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MENTAL IMAGES IN EPISODIC MEMORY: Comparison between Patients with Alzheimer's Disease and Healthy Control Subjects

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ZUSAMMENFASSUNG

Das episodische Gedächtnis, das von manchen auch als autobiografisches Gedächtnis bezeichnet wird, in dem vor allem bildhafte Erinnerungen repräsentiert sind, wird vermutlich bei Morbus Alzheimer (AD) beeinträchtigt. Zweck der vorliegenden Studie ist, das episodische Gedächtnis von AD Patienten zu analysieren und zu bewerten. Als einzig mögliches Verfahren kommt bei der Untersuchung des episodischen Gedächtnisses die Introspektion in Frage, will man Zugriff zu den persönlich bedeutsamen Bildern gewinnen. In Experiment I wurden die kognitiven Fähigkeiten bei gesunden und AD Patienten untersucht: 21 AD Patienten und 19 gesunde Testpersonen wurden miteinander verglichen. Die Testpersonen waren zwischen 55 und 70 Jahre alt und mit ihnen wurden in Korea standardisierte neuropsychologische Tests durchgeführt. Jede Testperson wurde aufgefordert, die bildlichen Erinnerungen aus dem episodischen Gedächtnis vom Vortag, von der vergangenen Woche, von dem vergangenen Monat und von einem Tag der lange in der Vergangenheit lag, zu beschreiben. Die Antworten wurden analysiert, wobei insbesondere auf begleitende Emotionen, mögliche Farben der Erinnerungsbilder und deren zeitliche Reihenfolge berücksichtigt wurde. Am darauf folgenden Tag wurden die Testpersonen gebeten, noch einmal alle am Vortag wiedergegebenen Bilder zu berichten, um mögliche Veränderungen des anterograden Gedächtnisses zu prüfen. Es wurde beobachtet, dass die Patienten die berichteten Bilder bei der Wiederholung nicht in die zeitliche Reihenfolge bringen konnten, die Bilder vom Vortag waren farblich unklar, und sie konnten sich nicht an Einzelheiten der Untersuchung

des Vortages erinnern, nur an den allgemeinen Ablauf. In einem weiteren Kapitel werden Ergebnisse von sechs Einzelfällen dargestellt, um genaueren Einblick in die individuelle Problematik bei AD Patienten und Gesunden zu erlangen. In einem weiteren Untersuchungsschritt wurde die emotionale Intensität beim Berichten der Erinnerungsbilder von unabhängigen Bewertern eingeschätzt; insbesondere wurde hierbei auf die Intonation der Stimmen geachtet. Übereinstimmend ergaben die Urteile der acht unabhängigen Bewerter, dass die emotionale Intensität bei AD Patienten geringer eingeschätzt wurde als bei Gesunden. Diese Beobachtung zeigt zum ersten Mal, dass bei AD Patienten bereits im Anfangsstadium ihrer Erkrankung der Ausdruck von Gefühlen bei Erlebnissen, die im episodischen Gedächtnis gespeichert sind, vermindert ist.

ABSTRACT

Episodic memory, i.e. memorization of information within a spatiotemporal environment, is affected by Alzheimer's disease (AD) but its loss may also occur in the normal aging process. The purpose of this study is to analyze and evaluate episodic memory in patients with AD by examining their cognitive skills in episodic memory through the introspection technique. A new method was used, wherein we assessed mental images of the subject's own past recalled in the mind like projected pictures and movies. Experiment 1 is designed to determine the effect and process of normal and pathological aging on cognitive skills in episodic memory using the introspection technique. Two groups were observed towards this purpose: 21 patients with AD and 19 normal control subjects. All subjects were chosen from ages from 55 to 70 and were administered standardized neuropsychological tests (K-DRS and MMSE-K). All subjects were asked to retrieve their episodic memory of the previous day, week, month, and a day remote from testing day. The answers were analyzed, focusing on their specific features such as emotional state, color, and time order. In the following day, the subjects were tasked to recall again all images that they reproduced in the previous day's test in order to observe impairment of anterograde memory. Results showed that patients failed to arrange the retrieved images in time order and their images of the previous day were unclear in color and were stationary like photographs, even when they reproduced the mental images at as much quantity as controls. They also could not remember particular events of yesterday, only their general

occurrence. These results suggest that in the early stage of AD, difficulties in the retrieval of recent episodic memory begin to occur, and qualitative impairment happens earlier than quantitative. The third chapter supports these results with further evidence, analyzing from a clinical viewpoint 3 patients with AD, 1 patient with mild depression and 2 controls. In Experiment 2 the emotional intensity of episodic memory within different categories of memory (yesterday, week, month, and remote) was investigated by comparing healthy elderly people and AD patients. The subjects' voice intonations were estimated by 8 valuators. As a result, the emotional intensity of AD patient was evaluated lower than controls. It appears that patients in the early stage of AD are impaired in the ability to express emotions during emotional episodic memory retrieval compared to healthy elderly adults.

INTRODUCTION

As a significant portion of the world's population begins to age, the health issues of senior citizens have gone mainstream in public discourse. In particular, Alzheimer's disease (AD) takes center stage because of its dramatic impact on the lives of patients and their families. To date, the exact cause, diagnosis, and treatment of the disease are still unknown, and research continues worldwide in the hopes of illuminating such crucial aspects of this complex disorder.

A keystone in the cure for AD is an accurate method of diagnosis. This is complicated by the slow progress of early AD symptoms. In the beginning, the only symptom may be mild forgetfulness, common enough in everyday life. During these early stages, patients may have trouble remembering recent events, activities, or the names of familiar people or things. Some patients are not able to solve simple mathematic problems (Braak and Braak, 1991; Alafuzoff, 1992). Such difficulties may be felt as an annoyance, but usually they are not serious enough to cause concern, as they also manifest in normal-aging people. It is therefore not easy to diagnose this disease in the early stage. However, as the disease gathers momentum, more alarming symptoms develop; for example, patients can no longer think clearly and begin to have problems speaking, understanding, reading, or writing. Later on, people with AD may become anxious or aggressive, or wander away from their homes. Such patients will eventually need 24-hour care.

Memory impairment is a hallmark deficit of this disease and is regarded as being essential for diagnosis in the early stages of AD (Morris and Kopelman, 1986; Bäckman, 1992). This

study in particular aims to analyze and evaluate episodic memory in patients with AD by running comparisons with healthy elderly controls.

Episodic memory (i.e. memory of events within a spatiotemporal frame) is affected in AD, but may also occur in the normal aging process. Episodic memory involves conscious retrieval of information acquired at a particular place and time (Tulving, 1983). The finding that episodic memory deficits in early stages of AD are widespread is consistent with certain histopathological (Braak and Braak, 1995) and morphological (Fox et al., 1996a; Fox et al., 1996b; Laakso et al., 1998) evidence that imply some of the earliest brain changes in AD occur in the hippocampus and related structures. These regions have been strongly implicated in episodic memory in both lesion (Vargha-Khadem et al, 1997) and brain imaging (Nyberg et al., 1996; Laakso et al., 1998) studies.

In the laboratory, episodic memory is typically assessed by having subjects recall and recognize specific information encountered in an experimental setting. Anterograde memory loss appears to be due to defective encoding and storage of new information, which increases sensitivity to pro-active interference and accelerates rates of forgetting (Granholm and Butters, 1988; Larsson et al. 1999; Leube et al., 2003). Remote memory by contrast has been investigated much less extensively. Although there is no doubt that patients with AD show impairment on a range of remote memory tests including naming and identification of famous faces or famous scenes (Greene and Hodges, 1996a), a number of clinical and theoretical questions concerning the efficacy of these tests on episodic memory remain unanswered. The first question is how to assess temporal order with these methods.

The question of temporal order has been previously studied in patients with alcoholic Korsakoff's syndrome (Seltzer and Benson, 1974; Kopelman, 1989). The same decline of this particular functional component can be observed in AD patients, as episodic events are by definition related to specific temporal and spatial contexts. The second question is how to assess remote memory in patients in mild stages of AD. In general, the majority of AD patients have well-established remote memory with respect to recent memory. Experimental settings can assess remote episodic memory quantitatively, but it is necessary to evaluate it qualitatively as well, because as mentioned above, remote memory in patients in the early stages of AD is not impaired in quantity but quality. The final question concerns the identification of famous people itself, as recalling the name of a famous person or object seems to be more of a mechanical task related to general loss of semantic memory. Also with regard to stimulus or cues, they tend to be more semantic and synthetic in their detection than that of episodic memory, as episodic memory is related to one's personal past and their relative emotions evoked through visual images.

Patients in the early stages of AD may have a different episodic memory process in comparison to people undergoing normal aging, even if the two groups appear to be similar at first glance. AD patients may experience memory decline in a more qualitatively and quantitatively significant manner than normal aging people. The questions raised in this study are "How much could AD patients remember of the previous day and/or week in free recall condition?", "What are the signs of this memory decline in patients with AD in comparison to people undergoing normal aging?" and "How is the process of this memory decline in patients with AD different from people

undergoing normal-aging?" Based on these questions, the following hypotheses have been drawn:

- AD patients show a deficit in time tag when compared to a central time tag, in contrast to healthy elderly people.
- AD patients will need to have more time (i.e. latency) to retrieve a mental image than the normal-aging group.
- The mental image of AD patients will not be highly related to emotion or to sensory modality (with less access to models such as auditory).
- With regard to anterograde memory in AD patients, the memory of yesterday will be very functional, whereas the memory of week and month will be deteriorated.
- In remote memory in AD patients, the quantity of this memory will be established in comparison to healthy elderly people, but it will be impaired qualitatively. For example, they could report a mental image of a remote event objectively, but they won't report specific feelings or thoughts.
- The encoding system of AD patients is impaired universally in the early stages. It will be tested, tasking subjects to memorize the context that the subject recalled during the interview and to recall it the following day.

This study is designed to evaluate the effect and the process of normal and pathological aging on cognitive skills in episodic memory using the technique of introspection. Two groups consisting of a total 40 subjects participated: 21 patients with AD (11 females and 10 males) and 19 normal control subjects (10 females and 9 males). All subjects were chosen from ages

55 to under 70. All subjects were administered the neuropsychological tests K-DRS (Korean-Dementia Rating Scale) and MMSE-K (Mini Mental State Examination-K). All patients were examined by a neurologist and psychiatrist before entry into study and underwent MRI scanning. Performances in healthy elderly subjects and in patients with AD are compared both quantitatively and qualitatively. In this study, free recall of one's own past was assessed on each measurement occasion in order to determine their relative importance in identifying persons at early stages of AD. The present study will pay particular attention to observing the mental images of episodic memory, the recall of an event and/or a thing with a mental image. The subjects are asked to retrieve his/her first image of the previous day, week, month and of remote. They are also asked for his/her sensory modality and emotional state etc. in the image. For example, “Did you smell or hear something?”, “How did you feel at this smell?” and/or “How were you?” In the following day, subjects were tasked to recall all the contexts which they recalled in the interview. The overall method will be described in more detail in chapter two.

The present study is constructed largely in three parts: theoretical, empirical, and clinical. This structure reflects the course of this study, its testing and possible verification of its hypotheses, and also the utilization of its results.

Chapter One assists the understanding and substantiation of the hypotheses of this study by giving a general overview of the ideas discussed. The concept of episodic memory will be described in the context of the practical and clinical work of Alzheimer’s disease, with citations from recent experiments. It will delve into how the particular concept of episodic memory was defined in neuroscience and list relevant

anatomical components. The common symptoms and process of AD will also be described, from the viewpoints of cognitive neuroscience and neurology. Finally, recent studies concerning episodic memory in AD patients shall be examined in order to see how episodic memory is observed in an experimental setting.

Chapter Two presents the experiment itself by describing the methods used in testing the hypothesis, and the results of the experiment. It includes an outline of the hypotheses, the material, and the method of the experiment, as well as a statistical analysis of the results done by category in order to try to falsify each hypothesis.

