Short-term memory (STM) has a very brief lifetime, probably not more than 30 seconds, and limited storage capacity. As incoming stimulus messages are passed to the brain from sensory memory, some part of the brain translates them into an appropriate code or representation which is maintained by rehearsal. This rehearsal also propels the memory into the long-term memory. Long-term memory (LTM), the final storehouse, is much more complex, as it stores many different aspects of an individual's experiences. The capacity and duration of long-term memory is infinite, at least in practical terms (Hintzman, 1978). It lasts for days, months, years, or even a lifetime.

These short-term and long-term distinctions are still accepted, however, these memories have been further divided into various categories. For example, STM is viewed as a diverse collection of temporary capacities that are distributed across multiple separate process modules. These temporary capacities, commonly known as "working memory," have been broadly divided into two slave systems – the phonological loop and the visuo-spatial sketch pad– coordinated and supervised by an attentional component, the “central executive” (Baddeley, 1992, 1993; Baddeley & Hitch, 1974). The phonological loop is responsible for storing and refreshing auditory information. It is made up of a passive phonological store of limited capacity and a subvocal rehearsal system, which is responsible for holding and manipulating material relating to speech, words and numbers (Gathercole & Baddeley, 1993) and helps to refresh the information and converts verbalizable stimulus into a phonological code. The visuo-spatial sketch pad is involved in maintaining spatial and verbal information, as well as forming and manipulating mental images. The role of central executive is to supervise and coordinate the information supplied by the slave systems and overseeing the transfer of information to long-term memory.

Recently, two major advances have contributed to Baddeley's model of working memory. The first of these is a formalization of executive functions which are the core of the central executive (Miyake et al., 2000). The second major innovation has come from Baddeley (2000, 2003; Repovs & Baddeley, 2006) who postulates the existence of a new temporary back-up store, the episodic buffer. The job of the episodic buffer is to act as a temporary storage system.
CHAPTER - I
INTRODUCTION

Memory function is not unique to human beings. The central role of memory in human behaviour has been implicitly recognized by psychologists and it is one of the most important cognitive functions, essential to human life. Memory is a hidden and very complex phenomena. It collects the countless experiences related to our existence into a single whole (Hering, 1920). It is the way in which individuals’ record the past for later use, in the future. People use their memories constantly to remember phone numbers, people’s faces, and names of people they once knew. It is an active system that receives, stores, organizes, alters and recovers information (Baddeley, 1990,1996). Without memory, there would be no then but only a now.

Memory process involves three basic processes— encoding, storage, and retrieval. Encoding refers to the process by which a physical, sensory input such as a word or a sound is transformed into a code that can be stored into memory. Storage refers to moving encoded information into a memory store that must leave some record in the nervous system (memory trace) and to maintaining the information. The final phase is retrieval, the point at which one tries to remember stored information from a memory store and moves the information into consciousness for use in active cognitive processing. However, all these processes depend on each other.

The multistage nature and richness of memory suggests that there are a number of memory systems. Traditionally, based on the retention interval, memory has been divided into three kinds: Sensory, Short-term and Long-term memory. Sensory memory refers to the brief persistence of stimuli following transduction. It permits stimuli to be available for selection via the attentional processes and entry into short-term memory. The sensory memory in the visual modality is known as the iconic memory while that in the auditory modality is known as the echoic memory.
Introduction

capable of integrating information from a variety of sources. It is assumed to be
controlled by the central executive.

Long-term memory can be mainly divided into declarative and non-declarative systems (Tulving, 1985; Zola-Morgan & Squire, 1990). This distinction is related to that made by Ryle (1949) between “knowing that” and knowing how”. **Declarative memory** corresponds to knowing that. It refers to knowledge of events, facts and concepts. Semantic and Episodic memory are further sub-divisions of declarative memory (Tulving, 1983). **Semantic memory** concerns not only the understanding and use of language (memory of words and concepts), but also the memory of “general facts of the world” including other kinds of stimuli (visual and spatial, etc.). **Episodic memory** is defined as the memory of personally experienced events, situated in temporal-spatial context of their acquisition. The basic characteristic of episodic memory is that it allows for the conscious recall of a previous experience. Episodic memory is the only form of memory which, at the moment of recall, is turned towards the past.

Non-declarative memory (sometimes referred to as “procedural” memory) corresponds to knowing how and it is the memory for skills and habits. Procedural memory allows us gradually to acquire skills through training, store them and reconstruct them without necessarily referring back to previous experiences. It is an automatic form of memory and cannot easily be accessed by one’s consciousness. Priming also comes under the rubric of non-declarative memory and it refers to an improved capacity for detecting or identifying perceptual stimuli based on recent experiences with non-target stimulus.

Recently, another type of memory—Prospective Memory (PM), has been proposed. **Prospective memory**, wherein an individual executes an intended action at some designated point in the future (McDaniel & Einstein, 2000), is categorized into event-based (performing an action when a particular event occurs), activity-based (executing an action at the end of another activity) and time-based types (carrying out an action at a specific time) (Einstein & McDaniel, 1990; Kvavilashvilli, 1998). Among these three types of PM, event- and activity-based types have explicit cues in the form of occurrence of an event and end of an activity respectively. The graphical representation of different types of memory is presented below:-
A large number of tasks and procedures have been used to assess the various memory systems and are useful in empirical conceptualization of these systems. These have been summarized in Table 1.1.

Figure 1.1 Classifications of Memory Systems
Table 1.1
Nature of various memory systems and tasks used to assess these systems

