)

   A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

   Time: ____" Om: ___ FP: ___ Score: ___/3 (UT: ___/2) Index: ____%

3. I want to see how quickly you can count by threes beginning with 1. Like this: 1, 4, 7, and so on. Go ahead. (Allow 45", bonus if w/i 20", 3 max.)

   1 4 7 10 13 16 19 22 25 28 31 34 37 40

   Time: ____" Om: ___ FP: ___ Score: ___/3 (UT: ___/2) Index: ____%

   {WMS-R Score: ___/9 (UT: ___/6)

4. I want to see how quickly you can say the months of the year, like this: Jan., Feb., ...

   Jan Feb Mar Apr May Jun Jul Aug Sept Oct Nov Dec

   Time: ____" Om: ___ FP: ___ Psv: ___ Hits: ___/12 Index: ____%

5. Now I want to see how quickly you can say the months of the year backwards, like this: December, November, ...

   Dec Nov Oct Sept Aug Jul Jun May Apr Mar Feb Jan

   Time: ____" Om: ___ FP: ___ Psv: ___ Hits: ___/12 Index: ____%

6. I want you to tell me all the letters in the alphabet that rhyme with the word *key*. (Demonstrate: B rhymes with *key*, but A doesn't.)

   B C D E G P T V Z False Positives: _____

   Response: _____

   Time: ____" Om: ___ FP: ___ Psv: ___ Hits: ___/9 Index: ____%

7. Now imagine the letters of the alphabet as they are written in large, capital letters. Tell me all the letters that have a curve in them. (Demonstrate with letters A and B.)

B C D G J O P Q R S U False Positives: _____

Response: _____

Time: ____" Om: ___ FP: ___ Psv: ___ Hits: ___/11 Index: ____%

Appendix C-14: Wechsler Memory Scale Visual Reproduction Figure Copy

Copy of WMS Visual Reproduction Figures

Name: _____ Date: _____ Subject #_____

	Criteria	Score	
A	Two lines crossed, four flags	1	
	Correctly facing one another	1	
	Accuracy (lines nearly equal, nearly bisected, nearly at right angles, flags nearly square)	1	
	Figure correctly reproduced and in approximate proportion	3	
B	Large square with two diameters	1	
	Four small squares within a large square	1	
	Two diameters in each small square	1	
	Sixteen dots, each alone in a small square	1	
	Accuracy of proportion (width of spaces around the four small squares between 1/4 and 1/2 the width of the 4 smallest squares)	1	
	If design is complete but with superfluous square or lines	3	
	Figure correctly reproduced and in approximate proportion	5	
C-1	Large rectangle with small rectangle inside	1	
	All vertices of inner rectangle connected to vertices of larger rectangle	1	
	Smaller rectangle correctly shifted to the right and approximately that of exposed figure	1	
	Figure correctly reproduced and in approximate proportion	3	
C-2	Open rectangle with correct loop at each end	1	
	Center and either left or right side correctly reproduced	1	
	Figure correct except one of loop incorrectly reproduced	1	
	Figure correctly reproduced and in approximate proportion	3	
	Total	14	

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Appendix D: Normative Data for the Dementia Version of the CVLT

Table D-1
The 9-Item CVLT: Normative Data

		AD		IVD		EC	
		Mean	SD	Mean	SD	Mean	SD
Demographic Data	Age	78.6	5.9	79.1	6.5	74.8	7.1
	Education	10.8	3.5	11.0	3.9	14.7	3.3
	MMSE	20.7	4.2	21.0	4.0	28.7	1.3
	GDS	6.9	5.0	6.6	5.0	2.6	2.9
CVLT-9	Trial 1	2.4	1.5	2.5	1.8	5.8	1.3
	Trial 2	3.3	1.8	3.9	1.7	7.5	1.1
	Trial 3	3.9	1.5	4.5	1.8	7.8	0.9
	Trial 4	4.2	1.6	4.9	1.9	7.9	1.0
	Trial 5	4.3	1.6	5.2	2.0	8.0	1.2
	Trials 1-5	18.4	7.4	21.3	8.2	37.1	4.3
	Trial 6 (Interference)	1.9	1.2	2.6	1.8	5.1	1.1
	SC Ratio	0.16	0.11	0.20	0.11	0.32	0.15
	Trial 7 (SD FR)	1.0	1.3	2.7	2.3	7.0	1.6
	Trial 8 (SD CR)	2.6	1.6	4.2	2.0	7.5	1.4
	Trial 9 (LD FR)	1.0	1.2	2.2	2.3	7.1	1.7
	Trial 10 (LD CR)	2.0	1.9	3.3	2.3	7.4	1.5
	Savings Score	15.3	26.6	38.2	34.7	88.9	20.0
	Recognition Discrimination	65.0	14.1	74.5	14.4	95.5	4.8
	Recognition Hits	6.9	1.7	7.6	1.4	8.3	1.0
	Recognition FP's	9.8	4.9	7.2	4.3	1.0	1.3
	% FR Intrusions	20.4	17.9	12.3	13.7	1.4	2.1
	% CR Intrusions	56.3	25.5	31.3	28.2	5.3	9.0
	% Perseverations	2.3	3.0	4.4	6.2	2.8	3.9

Note. AD = Alzheimer's disease, IVD = ischaemic vascular dementia, EC = elderly control, MMSE = Mini Mental State Exam, GDS = Geriatric Depression Scale, SC = Semantic Cluster, SD = Short Delay, LD = Long Delay, FR = Free Recall, CR = Cued Recall. After Mattson, Libon, Intrieri, & Socha, 1991.

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