Finally, Chapter Three reports 6 clinical cases: 3 cases from a normal-aging group and 3 cases from an AD patient group. Each case is analyzed independently in every category, reporting particular signs and symptoms. These analyses are compared in a consequent synthesis. In this synthesis, particular points of concentration are suggested for practitioners diagnosing AD.

CHAPTER I
THEORETICAL PART

The ability to learn and remember is one of the fundamental cognitive capacities besides perception, emotional evaluation or voluntary control. Current memory research tries to assess the deficits of episodic memory in Alzheimer's disease in comparison with the normal aging process.

This chapter is divided into three sections. The first considers the concept of episodic memory, a general definition of the episodic memory, and its concept in neuroscience and in particular in neuroanatomy. Furthermore, it describes the course of the disease, and the major regions of the brain which play an important role, and in which way the brain was investigated so far. The second section describes the concept of Alzheimer's disease, its pathogenesis, its neurocognitive symptoms, and its risk factor. The third section examines the method and/or experimental design to assess episodic memory in patients with Alzheimer's disease, including episodic memory in unaffected elderly people and the patients with Alzheimer's disease.

1.1. Definition of Episodic Memory

Memory commonly is subdivided into a number of forms (Tulving, 1995), and it is assumed that different brain regions contribute differently to the various forms of memory processing (Fink et al, 1996; Piefke et al., 2003). Two of the main forms of memory are episodic memory and semantic memory (Tulving, 1995), also subsumed under declarative or referential memory. Episodic memory is a type of memory for experienced events or for remembering what happened where

and when, whereas semantic memory contains general facts (e.g. knowledge about the world), which we need for verbal and nonverbal interaction with our environment, and which are not of private nature.

A person remembers personally experienced events always consciously and re-experiences them either as an observer and or as an actor in memory. Events are, thus, initially experienced consciously, either in association with an emotion or not, as a series of perceptual and semantic representations of objects that interact in space and time within a larger spatio-temporal context (Mayes & Roberts, 2001). This kind of the memory is called "episodic memory".

Some authors suggest autobiographical memory (Fink et al., 1996; Kopelman and Kapur, 2001; Conway, 2001) to be subsumed under episodic memory. According to Kopelman and Kapur (2001), autobiographical memory refers, characteristically, to a person's recollection of past incidents and events, which occurred at a specific time and place. Episodic memory, on the other hand, is a somewhat broader term, encompassing autobiographical memories as well as performance on certain learning tasks, such as the recall of a word-list. However, the term "autobiographical" and "episodic" are often used interchangeably. Conway's concept of autobiographical memory (2001) retains some features previously associated with episodic memory, but also includes some novel ideas, such as the temporal duration of episodic memory (short) and autobiographical memory (long) and different kinds of recollective experience (i.e., recollection and familiarity in episodic, and feelings of 'knowing ' in autobiographical memory). In the study of Fink et al. (1996) using imaging technology, autobiographical memory refers to a subsystem of episodic memory that implies emotional

processing. In my own study, episodic memory and autobiographical memory are not differentiated, because the definition of episodic memory in the present literature contains definitions of both forms of memory.

1.1.1. Episodic Memory in Neuroscience

Episodic memory was originally defined as a memory system that had to do with learning and retention of material presented in a particular place at a particular time. Episodic memory can, however, be regarded to be unique in neuroscience. Episodic memory and declarative memory differ with respect to their functions. As described above, episodic memory is concerned with remembering past experiences. It refers to the conscious recollection of previous experiences during events and situations. The other forms of memory, on the other hand, refer to facts and events in the physical world, i.e. the acquisition and use of knowledge. Episodic memory is oriented towards past, whereas all other forms of memory including semantic memory or procedural memory are oriented towards the present. Regarding cognitive processes, episodic memory is perhaps more complicated than the other forms of memory, because its encoding and retrieval mode have to be accompanied by the experience of 'reproducing the past events' or autonoetic remembering (Tulving, 1987; Tulving, 2001). Episodic memory is encoded in the brain with diverse components such as the sensory systems and emotions and it is retrieved with them again together (Sharot et al., 2004; Piefke et al., 2003; Nyberg et al., 1996). From the neuroanatomical point of view, both episodic and semantic memories depend on the integrity medial temporal lobe and diencephalic structures (Dolan et al., 2000). It has been demonstrate that episodic memory is controlled by

the frontal lobes in a different way than declarative memory (Tulving et al, 1994; Wheeler et al., 1995).

1.1.1.1. Emotion in Episodic Memory

When we recall soothing from the past, depending on the context of the events, people cry, laugh, or get angry while reproducing the memory. This leads to the conclusion that episodic memory is closely related to emotions. Episodic memory deals with individual episodes that are also defined by time when they happened and locus where they happened. Therefore, episodic memory implies a direct link to the awareness of the time course of one's life history which is depending by when and where something happened.

Episodic memory may involve emotional arousal (e.g. fear, happiness and anger, etc.) that were associated with the event and the particular emotion may be remembered when the linked scene, constituting the episode, is later retrieved (Graham et al, 1997; Montaldi et al, 1998; Mayes & Roberts, 2001).

The emotional response patterns consist of behaviors that deal with particular situations and physiological responses (both autonomic and hormonal), that support behavior (Carlson, 2000). In humans these responses are accompanied by feelings. Feelings are private events. The process of emotion might strike a person as being at odds with one's own experience (Ehrlichman & Halpern, 1988). The James-Lange theory of emotion implicitly recognizes the existence of such emotional behavior, but it is concerned with a subjective experience, the feeling, of emotion. These emotional feelings are based on the activity of peripheral autonomic and somatic response systems and their associated sensory systems.

Emotions are expressions of the activity of the whole brain

with the particular involvement of the limbic system. The limbic association cortex is located in the medial and ventral surfaces of the frontal lobe and the anterior tip of the temporal lobe. The limbic association cortex includes the orbital cortex, the cingulate region and parahippocampal area. It receives projections from other cortical regions, including prefrontal cortex. This provides a pathway in which emotions can affect motor planning. The structures of the limbic system are involved both in memory and emotional processing (Cahill et al., 1996; Maratos, 2001; Rolls, 2000; Medford et al, 2005). Support for this statement demonstrated from studies using fMRI (functional Magnetic Resonance imaging) (Fink et al., 1996; Piefke et al., 2003).

According to Nauta (cited in Fink et al., 1996), the limbic system is involved in affect-based information encoding, in particular, the amygdala and orbitofrontal cortex. The amygdala organizes emotional responses to different situations. The amygdala receives input from the association cortex of the temporal lobe, the frontal cortex and the other areas of the limbic system. Its output projects to the frontal cortex, the hypothalamus, the hippocampal formation, and brain stem nuclei that control autonomic functions and species-typical behaviors (Cited in Carlson, 2002). The activity in the amygdala is found to influence memory-related processes in the hippocampus (Iidaka et al., 2001). This activity has a bigger influence on the activity in the hippocampus or the cortex than vice versa. Emotional information about faces may be carried via backprojections from the amygdala to the hippocampus, where they become linked to episodic memory.

The orbitofrontal cortex is part of the limbic association cortex, having direct connections with limbic structures, such

as the amygdala. According to studies of Jacobson and other investigators, with lesioned animals, if the damage is limited to the orbitofrontal cortex, the normal aggressiveness and emotional responsiveness of primates is reduced (cited by Kupfermann, 1991). According to Rolls (2004), the orbitofrontal cortex is normally involved in executive behavior when the behavior is performed by evaluating the reinforcement associations of environmental stimuli. Evidently, the orbitofrontal cortex is involved when learning must be performed rapidly during acquisition or during reversal. Furthermore, Rolls (review, 2004) reports that stimuli to sensory systems influence motivational and emotional behavior via neural relays to the orbitofrontal cortex. In other words, areas of the orbitofrontal cortex are activated by pleasant touch, by taste, and by smell.

There is general agreement that in Alzheimer' disease, early stages are associated with impairments of emotional processing (Cadieux & Greve, 1997; Hargrave et al., 2002; Bucks & Radford, 2004). The finding that the adjacent limbic area to the entorhinal cortex is specially affected by brain pathology in early Alzheimer's disease is in good accordance with the observation of these behavioral deficits.

Expressions serve useful social functions; they provide other individuals with information how we feel and – even more important – what we are likely to do. Many animal species (including human beings) communicate their emotions to others by means of postural changes, facial expression and nonverbal sounds (such as sighs, moans and growls). We recognize other people's feelings by means of vision and audition, seeing their facial expressions and hearing their tone of voice and choice of words. In experiments on emotion, therefore, subjects listen to the meaning of words and say

whether they describe a situation in which someone would be happy, sad, angry or neutral. In another condition, they judge the emotional state from the tone of the voice.

1.1.1.2. Sensory Modality in Episodic Memory

The representation of episodic memory is multimodal, associating temporal and spatial properties from the visual, auditory, tactile, and other sensory modalities (Rolls, 2004). In general, in episodic memory, visual information is more salient (Kosslyn & Dror, 1992). However, information from other senses plays an important role and all this sensory information is likely to be interpreted automatically by the observer in terms of available semantic knowledge, and may be colored by emotion (e.g. vision, audition, and olfaction). All sensory information associates together in very different kinds of information, which include perceptual and sensitive aspects of objects, and how these are located in space and time relative to each other and the person itself.

Many sensory experiences seem to be a combination of certain basic "qualities" such as red and blue in the visual system or salty and sweet in taste. This suggests that there may be some fundamental receptors which, in combination, may result in the variety of sensations possible in each modality. That is, fundamental means of encoding within the sensory system work through stimulation of specialized sensory units.

Some stimuli also have characteristics of shape and movement. It seems obvious that the pattern of receptive elements that are stimulated can effectively "draw a picture" of such stimuli on the surface of the receptor.

The memory (information) is not only encoded by sensory stimuli, but also is recalled by these diverse stimuli (Cahill et

al., 1996; Royet et al., 2000). The task of sensory systems is to provide a reliable representation of biologically relevant events in the external environment. They are richer because they recall certain representations of objects, states, and events that are abstracted from the primitive sensory signal (Fink et al., 1996; Rolls, 2004). The sensory signal is encoded into the brain. Sensory processing does not end with the encoding of stimuli and its representation of objects and events in the context. These signals are modulated by messages from other sensory systems, from memory systems and from attentional systems. The visual information, dominates to encode information on the brain but many studies show that also olfactory (e.g. Degel et al., 2001) and auditory stimuli (e.g. Royet et al., 2004) are efficiently processed to encode and to recall the information.

1.1.1.3. Time in Episodic Memory

Time is one of the most important topics in the field of episodic research; where a temporally ordered sequence of scenes is experienced, a subject will also be aware of the duration of the different scenes constituting an episode. Episodic memory assists to retrieve and order past events and it is related to the memory of 'when.' It is important to know the relative order of events in order to merge and present information correctly. One would like to be able to ask when an event occurs, or what events occurred prior to a particular event.

This theoretical aspect relates to the Korsakoff psychosis as these patients have been shown to have worse temporal order memory than other amnesic patients. Elvevag et al. (2000) tested the memory for temporal order in patients with schizophrenia with verbal stimuli. Their patients were

impaired in placing the items in the correct temporal order. Some studies suggest that different brain structures such as the limbic-diencephalic and frontal regions may contribute to the processes that underlay temporal memory. Yasuno et al. (1999) investigated the role of the fornix for retrograde temporal order amnesia and they concluded that this type of memory impairment is probably due to the direct disconnection between the frontal lobe and the hippocampus by disruption of the fornix. These two brain regions, frontal lobe and hippocampus play an important role in episodic memory. Furthermore, the disruption of these brain areas is closely related to pathogenesis of AD. Patients with AD have been reported to have a variety of memory problems, although memory for the order of events has not been studied extensively so far.