<table>
<thead>
<tr>
<th>Concepts</th>
<th>Nature</th>
<th>Measurement Tools</th>
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</thead>
<tbody>
<tr>
<td><strong>Working Memory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phonological loop</td>
<td>Responsible for storing and refreshing verbal information</td>
<td>Forward verbal span</td>
</tr>
<tr>
<td>Visuo-spatial sketch pad</td>
<td>Involved in maintaining spatial and visual information</td>
<td>Forward visual span</td>
</tr>
<tr>
<td>Episodic buffer</td>
<td>Temporary storage system capable of integrating information from a variety of sources</td>
<td>Immediate prose recall; Integration task (Prabhakaran, Narayanan, Zhao, &amp; Gabrieli, 2000; Quinette et al., 2006b)</td>
</tr>
<tr>
<td>Central executive</td>
<td>Supervises and co-ordinates the slave systems (includes executive functions)</td>
<td>Backward spans; dual tasks; Trail-making test (mental flexibility); N-back test (updating); Stroop (inhibition) (Miyake et al., 2000)</td>
</tr>
<tr>
<td><strong>Long-term Memory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Episodic memory*</td>
<td>Memory of personally experienced events, situated in the temporal-spatial context of their acquisition</td>
<td>Wechsler Memory Scale (Wechsler, 1997), California Verbal Learning test (Delis, Kramer, Kaplan, &amp; Ober, 1987), Rey Figure test</td>
</tr>
<tr>
<td>Semantic memory</td>
<td>Memory of general facts of the world</td>
<td>Remember/Know paradigm (Tulving, 1985; Gardiner, 1988); Remember responses</td>
</tr>
<tr>
<td></td>
<td>Associated with <em>autonoetic consciousness</em></td>
<td>Explicit tasks: Pyramids and Palm Trees test (Howard &amp; Patterson, 1992)</td>
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<td></td>
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<td>Naming tasks; Verbal fluency tasks</td>
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<tr>
<td></td>
<td></td>
<td>Remember/Know paradigm (Tulving, 1985; Gardiner, 1988); Know responses, Implicit task: Category exemplar test</td>
</tr>
<tr>
<td>Perceptual representation system</td>
<td>Subtends perceptual priming effect</td>
<td>Perceptual identification tasks (Lebreton, Desgranges, Landeau, Baron, &amp; Bussière, 2001)</td>
</tr>
<tr>
<td>Procedural memory</td>
<td>Allows skills to be acquired through training</td>
<td>Rotor test (perceptual-motor); Mirror reading (perceptual-verbal); Tower tasks (cognitive) (Beaumieux et al., 2006)</td>
</tr>
</tbody>
</table>

* Most of episodic memory tasks assess accuracy, while the remember/known paradigm allows to evaluate the subjective experience.
Introduction

Brain Structures Involved in Memory

Karl Lashley was the first to systematically study the neural bases of memory. However, even after almost 35 years of his endeavour, he could not identify any concrete localization and accepted the equipotency of brain and commented, "It is not possible to demonstrate the isolated localization of a memory trace anywhere in the nervous system. Limited regions may be essential for learning or retention of a particular activity, but the engram is represented throughout the region" (Kolb & Whishaw, 1996). When an organism learns something, a number of brain systems can become engaged. However, in most cases there is one critical brain system which when damaged causes permanent impairment in a particular form of learning and memory. Some studies show preliminary findings regarding the specific structures involved in various kinds of memory, such as declarative and non-declarative memory. These studies show that temporal lobes, diencephalons, basal forebrain, frontal lobes, and hippocampus are the major brain areas that are linked with various kinds of memory. Many substructures of the diencephalons are also important for memory. Important among them are the dorsal medial nucleus (MD), anterior nuclei in the thalamus, and the mammillary body of the hypothalamus (Kolb & Whishaw, 1996). The idea that diencephalic structures have important role in memory gets strengthened by the fact that Korsakoff's patients, who show marked impairment of memory, frequently have damage or degeneration in mammillary nuclei and dorsal medial nucleus (Kolb & Whishaw, 1996; Zola-Morgan & Squire, 1993). It is believed that isolated damage of dorsal medial nucleus or in combination with mammillary nuclei can cause amnesia (Zola-Morgan & Squire, 1993). Basal forebrain comprises the area served by anterior communication artery. This includes the nucleus accumbens, septal nuclei, anterior hypothalamus, the nucleus of myenter and the diagonal band of Broca (Kolb & Whishaw, 1996; Zola-Morgan & Squire, 1993). Stroke or aneurysm of the anterior communication artery causes damage to the basal forebrain area. The basal forebrain is the primary source of cholinergic innervations of cortex (Zola-Morgan & Squire, 1993). Alzheimer's patients, who show marked impairment in memory, have decreased cholinergic activity and markedly reduced cell numbers in the basal forebrain (Coyle, Price, & DeLong, 1983). Another reason for memory disturbances following basal forebrain
damage can be the strong anatomical connections of this area with hippocampal formation (Kolb & Whishaw, 1996).

Prisko (1963) reported that patients with unilateral frontal lobe removal showed marked impairment in working memory. Bernard, Desgranges, Platel, Baron, and Eustache (2001) observed a predominantly left frontal activation associated with encoding and an exclusively right frontal activation associated with episodic retrieval. More precisely, during intentional coding, there was left frontal operculum activation which could reflect the use of a sub-vocal rehearsal strategy to memorize words (Kapur et al., 1996; Kelley et al., 1998). In addition, they also found bilateral activations, more extensive on the left of the anterior prefrontal and dorso-lateral prefrontal cortices which might reflect working memory processes associated with encoding.

Fletcher and Henson (2001) have reviewed various researches based on functional neuro-imaging techniques and found that during various stages of working and long-term memory; activations are seen in various frontal structures (e.g., dorsolateral, ventrolateral and anterior frontal cortex). In working memory, ventrolateral prefrontal cortex (VLFC) is more often activated during tasks requiring maintenance and dorsolateral prefrontal cortex (DLFC) during manipulation. Though the frontal cortex activations are often bilateral, comparison of verbal and spatial tasks suggests that left VLFC is primarily concerned with the maintenance of verbal information and right VLFC with maintenance of spatial information. DLFC and anterior frontal cortex (AFC) regions seem to be associated with executive component of working memory. Manipulation processes that operate on information already maintained in memory engage DLFC, whereas more complex processes that require maintaining the goals and output of one task while performing another engage AFC. For the short-term memory to be maintained during periods in which new stimuli are to be perceived, there must be separate networks for the perceptual and short-term memory functions, and indeed two coupled networks, one in the inferior temporal visual cortex for perceptual functions, and the other in the prefrontal cortex for maintaining the short-term
memory during intervening stimuli, provide a precise model of the interaction of perceptual and short-term memory systems (Renart, Parga, & Rolls, 1999).

In the long-term memory domain, the lesions in this part of the brain do not cause apparent amnesia as it is observed in temporal or diencephalic structural damages. But the studies have shown that frontal lobes play role in control processes such as memory for temporal order that aid and optimize memory encoding and retrieval (Fletcher & Henson, 2001). Frontal lobes play role at both encoding and storage stages of long-term memory. At the encoding level, the most common activation associated with tasks requiring simple retrieval of information from semantic memory is seen in anterior part of the left VLFC. But when the information must be kept online in verbal working memory, activation is more in the posterior VLFC region. When task condition requires selection from multiple possible responses or semantic features in working memory, activation of DLFC can be seen.