1.1.2. Neuroanatomical Aspect of Episodic Memory

1.1.2.1. Medial Temporal Lobe

Semantic and episodic memory depends crucially on medial temporal lobe structures (Dolan et al., 2000; Viskontas et al., 2000; Kounios et al., 2003). These structures are the hippocampus, the entorhinal cortex, parahippocampal cortex, and the perirhinal cortex. Lesions of these structures interfere primarily with the retention of new memory but they have relatively weak effects on prior memories. Thus, these structures are not themselves registers or savers for the memory storage, but are somehow involved in the process by which memories are placed into storage or are retrieved and read out from storage. Viskontas et al. (2000) studied the remote episodic memory deficits in patients with unilateral temporal lobe epilepsy and excisions. They indicated that

even minimal damage to medial temporal lobes results in significant impairment to autobiographical episodic memory. Actually, the neurosurgeon Wilder Penfield (cited in Kandel et al., 1991) investigated some time ago the function of the human temporal lobe, stimulating various points in the temporal lobe electrically in awake patients before he removed epileptic tissue. The patients were sometimes reexperiencing past events. This phenomenon after the stimulation of the temporal lobe appears to occur only in patients with epilepsy in the temporal lobe. Milner (Cited in Kandel et al., 1991) supported this observation with a few patients from whom both the left and right temporal lobe were removed. He has found irreversible impairment of the capacity to form certain types of long-term memories. Recently, neuro-imaging studies (Fink et al., 1996; Dolan et al., 2000; Dupont 2000; Kounios et al., 2003; Gilboa et al., 2005) have also shown that activation in the medial temporal lobe, including the hippocampus, is observed both, during encoding and retrieval. Dolan and his colleagues (2000) investigated whether neural systems known to be involved in episodic memory retrieval also subserve retrieval of emotional episodic memory by using functional imaging materials. They identified an anterior temporal pole activation that reflected the psychological set associated with emotional memory retrieval. There are many studies to indicate that memory deficits are combined with atrophy of medial temporal lobe in patients with AD using different methods (Visser et al., 1999; Pantel et al., 2002)

1.1.2.2. Hippocampus

To study the hippocampus and with respect to its importance in memory has continued to be of great interest to this day.

The most recent observations concentrate on the role of the hippocampal formation in the acquisition of episodic memory. Anatomically, the hippocampus lies at the end of the medial temporal lobe and is a recipient of convergent projections from each of the structures that proceed in the hierarchy. Many studies (Bäckman et al, 1999; Desgranges et al., 2002) suggest that the hippocampus plays a special role in memory tasks that depend especially on relating combined information from multiple sources, such as spatial information or information about specific events, as opposed to factual knowledge.

Damage to the hippocampal region results in a failure to remember spatial layouts or landmarks. This may be one reason why people with Alzheimer's disease become progressively unable to navigate in space despite normal vision. De Leon and coworkers (1997) found out that probable cases of Alzheimer's disease often emerge in people who start out with a small hippocampus and mild memory problems. Hippocampal volume declined from 20 to 50 percent in victims of Alzheimer's disease compared to healthy elderly controls.

Some studies suggest that the hippocampus regulates the episodic memory, but plays a very small role in the remembering factual information (Bäckman et al., 1999; Rombouts et al., 2000). However, in other studies suggest that "despite the hippocampus' powerful influence on episodic memory, other brain areas may independently gather" (Nyberg et al., 1996; Schacter et al., 1996; Nestor et al., 2002). It seems that all new experiences must pass through the hippocampus to form a new memory. When the region is damaged, patients become "prisoners of the past". Many patients with hippocampal damage remember things from

before an injury, but not since.

The hippocampus supports and extends operations of structures that send projections towards it (Dolan & Fletcher, 1997). Studies of lesions and behavior could not reveal deficits unique to the hippocampus that could not also be observed by damaging the perirhinal cortex, the parahippocampal cortex, or entorhinal cortex.

Memories are probably first processed and kept in the hippocampus for several weeks before they are transferred to the cerebral cortex for permanent storage. This may explain why people with brain damage within the hippocampal region retain previous memories of faces and places, which are stored in the cortex, but have difficulty forming new short-term memories

1.1.2.3. Frontal Lobe

The frontal lobe, located behind the forehead, is involved in controlling responses to the input from the rest of the central nervous system (brain and spinal cord). It is responsible for voluntary movement, emotion, planning and execution of behavior, intellect, memory, speech, and writing. The concept of the frontal lobes, however, in relation to behavior has not always been used consistently. It is commonly accepted that patients with damage restricted to the frontal lobes are not amnesic. It is also commonly thought that the frontal lobes are involved in the placement of such information into spatial and temporal contexts, and with the initiation and execution of complex mnemonic strategies. One important function of the frontal lobes is thought to be related to the capacity of the organism to weigh the consequences of future actions and to plan accordingly.

Some recent studies (Tulving et al., 1994; Buckner & Tulving,

1995) discovered that the frontal lobes do play a role on episodic memory. Episodic memory has been investigated using PET scanning to measure regional cerebral blood flow. These studies have consistently revealed frontal lobe activation during episodic memory tasks. For instance, patients with frontal lobe damage have great difficulty remembering the temporal order of two events. In some studies, right frontal regions show greater activation than left frontal regions during episodic retrieval, and left frontal regions show greater activation than right frontal regions during episodic encoding. Wheeler et al. (1995) observed the relation between the frontal lobes and episodic memory in comparison between frontal pathology and control subject, using test of recognition, cued recall and free recall. They report that frontal damage disrupts performance on all three tests, with the greatest impairment in free recall, and the smallest in recognition.

According to Buckner (1998), the prefrontal lobe is active when subjects engage in processing tasks that lead to effective episodic encoding of information, independent of whether these tasks are engaged intentionally by a subject or incidentally. Therefore, frontal lobe patients might perform more poorly at source recollection simply because it is more difficult and requires greater cognitive resources than item recognition. It would be particularly important to be able to relate prefrontal function to preserved memory ability in AD patients, because these areas are affected later in the course of the disease. Tulving et al. (1994), also have found more right prefrontal activity during episodic retrieval and left prefrontal activity during semantic retrieval or encoding new information. Grady et al. (2003) examined the neural correlates of episodic memory and semantic memory in

patients with AD by a neuro-imaging study. They demonstrated that patients with AD can engage additional prefrontal areas during memory task performance. Nakano et al. (2001) also observed this, investigating the effect of donepezil on regional cerebral blood flow in patients with mild to moderate AD.

1.1.3. Episodic Memory in Experiment

A prototypical laboratory experiment on episodic memory consists of an original study experience, during which individual items are encoded and stored by a learner, and a subsequent test during which some aspects of the experience is retrieved (Tulving, 1968). Episodic memory experiments have been concerned with a large variety of different kinds of information, for example, words, names, odors, faces, pictures, sounds, facts, sentences, paragraphs, stories, etc (Tulving & Patkau, 1962; Tulving 1965). Measures used to assess episodic memory have typically involved such tasks as reading short narrative passages and asking the subject to repeat these passages, recognition of previously shown pictorial, olfactory (e.g. Larsson & Bäckman, 1993; Larsson et al, 1999), or auditory stimuli (e.g. Tulving et al., 1994), facilitation of word identification upon repeated presentation (e.g. Hassing & Bäckman, 1997; Bäckman et al., 2001). The experimenter evaluates the amount of recall and degree of organization (Tulving et al., 1965; Slamecka, 1968). In the experiment, these forms of the tasks are utilized in different retrieval (recall) conditions (free recall, cued recall, etc.) and with different types of amnesia patients (e.g. Bäckman et al., 2001; Wheeler et al., 1995). According to Tulving's description of episodic tasks, free recall means to name the items in the study set or list, regardless of their order (e.g.

Tulving & Patkau, 1962; Tulving & Patterson, 1968). In studies on episodic memory, the subjects recall the past events without any cues easily. Cued recall means to name the item in the study list that represented for instance a category.

Recent studies are more interested in investigating whether episodic memory depends on special brain regions. They performed neuro-imaging studies (e.g. Dupont et al., 2000; Royet et al., 2000) using the above mentioned tasks in different kinds of amnesia patients (e.g. Butters et al., 1987; Greene et al., 1996a; Greene et al., 1996b; Bowler et al., 2000), or in delusional suspected people (Herlitz & Forsell, 1996), or in groups with different age (Larsson & Bäckman, 1993; Marcom et al., 2003), or gender (Herlitz et al., 1999).

However, the methods are limited to assess episodic memory in consideration of definition including the autobiographical memory concept, because these models seem to assess more semantically or to assess fundamental parts of episodic memory such as sensory-perceptual episodic memory. Episodic memory retains not only the knowledge in weeks, months and years, but also represents something experienced by a subject itself. This always accessed by its contents, does not need to give rise to recollective experience. Conway (2001) described and integrated the model to assess episodic memory considering both, its sensory-perceptual information and its autobiographical memory context.

As mentioned above, the diseases that are related to amnesia such as Alzheimer's disease and alcoholic Korsakoff's syndrome or head injured people had become subjects in episodic memory research to find the brain regions occupying this type of memory. In contrast, episodic memory could become an important tool in the investigation of the prediagnosis of dementia or to evaluate stages of AD.

1.2. Aspects of Alzheimer's Disease

Everyday you go to pick up your grandson from his school, but yesterday you forgot about it. Sometimes you find yourself in front of a burning pot on the gas range, but can't remember what you wanted to have, and more extremely, you have lost the way to find to your sons home, where you go to every week. In the process of aging, elderly people may expect a certain amount of forgetfulness. When slight memory loss is considered as normal, however, when is it a sign that something more serious is about to happen? Nowadays, if elderly people have these symptoms, they would suspect and worry to be affected by dementia. Dementia is a progressive decline in many areas of mental ability. Alzheimer's disease is the most prevalent type of dementia occurring in elderly people. About 70 percent of patients with symptoms of dementia are affected by AD.

When Alois Alzheimer described this disease in 1907, it was thought to affect only persons under the age of 65. Now it is understood that AD increases in prevalence as people get older. In fact, among people over the age of 65, AD has become the fourth leading cause of death. The number of people who have mild cognitive impairment is still unknown, however. Therefore, more research is needed to obtain knowledge regarding the symptoms of the early onset of AD.

AD is manifested by progressive impairments in memory, learning, language, visual-spatial skill, judgment, and behavior. At the end, patients become mute, incontinent, bedridden, and cannot move without a caregiver. The duration of the disease can differ widely among individuals, lasting from 5 to15 years. Many drugs (e.g. tacrine (Cognex), donepezil (Aricept), rivastigmine (Exelon), or galantamine

(Reminyl)) are being developed for treating it, but there is no prevention and definitive treatment to deal with.

The risk for Alzheimer's disease increases with each decade of adult life. People with a family history of Alzheimer's have a greater risk, implying that a genetic factor is involved (Sulkava, 1982). A clear inherited pattern of AD exists in less than 10% of cases. Some involve a mutation of the gene or the protein APP, found on chromosome 21 (Goate et al., 1991; Tanzi et al., 1992). Nearly all people with Down's syndrome (trisomy 21) who live into their 40s develop AD (Mann et al., 1984). A lot of the dementia research has focused on vascular risk factors, which are factors related to the blood circulation system. A great deal of evidence shows that disorders such as high cholesterol and high blood pressure which are in general factors that cause strokes and heart disease may also increase the risk for developing Alzheimer's (Jorm et al., 1991; Mortimer et al., 1991; Van Duijn et al., 1991). Adults who have had head injuries are three times more likely to develop Alzheimer's disease (Van Duijn et al., 1991). It is thought that gender plays a role because several studies suggest that women are affected with Alzheimer's disease more often than men. However, the evidence is inconsistent and some studies report that the disease is more prevalent in men (McPherson et al., 1999).

There are two abnormal structures in the brain associated with Alzheimer's disease. Amyloid plaques are clumps of protein fragments that accumulate outside of cells. Neurofibrillary tangles are clumps of altered proteins inside cells. Theses pathological changes on AD patients' brains are concentrated in the association areas of the parietal, temporal and frontal lobes and hippocampal formation (Delacourte et al., 1999). Areas of cortex subserving primary motor, somatosensory and

visual functions are relatively spared and subcortical structures typically do not become involved until late in the clinical course.