There is little doubt that the hippocampus plays a pivotal role in memory formation (acquisition and retention of new information) since it has been repeatedly demonstrated that bilateral, mesial temporal damage results in anterograde amnesia (e.g., Kapur & Brooks, 1999; Kartsounis, Rudge, & Stevens, 1995; Rempel-Clower, Zola-Morgan, Squire, & Amaral, 1996; Scoville & Milner, 1957; Zola-Morgan, Squire, & Amaral, 1986). Most researchers agree that interaction between the hippocampal system and the neocortex is necessary for permanent memory storage (Alvarez & Squire, 1994; Muree, 1996; Nadel & Moscovitch, 1997; Squire, 1992). Furthermore, the Multiple-trace theory (MTT) (Nadel & Moscovitch, 1997) proposes that the hippocampus and mesial temporal regions are involved only temporarily in the formation of semantic memories; according to the theory, once established, these memories can exist independently of the hippocampus. Studies done on the focal brain damaged cases and with functional neuro-imaging techniques have primarily implicated the role of frontal structures (especially the prefrontal structures) in prospective memory (Burgess, Quayle, & Frith, 2001; Cockburn, 1995; Okuda et al., 1998).

Okuda et al. (1998) obtained Positron Emission Tomography (PET) recording during event-based prospective memory tasks. The authors have found
activations in the right dorsolateral and ventrolateral prefrontal cortices, the left frontal pole and anterior cingulated gyrus, the left parahippocampal gyrus and the midline frontal lobe. These activations have been attributed to different cognitive processes involved in prospective memory. For example, right ventrolateral region and left frontal lobe can be responsible for holding the intention for future action, medial frontal region for divided attention between performing the intended plan and the routine activity, and left parahippocampal region for checking the novelty of the presented stimuli. The authors have concluded that the networks involving the right dorsolateral, ventrolateral prefrontal cortices, the left frontal pole and the medial frontal regions and the left parahippocampal regions provide the anatomical basis for prospective memory.

Burgess et al. (2001) have also conducted PET study on prospective memory with a slightly modified paradigm in which separate recordings has been done for controlled condition, event-based prospective memory condition and a novel condition in which subjects are instructed to perform a particular action whenever they see a target event but the target event is never presented. The purpose of the last condition is to see the nature of activation in a condition where intention is maintained but can never get executed. In both the conditions (i.e., when intention could be executed and when intention could not be executed), activations have been seen in the frontal pole bilaterally; right lateral prefrontal and inferior parietal regions plus the precuneus. Further, activation has been observed in the thalamus when the prospective memory stimuli occurs and is acted upon, with a corresponding regional cerebral blood flow decrease in the right lateral prefrontal cortex. Based on these two sets of activations, the authors have concluded that first set of regions play role in the maintenance of intentions with the second set involved additionally in its realization (Burgess et al., 2001). Studies on focal brain damaged cases have confirmed that damage to this lobe results in impaired prospective memory (Cockburn, 1995; Burgess et al., 2001).

The cerebral substrates of procedural memory comprise various subcortical structures, notably the striatum, as well as the cerebellum. Squire, Knowlton, and Musen (1993) argued that the main brain structures underlying declarative
Introduction

memory are located in the hippocampus and many structures of the medial temporal lobes have been found as candidate structures responsible for declarative memory. Among these medial temporal structures and hippocampus are considered to be most important for declarative memory. The other areas (entorhinal cortex, perihinal structure and parahippocampal structure) serve as major source of hippocampal input and output. Damage to the entorhinal cortex partially destroys afferents of the hippocampus and disrupts its function. Similarly, the parahippocampal and perihinal cortices provide about two third of the input to the hippocampus, which itself sends projections back to them as well as to other polysensory areas (Mayes, 1998). These adjacent hippocampal structures are not just routes of information to the hippocampus but seemingly play role in memory function as well. Damage incorporating hippocampus as well as adjacent areas results in higher degree of memory impairment as compared to the impairment due to hippocampal damage alone (Zola-Morgan & Squire, 1993). Similarly, subiculum and amygdala are two other important temporal lobe structures that play a role in memory (Kolb & Whishaw, 1996; I.eDoux, 1987; McGaugh, 1989).

Non-declarative seems to depend on the basal ganglia (Mishkin & Petri, 1984). However, the hippocampus seems to play a crucial role in complex learning (McCormick & Thompson, 1984), particularly in regard to the encoding of declarative information (Kolb & Whishaw, 1990; Zola-Morgan & Squire, 1990). The hippocampus also appears to be involved in the consolidation of encoded information in the long-term store. In addition, the cerebral cortex appears to play a minor but important role in long-term memory, particularly declarative memory (Zola-Morgan & Squire, 1990).

Eustache and Desgranges (2008) showed that the retrieval of recent memories was linked to cerebral structures involved in episodic memory, such as the hippocampus and the right prefrontal cortex. Conversely, the retrieval of remote memories was linked to cerebral structures involved in semantic memory, notably in the left middle frontal gyrus. According to the Hemispheric Encoding Retrieval Asymmetry (HERA) model, the right and left prefrontal cortices are preferentially involved in the retrieval of episodic memories and semantic information, respectively.
There is evidence that anterograde amnesia occurs in humans with bilateral damage to the hippocampus and nearby parts of the temporal lobe (Rempel-Clower et al., 1996; Squire, 1992). In addition, deficits in retrograde memory have been recorded in patients with lesions involving frontal (e.g., Baddeley & Wilson, 1986; Levine et al., 1998; O'Conner & Lafleche, 2004), posterior cerebral (Hunkin et al., 1995) or thalamic regions (Hodges & McCarthy, 1993; Isaac et al., 1998; Luchelli, Muggia, & Spinnler 1995; Markowitsch, von Cramon, & Schuri, 1993; Miller et al., 2001; Stuss, Guberman, Nelson, & Larochelle, 1988). The Consolidation theory and Multiple-trace theory (MTT) propose a role for the neo-cortex in the storage of long-term memories; therefore one might also expect deficits in retrograde memory as a consequence of temporal lobe lesions that spare the hippocampus. Markowitsch (1995) has proposed that anterolateral prefrontal and temporal polar cortices are necessary for retrieval of information from long-term memory. According to him, functions of the prefrontal cortex include effortful initiation of recall and temporal sequencing of information, while the anterior temporal cortex provides the connection to the posterior cortical regions where engrams are stored. Based on a review of single case reports and functional neuro-imaging studies of normal subjects performing tasks involving episodic and autobiographical memory recall, Markowitsch (1995) proposed that the left hemisphere may be essential for retrieval of semantic information from long-term memory and the right hemisphere may subserve episodic memory retrieval. Snowden, Thompson, and Neary (2004) have also proposed a model of semantic memory comprising a single interconnected network, with dedicated brain regions representing modality specific information i.e., the left temporal lobe is more important for the representation of words (including names) and the right temporal lobe for pictorial stimuli (including faces) (Howard & Patterson, 1992; Snowden et al., 2004). Studies have emphasized the role of the lateral temporal cortex in memory for semantic details related to public events, famous people, or vocabulary words, and its relatively limited importance to autobiographical event memory. In the domain of autobiographical memory, recall of episodes seemed to be related to the extent of the lesion in the mesial region. The short-term and long-term memory systems together with specific brain structures involved in each system are shown in Figure 1.2.
Figure 1.2  Brain Structures involved in various Memory Systems
Introduction

Brain Energy Metabolism

The understanding of the basic mechanisms of brain energy metabolism is an essential prerequisite to a full understanding of the physiology and pathophysiology of brain function. Abnormalities in brain energy metabolism are observed in a variety of pathological conditions such as neuro-degenerative diseases, stroke, diabetes, hypertension, and epilepsy. The human brain constitutes only 2% of the body weight, yet the energy consuming processes that ensure proper brain function account for approximately 25% of total body glucose utilization. Glucose is the obligatory energy substrate of the brain. In any tissue, glucose can follow various metabolic pathways. In the brain, glucose is almost entirely oxidized to carbon-dioxide (CO₂) and water. Indeed, the oxygen (O₂) consumption of the brain, which accounts for almost 20% of the oxygen consumption of the whole organism, is 160 mmol per 100g of brain weight per minute and roughly corresponds to the value determined for CO₂ production. This O₂/CO₂ relation corresponds to what is known in metabolic physiology as a respiratory quotient of nearly one and demonstrates that carbohydrates, and glucose in particular, are the exclusive substrates for oxidative metabolism. A striking characteristic of the brain is its high degree of structural and functional specialization. When an arm is moved, motor areas and their related pathways are activated selectively; intuitively, one can predict that as “brain work” increases locally (e.g., in motor areas), the energy requirements of the activated regions will increase in a temporally and spatially coordinated manner. Because energy substrates are provided through the circulation, blood flow should increase in the modality-specific activated area. Thus, under normal conditions, glucose is virtually the sole energy substrate for the brain and that it is entirely oxidized. Over the past few years, it has become clear that glucose has profound effects on the central nervous system (CNS). In primary fetal brain cell cultures, glucose plays an important role in the control of metabolism and growth. It also regulates key processes such as energy homeostasis, reproductive endocrinology, central action on peripheral glucose metabolism, learning, memory, and neuronal survival in adults. It seems that disturbances in glucose metabolism, especially insulin resistance, play a role in the promotion of most of the pathogenic processes. New
techniques that allow imaging of the three fundamental parameters of brain energy metabolism – namely, blood flow, oxygen consumption, and glucose utilization – provide a more refined level of spatial resolution and demonstrate that brain energy metabolism is regionally heterogeneous and is coupled tightly to the functional activation of specific neuronal pathways (Magistretti, Pellerin, Rothman, & Shulman, 1999).

Studies of memory formation have led to two conceptual sets of components important for understanding how memories are made. One set of events is comprised of the substrates of memory, those changes in the brain that are necessary to produce a neural representation of an experience. A second set of events, tested with modulators of memory formation, is comprised of the mechanisms by which the substrates are engaged and regulated. Activation of these modulators, which include several hormones and neurotransmitters, may be responsible for formation of memories. An early proposal, for which there is now considerable support, is that some hormonal consequences control or modulate the formation of new memory (Gold & McGaugh, 1975). One of the hormones most effective at regulating memory formation is epinephrine which is released into the circulation from the adrenal medulla. Glucose which is released from hepatic stores in response to epinephrine, is a widely investigated putative effector. In the past 20 years, extensive evidence has appeared indicating that glucose administration can regulate many brain functions (Gold, 1991, 1995; Korol & Gold, 1998). Glucose readily crosses blood-brain barrier, so it is plausible that glucose affects central processes directly to modulate memory performance. This fact is supported by researches where direct administration modulates memory (Darolia, Yadava, & Sharma, 2000; McNay & Gold, 1998; Stefani & Gold, 1999, 2001), strongly suggesting that changes in the amount of glucose present in the brain can affect memory processes. Thus, it is clear that in a wide range of circumstances, glucose can modulate memory processes via direct actions on the brain.
Causes of Memory Impairment

Although mild age-related memory loss is considered normal, more severe memory impairment is not. Many people assume that memory loss is exclusively caused by aging. Aging causes memory impairment but the truth is that it has a wide range of causes including medical disorders, medications and even lifestyle factors. Several health problems are now known to cause memory loss and increase the risk of dementia. Some of these problems, such as diabetes and hypertension, become more common with age and, together with age-related changes in the brain, help explain why people might become more forgetful as they grow old. The various causes of memory impairment are presented below:

Aging: Aging has been found to be a major contributor of memory impairment. Although, every individual need not suffer perceivable memory loss with age, aging results in slowing down or decline of various physiological processes. With age, neural processing speed slows down, therefore older adults require more time to register and process information (Fry & Hale, 1996). This is especially true when older adults work at complex tasks (Poon, 1987).

Age related physiological and psychological disorders result in the loss of particular cell types, including hippocampal, locus coeruleur and nucleus basal neurons (Flood & Coleman, 1988), changes in the neuronal plasticity as found in long-term potentation (Barnes & McNaughton, 1985), deficits in neuro-endocrine regulation of memory formation and atrophy of areas of the brain devoted to storing memories also occurs (Schacter, 1996). By the age of 65 years, a small, gradual loss of brain cells causes 5 to 7 percent reduction in the overall weight of the brain. When neurons are damaged or cannot function effectively, memory impairment and cognitive decline can occur.

Alzheimer’s disease: Alzheimer’s disease is a leading cause of dementia. It is extremely rare before age 60 and becomes much more common with further aging. With Alzheimer’s disease, there is a substantial loss of neurons along with the appearance of abnormal structures in the brain called “plaques” and “tangles”, particularly in regions of the brain associated with memory.
Cerebrovascular disease: Another leading cause of dementia is cerebrovascular disease. It refers to injury to the brain caused by hypertension, reduced blood flow and damage to the system of blood vessels that serves the brain. Reduction of blood to the brain produces impairments in the formation of new long-term memories (Corkin, Amaral, Gonzalez, & Johnson, 1997). A blow to the head that is strong enough to cause a concussion— a brief alteration of consciousness— can also impair memory. Among the other neurological disorders, that interfere with brain activities including memory are Parkinson’s disease, multiple sclerosis, epilepsy, Huntington’s disease and brain tumors.

Cardiovascular disease: Neuroscientists now know that what is bad for the heart is also bad for the brain. Conditions that have been linked with heart disease— high blood pressure, diabetes and high cholesterol— have also been linked to memory problems.