The clinical diagnosis of AD is based on the criteria defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR, American Psychiatric Association). However, a diagnosis of definite AD can be confirmed only in neuropathological examination of the brain tissue either from biopsy or autopsy. In the clinic, AD is diagnosed correctly, but not 100%. To diagnose AD generally, doctor's interview, some neuropsychological tests (e.g. DRS, MMSE, and CERAD), blood test, and brain scan (e.g. MRI) may be used. A diagnosis of the early onset of AD is very important because it helps patients and their families planning for the future and offers the best chance to treat the symptoms of the disease.

1.2.1. Alzheimer's Disease and Cognitive Aspects

Cognitive function (i.e. abilities such as language, critical thinking, reading and writing) is measured to detect early signs of AD (Grober & Kawas, 1997; Au et al., 2003; Graham et al., 2004; Joray et al., 2004). This has been labeled a mild cognitive impairment, for example, a memory disorder that is a strong early predictor of Alzheimer's disease (Hodges et al., 1990; Rombouts et al., 2000; Graham et al., 2004).

Memory impairment is the hallmark deficit of AD. Especially, the earliest symptom of AD in the majority of the patients is a more severe difficulty in encoding and/or retrieval new information than recalling their remote memory. It refers to anterograde memory impairment. This is revealed in everyday life by increasing forgetfulness for day-to-day events; first, patients may entirely forget a recent event from one week to

the next, then from one day to next, and finally from one minute to the next. In other words, this refers to the impairment of the episodic memory. In experiments, the episodic tasks reflect not only retrieval but also encoding of information to observe which of them is impaired in AD.

There is no doubt, that the impairment of episodic memory is a common cognitive manifestation of the preclinical phase of AD (Bäckman et al., 2001; Bayles, 2001; Souchay et al., 2002). Helitz and Bäckman (1990) and Bäckman and Helitz (1990) report that the episodic memory impairment in AD is global and AD is associated with a deficit in the ability to utilize task-relevant prior knowledge to enhance episodic memory in comparison with a normal aging group. For this reason, many studies of AD (Bäckman et al., 2001; Faust et al., 2001) are concentrated on episodic memory and suggest that episodic memory could be assessed for the preclinical diagnosis of AD. Some neuro-imaging studies (McGeer et al., 1990; Waldemar et al., 1994; Desgranges et al., 1998; Bäckman et al., 1999; Meguro et al., 1999; Meguro et al., 2005; Eustache et al., 2004) found out that certain brain regions are involved in the impairment of episodic memory in AD. For example, McGeer et al. (1990) and Waldemar suggest that the frontal lobe is involved in this decline. Bäckman et al. (1999) report that AD patients did not show increased activity in the left hippocampal formation during episodic retrieval.

The pathological hallmark of AD are neurofibrillary tangles and neuritic plaques, which are particularly deposited within the hippocampus pathways leading to and from the hippocampus (the entorhinal cortex and the subiculum, respectively) (Bäckman et al., 1999; Eustache et al., 2001). Mitchell et al. (2002) investigated how neurofibrillary tangles

relate to cognitive function and refer to the fact that neurofibrillary tangles are significantly correlated to measures of episodic memory. They also indicate that phosphorylated tau pathologies develop in the ventromedial temporal lobe prior to the onset of AD and their presence is associated particularly with the impairment of episodic memory.

There are also declines in the concentration of a number of neurotransmitters, the chemicals that are responsible for the transmission of nerve signals in the brain. One neurotransmitter in particular, acetylcholine, which is important for the normal human memory, declines by up to 70 percent in AD. Once neurons have died off during the processing of AD, memories are lost as well as cognitive ability. Alzheimer's patients experience changes in personality and other features of Alzheimer's disease begin to develop.

1.2.2. Alzheimer's Disease and Neurological Aspects

In 1906, Dr. Alois Alzheimer, a German doctor, noticed changes in the brain tissue of a woman who had died of an unusual mental illness. He found abnormal clumps (now called amyloid plaques) and tangled bundles of fibers (now called neurofibrillary tangles). Today, these plaques and tangles in the brain are considered signs of AD (Braak & Braak, 1995). In an Alzheimer's patient, within the parts of the brain that control memory and retention of learned information, nerve cells become extremely disorganized and form what are known as neurofibrillary tangles (Delacourte et al., 1999). This causes the neurons to stop working the activities that are controlled by those cells, such as memory, reasoning, and ability to take care of oneself, diminish as well.

The neuronal decay also seems to be associated with

accumulations of a protein called amyloid. These amyloid or "plaques" are most prevalent in the hippocampus and adjacent cortex of Alzheimer's brains. The amyloid protein (the beta protein) is responsible for the neuronal degeneration. Amyloid proteins are not only present in Alzheimer's patients, but also all normal people. In AD, however, amyloid filaments are accumulated. The plaques cause neuronal cell death by either disrupting the production of acetylcholine (neurotransmitter), or stimulating the over-production of acetylcholinesterase, which has an antagonistic effect on synaptic transmission.

Familial AD, a rare form of AD that usually occurs between the ages of 30 and 60, is inherited. One risk factor for this type of AD is a gene that makes a protein called apolipoprotein E (apoE). Everyone has apoE, which helps to carry cholesterol within the blood. The APP gene was found on chromosome 21 and is implicated in the occurrence of AD in Down's syndrome patients who survive beyond 40 years. Some families with a history of early-onset AD have a mutation on the APP gene and others have a mutation in the presenilin-1 gene found on chromosome 14. Another gene, the Apo E gene on chromosome 19, also has been implicated in the disease. ApoE is a protein found with beta amyloid in neuritic plaques. The apoE2 (E2), apoE3 (E3), and apoE4 (E4) are most frequently forms/alleles of ApoE. People inherit one apoE allele from each parent. Having one or two copies of the E4 allele increases a person's risk of getting AD (Reiman, et al., 1996). Having the E4 allele is a risk factor for AD (Bennett et al., 2003), but it does not mean that AD is certain. Some people with two copies of the E4 allele (the highest risk group) do not develop the disease while others with no E4s do. The rarer E2 allele appears to be associated with a lower risk of AD (Reiman et al, 1996). According to the study of Wilson

et al. (2002), the people who have E4 decline more rapidly in cognitive functions and possession of one or more E2 is associated to reduce decline in episodic memory. The E3 allele is the most common form found in the general population and may play a neutral role in AD. The exact degree of risk of AD for any given person cannot be determined based on apoE status.

CHAPTER II
EMPIRICAL RESEARCH

2.1. Introduction and Hypothesis

Complex cognitive abilities arise when different sets of component subsystems interact. Episodic memory usually involves a recall of a personally experienced event in the past. A person can recognize that he/she experienced a particular event from a picture or video of the occasion. Introspectively, visual mental images appear to embody spatial and temporal properties of objects and scene. These patterns are activated from episodic memory, not from the eye. Recollective experience is the sense or experience of the self in the past and is induced by images, feelings and other memory details that come to mind during the act of remembering (Conway, 2001). The memory awareness or feeling state (the sense of the self in the past) signals to the rememberer the mental representation associated with itself, and is in fact the memory of an experience that has actually occurred, not a fantasy, dream, plan, or such other mental construction. When recollection is present, the probability that the remembered event was one that had been previously experienced is high.

As mentioned above, an episodic memory is not about encoding and retrieving simple information, but about remembering one's own past event in its integrative detail. In other words, an individual recalls not only an occurred (past) event, but also the particular objects, emotions or feelings, thoughts, and senses related to that event.

Due to the complex nature of this encoding and retrieving process, measuring episodic memory in an objective and

precise way is not an easy task.

The assessment of episodic memory through testing for time and place according to the externally generalized definition of episodic memory may seen objective enough, but this experimental paradigm does not accurately assess episodic memory in its entirety. If episodic is simply defined as memory of time and place, the measuring of the retrieval of such can be in turn thought of as measuring episodic memory. It is difficult to say, however, that this method accurately measures episodic memory according to its correct definition.

The first aim of this study is to analyze the various detailed aspects of episodic memory in a more precise and objective way. Towards this purpose, for the present experiment the quality and quantity (feature, characteristic) of episodic memory will be evaluated by analyzing mental images projected on the brain when we recall an event.

Retrieval of episodic memory will vary depending on the quality (personal significance) and modality (period) of the event, as well as on the current state of the brain according to aging or head injury.

Numerous studies demonstrated that the decline of episodic memory is a major expression of cognitive impairment in the early stages of AD, and the brain regions known to regulate episodic memory actually coincides with those regions of which activities typically decrease in AD patients. Consequently, discovering the mechanisms of the decline of episodic memory caused by defective brain regions such as in the case of this neuro-degenerative disease is important not only for better elucidating the process of AD but also for that of normal aging. In fact, in the clinical setting it is critical to distinguish memory impairment typical of early stage AD from simple forgetfulness or false–dementia caused by

depression. In clinical practice, neuropsychological tests and neuro-imaging techniques such as MRI and PET are commonly used to diagnose AD. However, MRI and PET are used to clinically ascertain that patients have no brain infarction or extensive white matter hyperintensities or other types of dementia such as the stroke. Brain atrophy observed on the scan implies that the disease is moderated. Neuropsychological tests are useful tools in the diagnosis of AD, but their effectiveness is confounded by the influence of individual variables like education or intelligence, making their implementation somewhat limited for detecting AD in its early stage. There are also difficulties in distinguishing AD from false dementia caused often by depression because the only observable symptom for AD in its early stages is simple memory impairment.

In this study, the test of episodic memory is conducted with early-stage AD patients. Through a comparison of the encoding and retrieval process in both healthy elderly people and AD patients, the current study aims to understand the differences and characteristics of 'normal' and 'impaired' episodic memory. This study therefore tries also to discover differences and characteristics of the encoding and retrieval process of episodic memory between healthy elderly people and AD patients.

As noted, the retrieval of episodic memory is a complex process expressed through various dimensions of psychological behavior such as emotion and/or sensory modalities, as well as with diverse types of the images retrieved. In experiment 1, behaviors and phenomenon that are expressed in a complex fashion during the retrieval of episodic memory will be tested and analyzed. In experiment 2, the voice of the subjects is evaluated in order to assess the

level of the emotion related to episodic memory.
From the clinical perspective, findings from this study will contribute not only to establish better criteria or instruments for an early detection of AD in its early phase, but also towards the understanding of the normal evolution of episodic memory in normal aging. From the research perspective, these results may serve as more comprehensive and rigorous parameters to assess episodic memory in experimental settings.

Experiment 1

2.2. Method

2.2.1. Design

Performances in a diverse category of episodic memory are compared between patients with AD and healthy elderly controls. In this study, free recall of one's own past is assessed in each measurement in order to determine their relative importance in identifying persons at early stage of AD. In particular, the present study will observe the mental image of episodic memory.
In the first experiment, mental images of episodic memory emerged during retrieving tasks of memories of a day before, a week ago (previous week), a month ago (previous month), and the remote past will each be quantified and compared between groups. The features of the retrieval of episodic memory will be assessed and analyzed by investigating the following:

- retrieved emotions
- sensory modality involved in retrieval
- the color, position, and form of the mental image
- the position of the subject in the image
- images related to the event, retrieved objects

● the context of the image

2.2.2. Subjects

Subjects of this study comprised of 19 healthy elderly people and 21 patients with Alzheimer's disease (see table 2-1). Healthy elderly controls were volunteers recruited from the local community, and were all in good mental and physical health. Control subjects with a history of alcoholism, psychiatric illness, epilepsy, or cancer were excluded in order to eliminate the potential of including a person with cognitive symptoms of a dementing illness. 21 patients were in mild stages of AD in concordance with NINCDS-ADRDA and DSM-IV criteria, and were outpatients at KyungHee University Medical Centre. All subjects were between the ages of 55 and 70.

Table 2-1. Sample Characteristics

	Age	Sex	Education
Control (n = 19)	61.84 years SD = 3.74	Male: 9 Female: 10	11.26 years SD = 3.89
Patients (n = 21)	61.84 years SD = 5.2	Male: 10 Female: 21	9.19 years SD = 4.92

Subjects were administered two neuropsychological tests (K-DRS and MMSE-K). In addition, patients were examined by a neurologist and psychiatrist before entry into the study, and underwent MRI scanning to ascertain they had no focal abnormality such as stroke or Lewy body disease. The test was held at KyungHee University Medical Centre, and all subjects provided informed consent for study participation.