Hypertension: Adults with high blood pressure (hypertension) are more prone to memory impairment than people with normal blood pressure. Moreover, people with hypertension experience memory losses that are more severe than individuals who do not have hypertension. These differences hold true regardless of age. Hypertension may impair memory by damaging the brain’s white matter. The damage can be detected on MRI in the form of “white matter lesions”. These are pinpoint lesions in the brain’s message carrying axons that affect cognitive functions, especially weakening of memory and reasoning and significantly impacting quality of life (cf. Lawson, 2003). Hypertension is also related to pathological manifestations of Alzheimer’s disease (senile plaques, neurofibrillary tangles, hippocampal atrophy) (Skoog & Gustafson, 2006) and may lead to vessel wall changes in the brain, leading to hypoperfusion, ischemia and hypoxia which may initiate the pathological process of Alzheimer’s disease.

Diabetes: There are two features of diabetes that can impair memory. High blood sugar, the hallmark of the disease, depresses the function of the hippocampus. Middle-aged and elderly people with high blood sugar are likely to have a smaller hippocampus than younger adults (Convit, Wolf, Tarshish, & de Leon, 2003). The other feature of diabetes that can harm memory is high levels of
Introduction

Insulin and even moderately high insulin levels increase biochemical markers for inflammation, which is thought to promote Alzheimer’s disease.

High Cholesterol: In contrast to hypertension and diabetes, high cholesterol appears to increase the risk for mild cognitive impairment and Alzheimer’s disease. People with high cholesterol have a higher than average incidence of these two conditions. It is not clear how high cholesterol might lead to memory loss, or whether the crucial factor is excessive low-density lipoproteins (LDL, the “bad” cholesterol) or insufficient high-density lipoproteins (HDL, the “good” cholesterol).

Other factors such as hormonal imbalance, vitamin deficiency and over the counter medicines also influence memory. Experts are uncertain as to whether the decline in sex hormones that occurs naturally with age contributes to age-related memory loss. Many women experience particular trouble with memory during menopause, when their levels of estrogen fall sharply. Although men do not have such a dramatic decline of hormones as they get older, research shows that men with high levels of testosterone have better visual and verbal memories than men with lower levels. Vitamin B₁₂ keeps neurons healthy by helping to make and preserve the myelin sheath that surrounds the axons. A deficiency of this vitamin sometimes occurs in older people and can be caused by dietary factors or an inability of the intestine to absorb Vitamin B₁₂. Lack of Vitamin B₁₂ can lead to permanent neuronal damage, including memory loss. Heavy drinking, smoking, or drugs (opioids and over-the-counter medicines) can impair memory. Anticholinergic agents, such as those used to treat bladder dysfunction, affect the activity of certain neurotransmitters in the brain that are crucial to memory. The tricyclic class of anti-depressants also has potent anti-cholinergic side effects that can impair memory and other elements of cognitive function. Other medicines that can cause memory loss include narcotic pain killers, beta blockers for hypertension, cimetidine for ulcers, amantadine for Parkinson’s disease, benzodiazepins for anxiety, eye drops for glaucoma and chemotherapy for cancer.

Considered together, the above evidence indicates that cognitive functioning is strongly affected by aging. Adults with arteriosclerosis,
cerebrovascular, cardiovascular disease, diabetes and untreated hypertension score more poorly on tests of cognitive functioning, perhaps as a result of reduced flow of blood and oxygen to the brain (Zelinski, Crimmins, Reynolds, & Seeman, 1998). When age-related memory declines, it mostly involves declarative and short-term memory. However, older persons can be taught more efficient memorization and recall techniques, to compensate for the reduced neural functioning (Perlmutter, Kaplan, & Nyquist, 1990).

The present research work focused on two chronic disorders i.e., diabetes and hypertension, because of high rate of prevalence, complications, and physical and mental burden placed on the patient by these diseases. In 2006, according to the World Health Organization (WHO), at least 171 million people worldwide were suffering from diabetes. Its incidence is increasing rapidly, and it is estimated that by the year 2030, this number will double. Diabetes mellitus occurs throughout the world, but is more common in the more developed countries. WHO has warned that there is a real danger of India becoming the diabetes capital of the world. According to an estimate by 2010, there will be 37 million diabetic patients and by 2025 it is likely to reach 70 million. Similarly, the prevalence of hypertension has also been reported very high worldwide. Kearney et al. (2005) reported the total number of adults worldwide who had hypertension in 2000 was 26.4% i.e., 972 million (333 million in economically developed and 639 million in economically developing countries). The number was predicted to increase to 29.2% (i.e., 1.56 billion) by 2025. Epidemiological studies have also shown that hypertension is present in 25% of urban and 10% of rural population in India (Gupta, 2004). Further, hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India (Rodgers, Lawes, & MacMohan, 2000).

Medical practitioners pay little heed to the accompanying memory losses in patients with diabetes or hypertension which are actually caused by the diseases. However, these impairments are a major cause of stress to the patient who is unable to account for the subjectively perceived memory loss. Generally, this
memory loss is attributed to aging which leads to reduction in motivation and conscious efforts to operate at the maximum possible level.

Thus, it was felt that a study of the specificity of memory impairments in diabetes and hypertension could provide the basis for developing mental strategies to delay or at least compensate for the memory impairments associated with these diseases.

**Diabetes and Memory**

Diabetes mellitus is one of the largest health care problems in terms of prevalence, cost and the physical and psychological burden it places on individuals living with the illness. Diabetes is also one of the most challenging of the chronic diseases from a psychosocial and behavioural perspective (Cox & Gonder-Frederick, 1992). The body needs glucose to fuel metabolic processes, but too much of it in the blood over a long period of time, a condition called hyperglycemia, is the mark of diabetes mellitus. The body normally controls the blood sugar levels with the hormone insulin produced by the pancreas. In diabetes, abnormal levels of glucose accumulate in the blood because the pancreas do not produce sufficient insulin (American Diabetes Association [ADA], 2000) or when cells cannot make use of the available insulin. There is no cure for diabetes and its cause remains a mystery, although heredity, age and lifestyle factors appear to play a major role.

There are several kinds of diabetes mellitus but Type I and Type II are the two most common types. Type I Diabetes (Insulin Dependent Diabetes Mellitus, IDDM) is characterized by decreased production or absence of insulin. It is an auto-immune disease and its onset is generally during adolescence or young adulthood and accounts for only 5 to 10% of diabetes cases. There is substantial evidence that Type I diabetes has a genetic component.