2.2.3. Materials

2.2.3.1. K-DRS (Korean-Dementia Rating scale)

The Dementia Rating Scale (DRS) [ages 55-89+ years] developed by Mattis (1988) measures cognitive functioning at lower ability levels and can also be used to track changes in cognitive status for adults with cortical impairment, particularly that of the degenerative type. The DRS is very useful in the assessment and progression of dementia of Alzheimer's, vascular dementia, Parkinson's disease, Huntington's disease, age-related dementia in mental retardation, and Down's syndrome.

Table 2-2. K-DRS and MMSE

	GROUP	N	Mean	SD	SE	P-Value
Attention	HEP	19	35.684	.8852	.2031	*
	AD	21	33.952	2.6358	.5752	
Initiation/ Preservation	HEP	19	33.737	3.3968	.7793	
	AD	21	31.429	5.0850	1.1096	
Construction	HEP	19	5.89	.315	.072	*
	AD	21	5.05	1.499	.327	
Conceptualization	HEP	19	36.737	1.7270	.3962	**
	AD	21	33.857	3.9659	.8654	
Memory	HEP	19	23.474	1.5409	.3535	***
	AD	21	16.952	3.5281	.7699	
Total	HEP	19	135.5263	4.91447	1.12746	***
	AD	21	121.2857	9.74240	2.12597	
MMSE-K	HEP	19	27.895	1.2865	.2951	***
	AD	21	23.190	3.6279	.7917	

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

HEP (Healthy Elderly People) indicates Healthy controls

AD (Alzheimer's Disease) indicates the patients

The five DRS subscales provide additional information on

five specific abilities: Attention (8 items), Initiation/Preservation (11 items), Construction (6 items), Conceptualization (6 items), Memory (5 items). The maximum score is 140. Any score of 106 or lower is indicative of the suspect of dementia. The tasks can be easily administered individually and are scored from 15 to 45 minutes. In the experiment, the K-DRS validated by Choi (1998) was utilized. Results in table 2-2 indicated that healthy controls performed better than AD patients in the total score, especially in memory.

2.2.3.2. MMSE-K (Mini Mental State Examination-Korean)

The Mini Mental State Examination – Korean Version (MMSE-K) (Kwon & Park, 1989) is a brief and widely used instrument to assess cognitive mental status for adults (ages 18 and older). The MMSE has been used to detect impairment in the clinical setting. It has also been used as a research tool of screening for cognitive disorders in epidemiological studies. This brief 11-item measure tests five areas of cognitive functions: orientation, registration, attention and calculation, recall, and language. The maximum score is 30. The score of 23 or lower is indicative of cognitive impairment. Administration of MMSE takes only 5-10 minutes. In the result, healthy elderly people performed significantly better than AD patients.

2.2.3..3. Picture and Film

Pictures and a short film were used as examples for helping with understanding the procedure of the experiment. The pictures were of a wedding, war, and birthday party, and daily photos (see appendix I). The short film contained the sounds and the movement of a child, showed to illustrate the mental image of a retrieved event.

2.2.3.4. Question List of Episodic Memory Interview

Questions were constructed for assessing the elements of episodic memory (See Appendix II). For example, this experiment analyzes and evaluates the color and the feeling of an image of episodic memory. The experimenter gives some formed questions for each element to the subject. Questions were constructed toward checking out all elements of episodic memory, and this helps the experimenter for performing the test. However, the experimenter does not need to read out the exact questions. The experimenter can change the question in order to help the subject understand better in the context of each element.

2.2.4. Procedure

The subjects are informed about the procedure of test. The experimenter explains how to recall an event with the prepared picture and a short film and what the subjects will be asked during the test. Pictures of the wedding, the war, and the birthday party, and a daily photo of no significance and the short film containing the sounds and the movement of a child are showed to explain the mental image of a retrieved event. Both color and black and white photos were prepared and showed. The subjects were then asked to retrieve his/her first memory of the previous day and/or week without any cues (free recall). The subjects were instructed to record by themselves the entire context of the interview and are informed that they will be asked to retrieve it the following day. In the experiment, the experimenter measures latency to response and the duration and sequence of response by a stopwatch chronometer. An MP3 player records verbal response during the test. The experimenter asks them to tell everything that they remember about/in an image according

questions, which are designed for measuring diverse categories of memory retrieval. For example, “Did you smell or hear something?”, “How did you feel at smell?” and/or “How were you?” The subjects are then asked to retrieve other memories in the same way. On the following day, subjects are tasked to recall all contexts that they were able to remember in the telephone interview. The content of the response will be interpreted by category, time order and number of image, congruence etc. and can be marked for frequency for each category on the prepared table and then calculated for percentage of frequency.

2.2.5. Data Analysis

The data were analyzed using Statistical Package for the Social Sciences (SPSS version 11.0.). Scores between two groups in different tasks were compared using independent t-tests and the chi-square test according to the way of the quantifying. Statistical significance was set at $p < .05$ (two-tailed). Scores between four different categories of memory (yesterday, week, month, and remote) were compared using one-way ANOVA and consequently post-hoc test.

2.3. Results

2.3.1. Time

The total duration of the interview was measured, from when the first question was given to when the subject answered the last question. Latency is measured from the end of the question to the first reaction to the question. An independent t-test compared means between two groups.

Table 2-3. Total duration and Latency

	GROUP	N	Mean	SD	S	P-value
Total Duration	HEP	19	1149.1411	287.60428	65.98095	
	AD	21	1314.5043	334.99521	73.10195	
Latency Yesterday	HEP	19	4.2342	3.93253	.90219	*
	AD	21	11.5405	13.74662	2.99976	
Latency Week	HEP	19	8.4279	9.49945	2.17932	
	AD	17	13.8776	15.06137	3.65292	
Latency Month	HEP	18	10.1428	8.43270	1.98761	
	AD	8	9.3888	10.15943	3.59190	
Latency Rmote	HEP	19	4.1637	3.55566	.81572	**
	AD	20	9.1575	6.37846	1.42627	

* $p < .05$, ** $p < .01$.
HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

As in figure 2-1, the AD patient's group took more time to perform this test than healthy elderly people, but this is not a significant result statistically (See table 2-3).

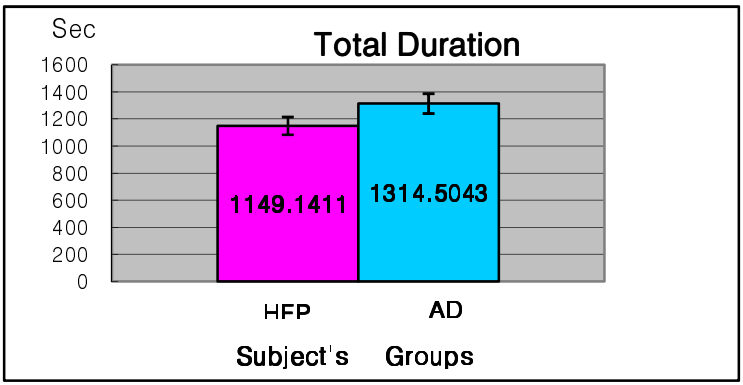

Figure 2-1. Mean (±SE) total duration of interview in Alzheimer's disease and Healthy elderly people.
HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

AD patients took more latency in yesterday (p = .029 < .05) and remote memory (p = .005 < .01) significantly than healthy elderly people (See table 2-3 and fig 2-2).

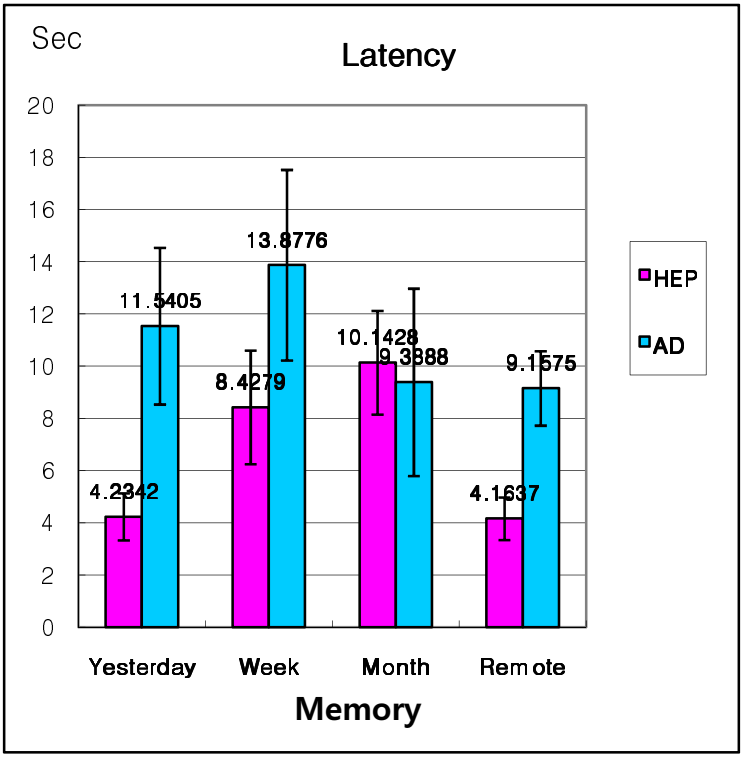

Figure 2-2. Mean (±SE) Latency in Alzheimer's disease and Healthy elderly people.
HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

2.3.2. Number of Images

This measurement is for evaluating the quantity of the retrieval of episodic memory. The number of the retrieved mental images are quantified and then compared between groups by using an independent t-test. In the retrieval of a week ago and a month ago, the experiment checked only that the subject was able to retrieve an event or not. Once the subject retrieved more than an event spontaneously, the experimenter does not interrupt, and at the same time, the experimenter does not demand to retrieve more events. An independent t-test compared means between two groups. The retrieved mental images were quantified. The mean between two groups was compared in total Number of, and different categories of the memory using an independent t-test. The mean of the patients' group from all categories was lower significantly than health elderly people (HEP). An in Fig., this result is caused by the low level of retrieval in episodic memory in AD patients.

Table 2-4 Number of Images

	GROUP	N	Mean	SD	SE	P-value
Total	HEP	19	20.368	3.2009	.7343	**
	AD	21	12.619	3.4420	.7511	
Yesterday	HEP	19	8.789	1.0317	.2367	**
	AD	21	5.333	1.8797	.4102	
Week	HEP	19	3.05	1.268	.291	**
	AD	21	1.48	1.078	.235	
Month	HEP	19	1.79	.855	.196	**
	AD	21	.43	.598	.130	
Remote	HEP	19	6.74	1.628	.373	*
	AD	21	5.38	1.962	.428	

* $p < .05$, ** $p < .001$.
HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

The number of images in episodic memory is shown Figure 2-3. In total Nr (p = .000 < .001) and four different categories memory, yesterday (p = .000 < .001), week (p = .000 < .001), month (p = .000 < .001), and remote (p = .023 < .05), there are significant mean differences between AD patient and controls (See Table 2-4).

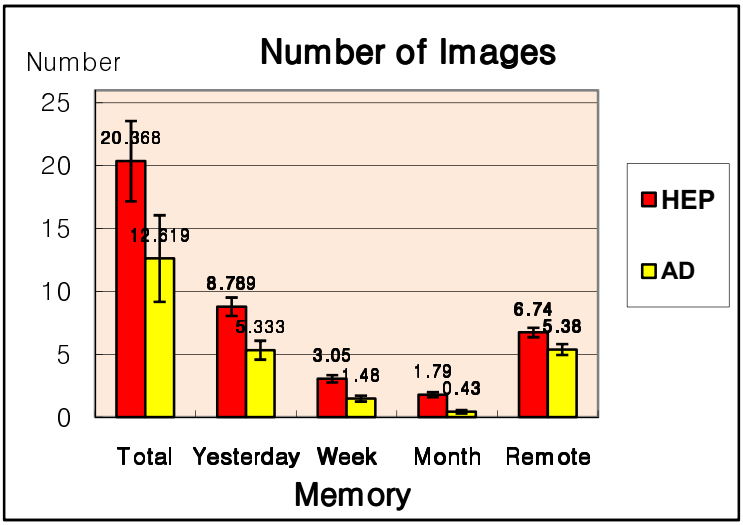

Figure 2-3. Mean (±SE) Number of images in Alzheimer's disease and Healthy elderly people.
HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

The frequency of recall ability is assessed. Recall ability means that the subject can recall an event during retrieving tasks of memories of a day before, a week ago, a month ago and remote past.

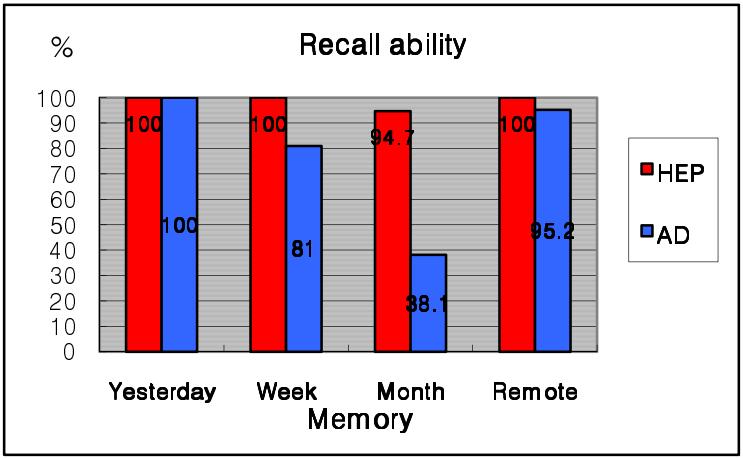

Figure 2-4. Frequency for recall ability in Alzheimer's disease and Healthy elderly people.

HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

The frequency of the subjects is quantified, and then compared between groups by using a chi-square test. The results of recall ability are shown in Figure 2-4. As noted in Fig.2-4, recall ability of the AD group is lower significantly in week ($p < .05$) and month ($p < .001$) episodic memory than controls (See Table 2-5).

Table 2-5 Recall ability

		Value	Df	Asymp. Sig. (2-sided)
Yesterday AD patients (N=21) HEP (N=19)	Pearson Chi-Square			
	N of Valid Cases	40		
Week AD patients (N=21) HEP (N=19)	Pearson Chi-Square	4.021[b]	1	.045
	Likelihood Ratio	5.556	1	.018
	Linear-by-Linear Association	3.921	1	.048
	N of Valid Cases	40		
Month AD patients (N=21) HEP (N=19)	Pearson Chi-Square	14.067[c]	1	.000
	Likelihood Ratio	16.050	1	.000
	Linear-by-Linear Association	13.715	1	.000
	N of Valid Cases	40		
Remote AD patients (N=21) HEP (N=19)	Pearson Chi-Square	.928[d]	1	.335
	Likelihood Ratio	1.312	1	.252
	Linear-by-Linear Association	.905	1	.342
	N of Valid Cases	40		

a. No statistics are computed because Yesterday is a constant.
b. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.90.
c. No cell (.0%) has expected count less than 5. The minimum expected count is 6.65.
d. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .48.

2.3.3. Episodic Memory Retrieval on the Following day

This section was constructed for evaluating the abilities of encoding and retrieval anterograde episodic memory by quantifying of mental images, which the subject can recall on the following day from mental images, which are retrieved

during the interview.

Table 2-6 Following day

	GROUP	N	Mean	SD	SE	P-value
TOTAL	HEP	19	.9311	.07716	.01770	**
	AD	21	.3433	.30578	.06673	
Yesterday	HEP	19	.9200	.11363	.02607	**
	AD	21	.3524	.31824	.06945	
Week	HEP	19	.8947	.25574	.05867	*
	AD	17	.4412	.58316	.14144	
Month	HEP	17	.9512	.14106	.03421	*
	AD	8	.2500	.46291	.16366	
Remote	HEP	19	.9621	.09396	.02156	**
	AD	20	.3520	.33706	.07537	

* $p < .01$, ** $p < .001$.
HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

At the beginning of the interview, the subjects are informed that they have to memorize the context of the interview and to recall again to tomorrow (the next day of interview). The base rate of 100 is the total number of the mental images which are retrieved in the previous day (during the interview) and then the number of the mental images retrieved in the following day is calculated for percentage. An independent t-test compared means between two groups.

Following day as retrieval of anterograde episodic memory is shown in Figure 2-5. Healthy elderly people performed significantly better in all four categories (yesterday, $p = .000 < .001$; week, $p = .007 < .01$; month, $p = .003 < .01$; remote, $p = .000 < .001$) and total score ($p = .000 < .001$) than AD patients.

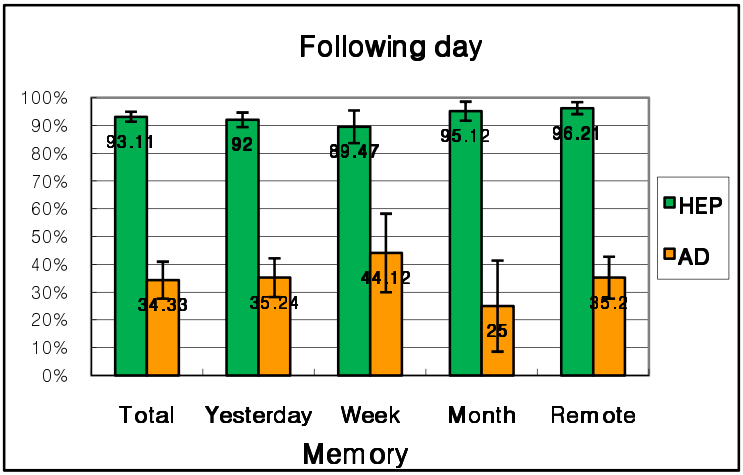

Figure 2-5. Mean (±SE) following day in Alzheimer's disease and Healthy elderly people.

HEP (Healthy Elderly People) indicates Healthy controls

AD (Alzheimer's Disease) indicates the patients

2.3.4. Time Order Memory

This section assesses the subject's capability to recall mental images in time order. In the experiment, the subjects are tasked to first recall an image at the time without time order. And then the subjects are asked to recall the mental images in time order from waking up to going to sleep including the mental images retrieved in the previous task. The time order memory is estimated only in yesterday memory. The frequency of the subjects is quantified, and then compared between groups using a chi-square test.

Table 2-7 Time order memory

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	15.510[b]	1	.000		
Continuity Correction[a]	12.908	1	.000		
Likelihood Ratio	20.187	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	15.122	1	.000		
N of Valid Cases	40				

a. Computed only for a 2x2 table

b. 0 cell (.0%) has expected count less than 5. The minimum expected count is 5.70.

There are significant results in time order memory (See Fig. 2-6). The control group performed significantly better than AD patients (p = .000 < .001). These effects indicate that time order memory declines in the early stage of AD.

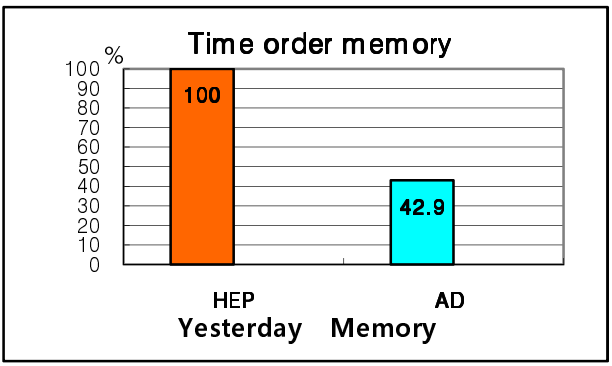

Figure 2-6 Frequency for time order memory in AD patients and Healthy elderly people

HEP (Healthy Elderly People) indicates Healthy controls

AD (Alzheimer's Disease) indicates the patients

2.3.5. Details

This part evaluates subjects' recollection of an event in coherence and detail, and sees whether they can describe the event logically with consideration for what comes before and after the events. The subjects are tasked to describe the event according to 5W1H (When, where, what, who, why, and how).

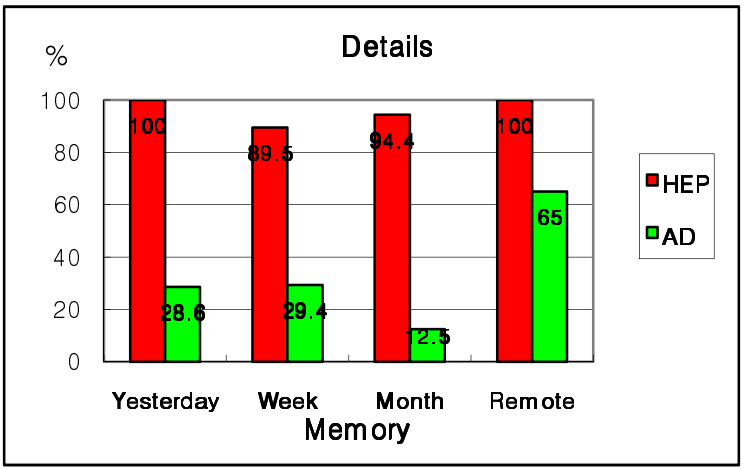

Figure 2-7 Frequency for Details in AD patients and Healthy elderly people

HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

Table 2-8 Details

		Value	df	Asymp. Sig. (2-sided)
Yesterday	Pearson Chi-Square	21.714[a]	1	.000
	Likelihood Ratio	27.798	1	.000
AD patients (N=21)	Linear-by-Linear Association	21.171	1	.000
HEP (N=19)	N of Valid Cases	40		
Week	Pearson Chi-Square	13.619[b]	1	.000
	Likelihood Ratio	14.730	1	.000
AD patients (N=17)	Linear-by-Linear Association	13.241	1	.000
HEP (N=19)	N of Valid Cases	36		
Month	Pearson Chi-Square	17.459[c]	1	.000
	Likelihood Ratio	18.344	1	.000
AD patients (N=8)	Linear-by-Linear Association	16.787	1	.000
HEP (N=18)	N of Valid Cases	26		
Remote	Pearson Chi-Square	8.105[d]	1	.004
	Likelihood Ratio	10.810	1	.001
AD patients (N=20)	Linear-by-Linear Association	7.897	1	.005
HEP (N=19)	N of Valid Cases	39		

a. 0 cell (.0%) has expected count less than 5. The minimum expected count is 7.13.
b. 0 cell (.0%) has expected count less than 5. The minimum expected count is 6.61.
c. 1 cell (25.0%) has expected count less than 5. The minimum expected count is 2.46.
d. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 3.41.

This is assessed in a way that the subject gets a point for every time the subject is able to describe the event completely according to those six questions. The frequency of the subjects is quantified, and then compared between groups by using a chi-square test. Details as a function of logical memory is shown Figure 2-7. In all four categories, there are

significant results. Healthy elderly people perform better than AD group in yesterday ($p = .000 < .001$), week ($p = .000 < .001$), month ($p = .000 < .001$), and remote ($p = .004 < .01$).

2.3.6. Event Related Memory

This measure assesses how to relate the retrieved mental images to the particular event between the categories of memory. In the yesterday memory, the mental images which are related to daily life events such as washing oneself, having a meal etc. are not included. In the remote memory, the mental images which are not related to a particular event and which are retrieved only as the image such as the house or the school where the subject lived/went to in childhood, are not included. The frequency of the subjects is quantified, and then compared between groups by using a chi-square test.