Type II Diabetes (Non-Insulin Dependent Diabetes Mellitus, NIDDM) is characterized by body tissue resistance to insulin action, though decreased secretion of insulin can also occur concomitantly. About 90% of those with diabetes are in the Type II category. Most, but not all, people with Type II diabetes
can manage their glucose levels by carefully following special diets and taking medication (ADA, 2000; Guare, Myers, & Marrero, 1999). Although Type II diabetes can develop at any age, it usually appears after the age of 40.

Research has shown that uncontrolled diabetes can lead to mental decline, including memory loss. Under normal conditions, the brain’s main source of fuel is glucose (Sieber & Traystman, 1992). The entry of glucose into the brain is regulated at the blood-brain barrier. This barrier, which is formed by the cells that line brain capillaries (very small blood vessels), controls the brain’s environment. Diabetes harms blood vessels that supply the brain, heart and other organs.

Blood Glucose (BG) accounts for more than 90% of the metabolic fuel used by the brain as storage of glucose in the brain is very limited. Therefore, a person needs a constant supply of glucose from the blood for normal brain functioning. The brain uses glucose as its primary substrate for cognitive functioning (Raichle, Herscovitch, Mintun, Martin, & Powers, 1984). The positive effect of glucose on complex cognitive tasks such as declarative memory, working memory, procedural learning has been demonstrated by Craft, Murphy, and Wemstrom (1994).

Proposed pathogenetic mechanisms of cognitive dysfunction in diabetes include chronic hypoglycemia, vascular disease, and cumulative effects of insulin on the brain (Biessels, van der Heide, Kamal, Bleys, & Gispen, 2002). It is unclear whether these factors individually, or in combination, mediate the pathogenesis of the cognitive dysfunction. In diabetes, there is a significant cumulative burden of cerebrovascular disease resulting from diabetic microangiopathy, hyperlipidaemia, and potentiation of other vascular risk factors such as hypertension. Another key mechanism of neurodegeneration in diabetes may be insulin dysregulation (Craft & Watson, 2004). This may result in increased inflammation, oxidative stress, advanced glycation end products, decreased neuronal repair and neurogenesis. Insulin can promote the release of intracellular Aβ in neuronal cultures (Gasparini et al., 2001) and intracellular accumulation of Aβ has been considered as a pertinent factor in the pathogenesis of Alzheimer’s disease (AD) (Oddo et al., 2003). These findings indicate that diabetes, through neurodegenerative processes
resulting from dysfunctional metabolism, may lead to direct neuronal injury manifested as brain atrophy and may form a structural basis for dementia.

Both extended periods of elevated glucose levels (hyperglycemia) and very low glucose levels (hypoglycemia) are believed to contribute to the development of memory problems in people with diabetes. It is well established that hyperglycemia causes oxidation stress which contributes to cerebral ischemic injury and neuronal apoptosis. Collectively, insulin resistance and hyperglycemia can induce elevated glucose levels in the brain, causing oxidative stress and neuronal loss, especially in hippocampus.

High blood sugar is thought to contribute to brain dysfunction by altering cerebral blood flow, affecting brain energy metabolism and impairing blood-brain-barrier function. Many studies suggest that high blood sugar decreases the efficiency with which glucose is transferred from blood capillaries into the brain across the blood-brain barrier. Insulin enters in the brain by means of a receptor-mediated active transport system (Baskin, Figlewicz, Woods, Porte’, & Dorsa, 1987). Insulin receptors have also been identified in specific brain regions—particularly the hypothalamus and the limbic system—and researchers have found that insulin modulates synaptic activity, perhaps by inhibiting the firing of neurons in these brain regions or by regulating the synthesis of specific neurotransmitter reuptake transporters for dopamine and norepinephrine (McCall & Figlewicz, 1997). Low blood sugar is thought to alter brain function through its effects on neurotransmitters, by which nerve cells in the brain communicate biochemically. Although the brain represents only about 2% of the body’s weight, it consumes 20% of the body’s energy in adults and up to 50% in children. The brain’s high metabolic rate and the corresponding need for a constant supply of sugar from the bloodstream are required to fuel neurotransmission. Since learning and memory depend on neurotransmission, any lapse in the system will affect the ability to learn and remember.

Low or high blood glucose also causes the hippocampus to malfunction bio-chemically, and the hippocampus has been found to be responsible for short-term memory. The result is often impaired concentration and attention, memory
loss and slowing of information processing speed. More than 20 case control studies of cognitive function have now been conducted in older adults with Type II diabetes and virtually all of them have found evidence of impairment. Learning and memory deficits appear most prominently and consistently (Perlmuter et al., 1984; Reaven, Thompson, Nahum, & Haskins, 1990; U’ren, Riddle, Lezak, & Bennington-Davis, 1990), but deficits may also occur on measures of attention, psychomotor speed and problem solving (Strachan, Deary, Ewing, & Frier, 1997). Chronic hyperglycemia is the best, albeit imperfect, predictor of cognitive dysfunction. Case control studies that have evaluated relatively healthy, high-functioning diabetic adults have also reported evidence of significant memory dysfunction, which was best predicted by glycosylated hemoglobin levels (Reaven et al., 1990).

One important question that remains unanswered is whether all Type II diabetic patients have an equal vulnerability to developing cognitive problems. The preliminary research suggests that age may be a critical factor, with younger patients having a substantially lower risk. On the other hand, Ryan and Geckle (1999) compared adults (mean age 49 years) with and without Type II diabetes and found little evidence of learning and memory impairments. One of the few studies to examine the relationship between Type II diabetes and brain morphology has reported an interaction with age as well as with hypertension. Using computerized tomography techniques to estimate degree of brain atrophy in 416 medical patients, Pirttilä, Jarvenpaa, Laippala, and Frey (1992) found that age, diabetes, hypertension, chronic cerebrovascular disorders and number of medications were all associated, to some extent, with brain atrophy. Only 12% of the patients under age 65 showed cortical atrophy in the absence of both diabetes and hypertension, whereas atrophy was present in 27% of those with hypertension, 40% of those with diabetes, and in 36% of those with both disorders.

Convit et al. (2003) showed that middle-aged and elderly people with high blood sugar actually had a smaller hippocampus, the brain region so crucial for recent memory. This study also found that people’s memory may be harmed long before they ever develop full-fledged diabetes— and it’s a problem of fuel. Unlike
most other tissues that have multiple fuel sources, the brain depends on blood sugar for almost all its energy. The longer that glucose stays in the bloodstream instead of being metabolized into body tissues, the lesser fuel the brain has to store memories. Convit et al. found no specific threshold at which memory automatically worsened. It is intriguing why only the memory crucial hippocampus gets harmed. Previous animal and human research shows that it is the region most likely to be damaged by any brain insult. Conversely, it is also a very adjustable region, with the potential for some recovery if people bring their blood sugar under control.

Consistent with results from small case control studies, the larger community-based investigations again demonstrate that diabetes is associated with a greatly increased risk of cognitive dysfunction. Analyses of stroke-free cohort of 249 older adults (mean age 71 years) showed that diabetes was a significant independent predictor of deficits on measures of abstract reasoning and visuospatial functioning (Desmond, Tatemichi, Paik, & Stern, 1993). Assessment of more than 1,300 community-dwelling individuals, 24 to 81 years of age, also revealed a strong relationship between diabetes and cognitive functioning (van Boxtel et al., 1998). It is important that when the effects of Type I and Type II diabetes were examined separately, both were found to be associated with poorer memory, slower sensory-motor performance, and lower scores on measures of cognitive flexibility and psychomotor efficiency. An even larger study of nearly 4,000 older community-dwelling adults also showed a relationship between diabetes and cognitive performance as measured by the Mini-Mental State Examination (Launer, Dinkgreve, Jonker, Hooijer, & Lindeboom, 1993). Although the pathophysiological mechanism underlying the link between Type II diabetes and cognitive dysfunction remains poorly understood, but most researchers now argue that it is more likely a direct consequence of one or more metabolic aberrations. Chronic hyperglycemia could affect the CNS and other systems throughout the body by triggering the development of advanced glycosylated end products, largely because these oxidation products have been found in the senile plaques and neurofibrillary tangles that are characteristic of Alzheimer’s disease (Stewart & Liolitsa, 1999).
Thus, Type II diabetics are likely to show clinically significant cognitive impairments—particularly on measures of learning and memory.

### Hypertension and Memory

Hypertension which is very common in people with diabetes, is one of the earliest manifestations of cardiovascular disease and foretells human suffering, deteriorating quality of life, and increased financial burden. The term hypertension is used to indicate high blood pressure (BP). Blood pressure is the force exerted by the blood as it pushes out against the walls of the arteries. Hypertension is usually called the silent killer because it has no specific symptoms. Patients may have hypertension for many years without knowing it because there is no specific perceived sensory information associated with high BP. Like diabetes, hypertension cannot be cured but it can be treated and managed.

Although hypertension can occur at any age, it is more prevalent in adults over the age of 35 years. It is particularly prevalent among African Americans, middle-aged and elderly people, obese individuals, and heavy drinkers (MacMahon, Cutler, Brittain, & Higgins, 1987; Neaton & Wentworth, 1992; Stamler et al., 1989; Whelton, 1985). However, there is a high heterogeneity in hypertension prevalence related to heterogeneity in underlying pathophysiological processes. Cultural and psychosocial factors, as well as responsiveness to interventions may also contribute to differences in hypertension prevalence (Horan & Mockrin, 1992).

When blood pressure (BP) is measured, it is defined as two numbers: systolic and diastolic. Systolic BP represents the force at which blood flows when the heart beats. Diastolic BP, on the other hand, is an estimate of the force of blood flow when the heart relaxes (in between heart beats). Hypertension is recorded in millimeters of mercury (mm Hg). The Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC, 1997) and the American Heart Association (AHA) have put forth recommendations on the classification of BP levels. The recommendations are as follows: First, optimal BP is systolic less than 120 mm Hg and diastolic less than 80 mm Hg. Second, normal
BP is systolic less than 130 mm Hg and diastolic less than 85 mm Hg. Third, high normal BP is systolic 130 to 139 mm Hg or diastolic 85 to 89 mm Hg. Fourth, Stage 1 (mild) hypertension is systolic 140 to 159 mm Hg or diastolic 90 to 99 mm Hg. Fifth, Stage 2 (moderate) hypertension is systolic 160 to 179 mm Hg to diastolic 100 to 109 mm Hg. Finally, Stage 3 (higher) hypertension is systolic 180 or higher mm Hg or diastolic 110 mm Hg or higher.

Hypertension increases workload on the heart and contributes to myocardial cell enlargement and left-ventricular hypertrophy. As BP increases, the pumping action of the heart requires more effort and energy. Under the condition of high BP, the arteries carry blood that is moving under greater pressure. Chronically, this state eventually leads to various structural changes in the heart and blood vessels, leading to the hardening of arteries and other organs may also get directly affected, leading to the sequel of hypertension, including stroke, congestive heart failure, kidney failure, heart attack, and cognitive dysfunction including memory loss.

It is estimated that one in four adults has high BP (American Heart Association [AHA], 1998). Approximately 90-95% of all cases on adult-onset hypertension are essential (primary) hypertension, a term that refers to a sustained BP elevation of unknown cause. Elevated BP that is attributable to a known medical disorder is called secondary hypertension. Despite no clear identification of the pathophysiology of essential hypertension, the role of psychological variables in hypertension has occupied a prominent position within the field of behavioural medicine (Alexander, 1939). Numerous life style and behavioural risk factors for hypertension are suggested; they include excess body weight, physical inactivity, dietary factors, excessive alcohol consumption, oral contraceptive use, various psychosocial factors and stress related cardiovascular reactivity (AHA, 1998; JNC, 1997; Kaplan, 1998).

People who had high blood pressure for many years and even those who were treated had more shrinkage in certain parts of the brain, and this was different than healthy group (Salerno et al., 1992). The brain is thus one of several target organs (e.g., heart, kidneys, eyes) that are damaged by hypertension. The
primary peripheral hormone produced by the adrenal cortex, cortisol, is essential to the maintenance of normal vascular tone. Cortisol has ready access to the central nervous system, affecting areas of the brain that are involved in the control of blood pressure (e.g., hypothalamus, limbic system) (Wilson & Foster, 1992). Cortisol also inhibits the production of prostaglandin and arachidonic acid, bradykinin, serotonin and histamine (Wilson & Foster, 1992), leading to vasoconstrictive effects. These properties of cortisol increase the effects of cardiovascular activation on the heart and blood vessels. Since neural effects of cortisol have been reported, they may play a role in memory impairments observed in hypertensives. In fact, prior to clinically evident cerebrovascular complications, hypertension-related changes in the brain and cognition are detectable with methods such as neuropsychological assessment and neuro-imaging.

The impact of hypertension on the brain has long been recognized in the form of severe disturbances termed as hypertensive encephalopathy (Oppenheimer & Fischberg, 1928). Case control studies of hypertension and cognition generally compare the performance of persons with normal BP (normotensives) with that of unmedicated essential hypertensives.