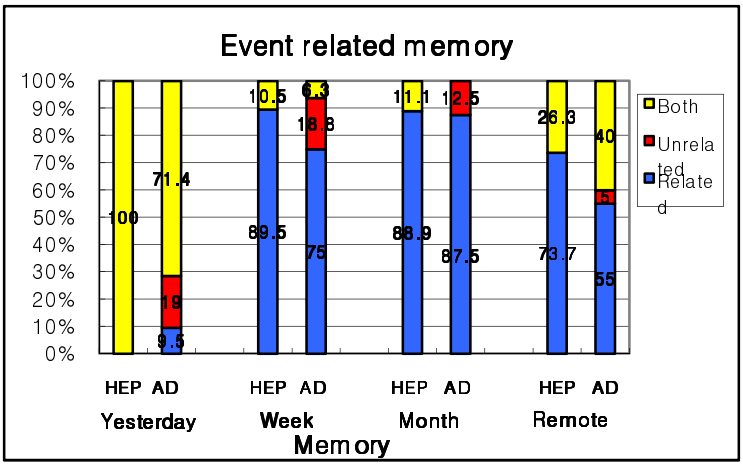

Figure 2-8 Frequency for Event related memory in AD patients and Healthy elderly people

HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

Table 2-9 Event related memory

		Value	df	Asymp. Sig. (2-sided)
Yesterday	Pearson Chi-Square	6.387[a]	2	.041
	Likelihood Ratio	8.689	2	.013
AD patients (N=21) HEP (N=19)	Linear-by-Linear Association	5.429	1	.020
	N of Valid Cases	40		
Week	Pearson Chi-Square	3.967[b]	2	.138
	Likelihood Ratio	5.108	2	.078
AD patients (N=16) HEP (N=19)	Linear-by-Linear Association	.242	1	.623
	N of Valid Cases	35		
Month	Pearson Chi-Square	3.140[c]	2	.208
	Likelihood Ratio	3.829	2	.147
AD patients (N=8) HEP (N=18)	Linear-by-Linear Association	.163	1	.687
	N of Valid Cases	26		
Remote	Pearson Chi-Square	2.028[d]	2	.363
	Likelihood Ratio	2.420	2	.298
AD patients (N=20) HEP (N=19)	Linear-by-Linear Association	1.131	1	.288
	N of Valid Cases	39		

a. 4 cells (66.7%) have expected count less than 5. The minimum expected count is .95.
b. 4 cells (66.7%) have expected count less than 5. The minimum expected count is 1.37.
c. 4 cells (66.7%) have expected count less than 5. The minimum expected count is .31.
d. 2 cells (33.3%) have expected count less than 5. The minimum expected count is .49.

As can be seen from Figure 2-8, both groups emerge with similar results in event related memory. Only in yesterday memory ($p = .041 < .05$), there is significant difference between two groups. In the other categories of memory, there are no significant results (See table 2-9).

2.3.7. Color, Moving/stationary, and Subject's Position in the Image and Position of Image

In this section, features of the retrieved images are investigated. Specifically, the color of retrieved images (color or black and white), the nature of the image (whether they are a moving image like a movie or a stationary image like a photo).

Once the subject retrieves a mental image or an event, the subject is asked whether their mental image is colorful or B&W (black and white). When the subjects have difficulties understanding it, they are asked to retrieve the color of the objects and of the clothes of the person which/who is retrieved in the mental image and the color of the background of the mental image. This measure is marked as 'color', 'B&W' and 'Both'. The frequency of the subjects is quantified, and then compared between groups using a chi-square test.

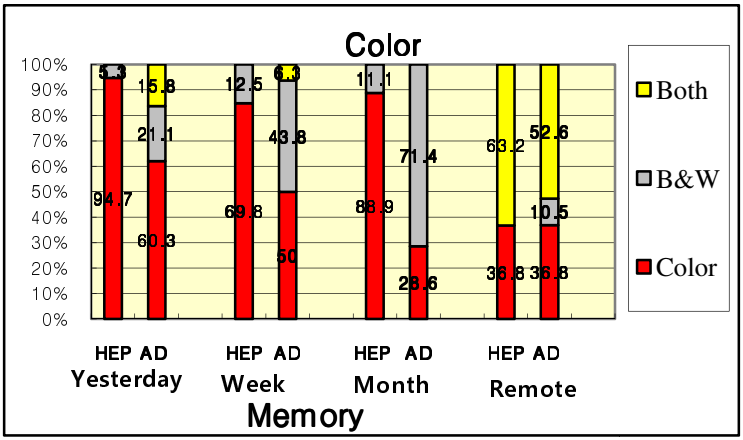

Figure 2-9 Frequency for colorful image in episodic memory in AD patients and Healthy elderly people

HEP (Healthy Elderly People) indicates Healthy controls

AD (Alzheimer's Disease) indicates the patients

Table 2-10 Color

		Value	Df	Asymp. Sig. (2-sided)
Yesterday	Pearson Chi-Square	6.000[a]	2	.050
	Likelihood Ratio	7.294	2	.026
AD patients (N=19)	Linear-by-Linear Association	5.709	1	.017
HEP (N=19)	N of Valid Cases	38		
Week	Pearson Chi-Square	9.156[b]	2	.010
	Likelihood Ratio	10.138	2	.006
AD patients (N=16)	Linear-by-Linear Association	8.397	1	.004
HEP (N=19)	N of Valid Cases	35		
Month	Pearson Chi-Square	9.095[c]	1	.003
	Likelihood Ratio	8.714	1	.003
AD patients (N=7)	Linear-by-Linear Association	8.732	1	.003
HEP (N=18)	N of Valid Cases	25		
Remote	Pearson Chi-Square	2.182[d]	2	.336
	Likelihood Ratio	2.955	2	.228
AD patients (N=19)	Linear-by-Linear Association	2.182	1	.736
HEP (N=19)	N of Valid Cases	38		

a. 4 cells (66.7%) have expected count less than 5. The minimum expected count is 1.50.
b. 4 cells (66.7%) have expected count less than 5. The minimum expected count is .46.
c. 1 cell (25.0%) has expected count less than 5. The minimum expected count is 1.96.
d. 2 cells (33.3%) have expected count less than 5. The minimum expected count is 1.00.

Results in color of the image are shown in Figure 2-9. As shown in Table 2-10, there are significant results in week (p = .01 < .05) and month (p = .003 < .01) between the two groups. In yesterday ((p = .05), there is considerable difference between two groups, but this is not significant statistically and there are no significant results in remote.

Table 2-11 Moving image

		Value	df	Asymp. Sig. (2-sided)
Yesterday	Pearson Chi-Square	17.597[a]	2	.000
	Likelihood Ratio	19.715	2	.000
AD patients (N=21) HEP (N=19)	Linear-by-Linear Association	12.417	1	.000
	N of Valid Cases	40		
Week	Pearson Chi-Square	18.137[b]	2	.000
	Likelihood Ratio	20.936	2	.000
AD patients (N=16) HEP (N=19)	Linear-by-Linear Association	1.709	1	.191
	N of Valid Cases	35		
Month	Pearson Chi-Square	4.787[c]	1	.029
	Likelihood Ratio	6.952	1	.008
AD patients (N=8) HEP (N=18)	Linear-by-Linear Association	4.609	1	.032
	N of Valid Cases	26		
Remote	Pearson Chi-Square	.174[d]	2	.916
	Likelihood Ratio	.176	2	.916
AD patients (N=20) HEP (N=19)	Linear-by-Linear Association	.014	1	.905
	N of Valid Cases	39		

a. 2 cells (33.3%) have expected count less than 5. The minimum expected count is 2.38.
b. 2 cells (33.3%) have expected count less than 5. The minimum expected count is 1.83.
c. 1 cell (25.0%) has expected count less than 5. The minimum expected count is 2.37.
d. 4 cells (66.7%) have expected count less than 5. The minimum expected count is 2.44.

In the nature of the mental image, the subjects are asked whether they can observe some movement in the image. If they had difficulties understanding this question, the experimenter asked them whether their image is like a film or a photo like the examples demonstrated in the beginning of

the interview. This measure is also marked 'moving', 'stationary' or 'both'. The frequency of the subjects is quantified, and then compared between groups using a chi-square test.

As Table 2-11 indicates, moving image as a feature (characteristic) of the retrieval of episodic memory emerged with significant result in yesterday (p = .000 < .001), week (p = .000 < .001), and month memory (p = .029 < .05), but there were no significant difference between two groups in remote memory (p = .916 > NS). Interestingly, both groups emerged with similar results in remote memory.

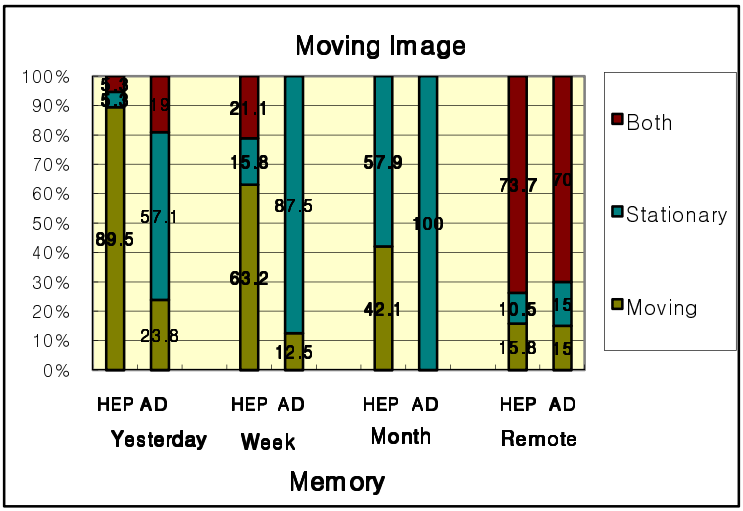

Figure 2-10 Frequency for Moving image in episodic memory in AD patients and Controls

HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

The retrieved position of the mental image is assessed. The

subjects are asked to indicate the position of the mental image, and also the experimenter observes where the subject gazes at during the retrieval. The position is classified as the front, right, left, upper, under, and panoramic round the subject as a center. The panoramic means that a mental image surrounds the subject; in this case, the subject reproduces the mental image indicating the objects in the image from him/herself. The frequency of the subjects is quantified, and then compared between groups using a chi-square test.

Table 2-12 Subject's Position in the image

		Value	df	Asymp. Sig. (2-sided)
Yesterday	Pearson Chi-Square	2.000[a]	2	.368
AD patients (N=19)	Likelihood Ratio	2.773	2	.250
HEP (N=19)	Linear-by-Linear Association	.204	1	.651
	N of Valid Cases	38		
Week	Pearson Chi-Square	2.889[b]	1	..089
AD patients (N=14)	Likelihood Ratio	3.606	1	.058
HEP (N=19)	Linear-by-Linear Association	2.802	1	..094
	N of Valid Cases	33		
Month	Pearson Chi-Square	10.286[c]	1	.001
AD patients (N=6)	Likelihood Ratio	9.767	1	.002
HEP (N=18)	Linear-by-Linear Association	9.857	1	.002
	N of Valid Cases	24		
Remote	Pearson Chi-Square	5.478[d]	1	.065
AD patients (N=20)	Likelihood Ratio	6.043	1	.049
HEP (N=19)	Linear-by-Linear Association	1.350	1	.245
	N of Valid Cases	39		

a. 4 cells (66.7%) have expected count less than 5. The minimum expected count is .50.
b. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .85.
c. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .75.
d. 4 cells (66.7%) have expected count less than 5. The minimum expected count is 2.92.

The position of the subject is investigated in the mental image. It observed that in the mental image, the subject is an actor or an observer in the mental image. If the subjects had difficulty understanding it, the experimenter asked them whether they could see themselves in the image or whether they were looking at the image. The frequency of the subjects is quantified, and then compared between groups using a chi-square test.

The subject's position in the image as a feature of the retrieval of episodic memory is reported in table 2-12. There was significant difference statistically between two groups only in month memory ($p = .001 < .01$). This phenomenon will be considered again in the discussion.

As Figure 2-11 indicates, however, we can note a very interesting phenomenon in the differences of the frequency between two groups that rise gradually going back to the past.