Decreased cerebral blood flow, metabolism, or both, has been noted in hypertensives, with some suggestions that frontal, temporal, and subcortical (e.g., basal ganglia) regions are most affected (Fujishima, Ibayashi, Fujii, & Mori, 1995; Mentis et al., 1994; Rodriguez et al., 1987; Salerno et al., 1995). Fujishima et al. (1995) found that spontaneously hypertensive rats, as compared to normotensive rats, had decreased cerebral blood flow and glucose utilization in a variety of cortical and subcortical regions that correlated with poorer spatial learning and memory in maze tests. However, these changes were reversible with anti-hypertensive treatment. Cerebral perfusion has also been found to be better among treated than untreated hypertensives (Nobili et al., 1993). Recent findings have also noted that hypertensives show smaller cerebral blood flow response during memory tasks (Jennings et al., 1998). More specifically, hypertensives displayed less activation in right hemisphere regions but enhanced (possibly compensatory)
left hemisphere activation during two memory tasks. Researchers have found that when people with hypertension perform memory tasks, they have less blood flow to parts of the brain involved in memory and more blood flow to other brain regions than people with normal blood pressure (Mercado & Hilsabeck, 2005). Hypertension is also known to affect the autoregulation of cerebral blood flow (Baumbach & Heistad, 1988). Specifically, hypertension shifts both the lower and upper limits of the autoregulatory range to the right, at least in part as a result of vascular hypertrophy and remodeling. This can lead to impairment in autoregulatory vasodilation during episodes of hypertension, thus rendering hypertensives vulnerable to hypoxic effects associated with decreases in perfusion pressure.

Hypertension is also associated with subtle alterations in brain structure that mark the gradual emergence of cerebrovascular disease. In this regard, hypertensives display increased hyperintensities in periventricular and deep white matter on magnetic resonance imaging that indicate the presence of cerebral white matter disease (Liao et al., 1996; Manolio et al., 1994; Schmidt et al., 1995; van Swieten et al., 1991). Treated hypertensives display less white matter disease than untreated hypertensives (Fukuda & Kitani, 1995). Among treated hypertensives, those who exhibit poorer BP control show the most extensive pathology (Liao et al., 1996). Also noted among hypertensives is a greater prevalence of silent lacunar infarction (Hougaku et al., 1992), a greater degree of cerebral atrophy and ventricular enlargement (Manolio et al., 1994; Salerno et al., 1992; Schmidt et al., 1995), and increased carotid atherosclerosis (Ferrara et al., 1995) as compared to normotensives.

Hypertension has also been related to pathological manifestations of Alzheimer’s disease (Senile plaques, neurofibrillary tangles, hippocampal atrophy) (Skoog & Gustafson, 2006). It may initiate the pathological process of Alzheimer’s disease as a result of vessel wall changes in the brain, leading to hypoperfusion, ischemia and hypoxia. In several investigations, dose-response relations have been noted between progressive increments in BP level and reduced

Results of the numerous available case control studies of hypertension and cognition generally reveal that hypertensives perform more poorly than normotensives across multiple domains of neuropsychological function (Waldstein, Manuck, Ryan, & Muldoon, 1991). Some of the most prominent and consistent findings are noted within the domains of learning and memory, attention, abstract reasoning, and other executive functions (Boller, Vrtunski, Mack, & Kim, 1977; M. F. Elias, Robbins, Schultz, & Pierce, 1990; M. F. Elias, Robbins, Schultz, Streeten, & Elias, 1987; Robbins et al., 1994; Waldstein, Ryan, Manuck, Parkinson, & Bromet, 1991; Waldstein et al., 1996). Compromised performance is also evident on tests of visuo-spatial, visuo-constructive, perceptual, and psychomotor abilities (Blumenthal, Madden, Pierce, Siegel, & Appelbaum, 1993; Boller et al., 1977; M. F. Elias et al., 1987; Robbins et al., 1994; Shapiro, Miller, King, Ginchereau, & Fitzgibbon, 1982; Waldstein et al., 1996).

Although hypertension related cognitive deficits have been noted in individuals of all ages, several studies have revealed more pronounced performance differences between young (less than 40 or 50 years of age) than middle-aged (upper limits ranging from 56 to 72 years) hypertensive and normotensive groups on tests of attention, memory, executive functions and psychomotor abilities (M. F. Elias et al., 1990; Schultz, Dineen, Elias, Pentz, & Wood, 1979; Waldstein et al., 1996). This may be attributed to the normal cognitive dysfunction which sets in with aging.

Hypertension may also interact with other cardiovascular diseases (CVD) and metabolic diseases to affect cognitive function. In this regard, data from the Framingham Heart Study (P. K. Elias et al., 1997) reveal an interaction of BP with non-insulin-dependent diabetes mellitus (Type II diabetes) such that hypertensives with Type II diabetes showed the poorer performance on tests of visual organization and memory. Although hypertensives are not clinically impaired, their diminished levels of cognitive performance could affect their perceived quality of life.
Hypertension has thus been one of the most extensively investigated of the CVDs with respect to cognitive functioning (Waldstein, Snow, Muldoon, & Katzel, 2001).

From the above discussion, it is evident that the mnemoactive effects of diabetes and hypertension are due to their physiological effects which in turn influence the functioning of the brain. There is extensive evidence, emanating from studies employing a variety of methodologies, indicating that diabetes and hypertension are associated with poorer cognitive performance and severity and chronicity also predicts profound cognitive decline over time. Since, these two diseases are also been known to co-exist specifically along with obesity, their influence on brain functioning could be further magnified. Research findings indicate that the two diseases affect different aspects of memory, i.e., diabetes has a more profound effect on short term memory and visual memory while hypertension has been reported to impair attention and executive functions. Both these diseases are chronic and require prolonged treatment where emphasis is on management i.e., control of BP or BG levels. Very few attempts have been made to study which specific areas of cognitive functioning are impaired as a consequence of the diseases. Research findings implicate impairments in various physiological/neural processes as a consequence of these diseases. Specifically, diabetes has been reported to result in hippocampus malfunctioning while hypertension leads to reduced right hemisphere activation. Both the disorders are related to pathological manifestations of Alzheimer’s disease (AD), reduced blood flow/fuel to the brain, neural damage, and cognitive mutilation. Impairment in a wide variety of cognitive functions has been reported as a consequence of these diseases (attention specifically visuo-spatial, perceptual processes, psychomotor efficiency, abstract reasoning, executive functions etc.). Since recent researches have implicated the involvement of specific brain areas in the functioning of specific memory systems, it was felt that diabetes and hypertension could have specific mnemonic effects via an influence on specific neuropsychological functions.

A review of researches related to cognitive dysfunctioning as a consequence of these two diseases has been presented in the next chapter.