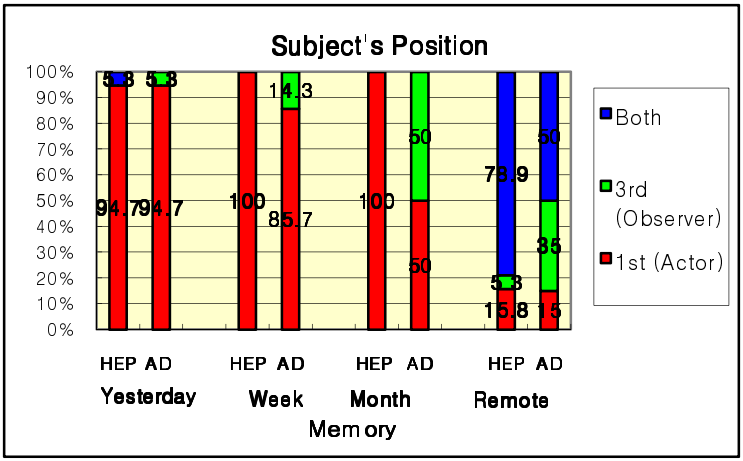

Figure 2-11 Frequency for Subject's Position in the image in episodic memory in AD and Controls

HEP (Healthy Elderly People) indicates Healthy controls

AD (Alzheimer's Disease) indicates the patients

2.3.8. Objects in the Image

The people, objects, building, and/or place that is recalled in the mental image are investigated. They are observed in the verbal responses of the subject.

The total number of all objects retrieved in the metal image is first estimated without reference to the kind of object. Means between the two groups were compared using an independent t-test.

Table 2-13 Number of Object

	GROUP	N	Mean	SD	SE	P-value
Yesterday	HEP	19	6.632	1.4985	.3438	**
	AD	21	3.762	1.6403	.3579	
Week	HEP	19	3.11	1.197	.275	
	AD	16	3.00	1.549	.387	
Month	HEP	18	2.56	1.199	.283	
	AD	8	2.00	1.604	.567	
Remote	HEP	19	5.47	.841	.193	*
	AD	21	4.38	1.532	.334	

* $p < .01$,* * $p < .001$

HEP (Healthy Elderly People) indicates Healthy controls

AD (Alzheimer's Disease) indicates the patients

Number of Object as a function of the retrieval of episodic memory emerged from Table 2-13. As Figure 2-12 indicates, Healthy elderly people retrieved more objects in yesterday (p = .000 < .001), and remote memory (p = .008 < .01) than AD patients. There were no significant differences in week and month. This may be caused by which the subject was tasked to recall one or two particular events, as well as, did not recall many episodic images like the memory of yesterday and remote.

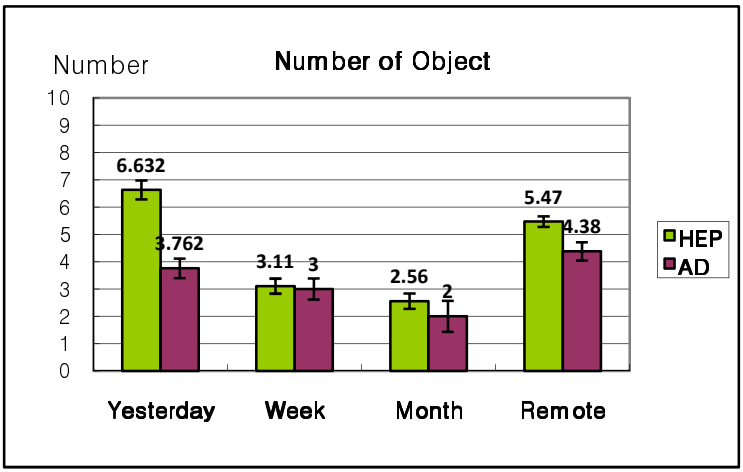

Figure 2-12. Mean (±SE) Number of Object in Alzheimer's disease and Healthy elderly people.

HEP (Healthy Elderly People) indicates Healthy controls

AD (Alzheimer's Disease) indicates the patients

2.3.9. Context in the Image

The context is analyzed by classifying according to the content of the events, for example, events related to relationships, the death/birth of an important person or the Korean War. The frequency of the subjects in each sort is quantified, and then compared between groups using a chi-square test.

Context of the image as a feature of the retrieval of episodic memory emerged from Table 2-14. Interestingly, these results concern more with the comparison between memory of yesterday and remote than between groups. It means that the histograms in Figure 2-13 demonstrate different forms of the distribution in memory of yesterday and remote.

Table 2-14 Context of the image

	Context	HEP	AD Patients	P-value
Yesterday AD patients (N=21) HEP (N=19)	Trip	36.8%	19%	
	Meeting	63.2%	57.1%	
	Work	57.9%	47.6%	
	Family event	10.5%	4.8%	
	Health	5.3%	23.8%	
	Human relationship	31.6%	-	*
	Daily life	100%	57.1%	*
Remote AD patients (N=20) HEP (N=19)	Trip	15.8%	15%	
	Meeting	5.3%	5%	
	Work	36.8%	50%	
	Family event	15.8%	20%	
	Human relationship	31.6%	35%	
	K-war	84.2%	65%	*
	Unmean. Ima.	31.6%	45%	
	Negative event	47.4%	45%	
	Bir. of fam. Mem.	15.8%	20%	
	Personal	%	-	

* $p < .01$,* * $p < .001$

HEP (Healthy Elderly People) indicates Healthy controls

AD (Alzheimer's Disease) indicates the patients

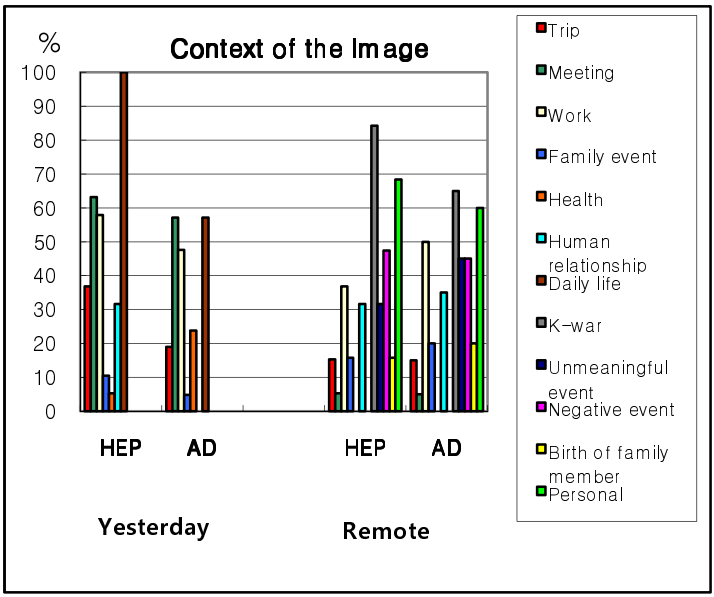

Figure 2-13. Frequency for Context of the image in Alzheimer's disease and Healthy elderly people.
HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

2.3.10. Emotion

The emotion in experiment 1 is to investigate which emotion is more recalled and related during the retrieval of episodic memory. In the experiment, the six basic emotions (happiness, anger, fear, sadness, surprising and disgust) are defined in accordance to Ekman, Friesen and Ellsworth (1972). Once the subject retrieves a mental image or an event, he/she is tasked to respond how he/she felt in the image. Once an emotion, which consists of context of the mental image, is observed, it is also marked. According to theory, happiness is included all positive emotion such as joy and calm, and anxiety,

aggression, and fatigue are marked as fear. The frequency of the subjects in each emotion is quantified, and then compared between groups by using a chi-square test.

Table 2-15 Emotions

	Emotion	AD	HEP	P-value
Yesterday AD patients (N=21) HEP (N=19)	Happy	76.2%	89.5%	
	Anger	9.5%	31.6%	
	Fear	9.5%	57.9%	*
	Sadness	14.3%	5.3%	
	Surprising	-	5.3%	
	Disgusting	-	5.3%	
Week AD patients (N=17) HEP (N=19)	Happy	64.7%	57.9%	
	Anger	5.9%	31.6%	
	Fear	23.5%	36.8%	
	Sadness	5.9%	10.5%	
	Surprising	-	-	
	Disgusting	-	-	
Month AD patients (N=8) HEP (N=18)	Happy	62.5%	38.9%	
	Anger	-	38.9	*
	Fear	12.5%	22.2%	
	Sadness	-	22.2%	
	Surprising	-	-	
	Disgusting	-	-	
Remote AD patients (N=20) HEP (N=19)	Happy	80%	73.7%	
	Anger	15%	21.1%	
	Fear	75%	78.9%	
	Sadness	60%	68.4%	
	Surprising	-	21.1%	*
	Disgusting	-	5.3%	

* $p < .05$.

HEP (Healthy Elderly People) indicates Healthy controls

AD (Alzheimer's Disease) indicates the patients

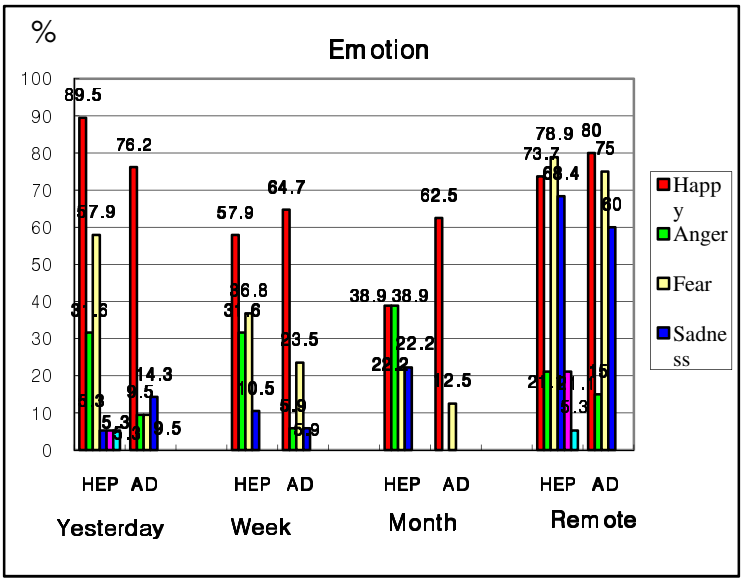

Figure 2-14. Frequency for emotion in Alzheimer's disease and Healthy elderly people.

HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

Figure 2-14 is shows the frequency for retrieved emotion in episodic memory. There are significant differences statistically in fear of yesterday ($p = .001 < .01$), anger of month ($p = .039 < .05$) and surprise of remote ($p = .030 < .05$) between the two groups (See table 2-15). Healthy elderly people recall more multiple emotions than AD patients. However, in the memory of remote, both groups demonstrate similar form in the histogram (See Figure 2-14). Happiness is recalled more easily in all four categories of memory and also in both groups.

2.3.11. Sensory Modality

In this part, five different sensory modalities related to the retrieved mental image are evaluated. Once the subject retrieves a mental image or an event, the subjects are asked which sensory modality is retrieved for each mental image. This is estimated by which sensory modality is more recalled in the four different memory categories during the episodic memory retrieval. The frequency of the subjects in each sensory modality is quantified, and then compared between groups by using a chi-square test.

Table 2-16 Sensory modalities

Memory	Sensory modality	AD	HEP	P-value
Yesterday AD patients (N=21) HEP (N=19)	Vision	100%	100%	
	Audition	47.6%	73.7%	
	Olfaction	28.6%	42.1%	
	Taste	38.1%	63.1%	
	Tactile	9.5%	15.8%	
Week AD patients (N=17) HEP (N=19)	Vision	94.1%	100%	
	Audition	23.5%	31.6%	
	Olfaction	-	10.5%	
	Taste	11.8%	15.8%	
	Tactile	11.8%	5.3%	
Month AD patients (N=8) HEP (N=18)	Vision	88.9%	100%	
	Audition	11.1%	22.1%	
	Olfaction	-	5.6%	
	Taste	-	16.7%	
	Tactile	11.1%	-	
Remote AD patients (N=20) HEP (N=19)	Vision	100%	100%	
	Audition	65%	57.9%	
	Olfaction	5%	5.3%	
	Taste	10%	10.5%	
	Tactile	30%	10.5%	

* $p < .05$.

HEP (Healthy Elderly People) indicates Healthy controls

AD (Alzheimer's Disease) indicates the patients

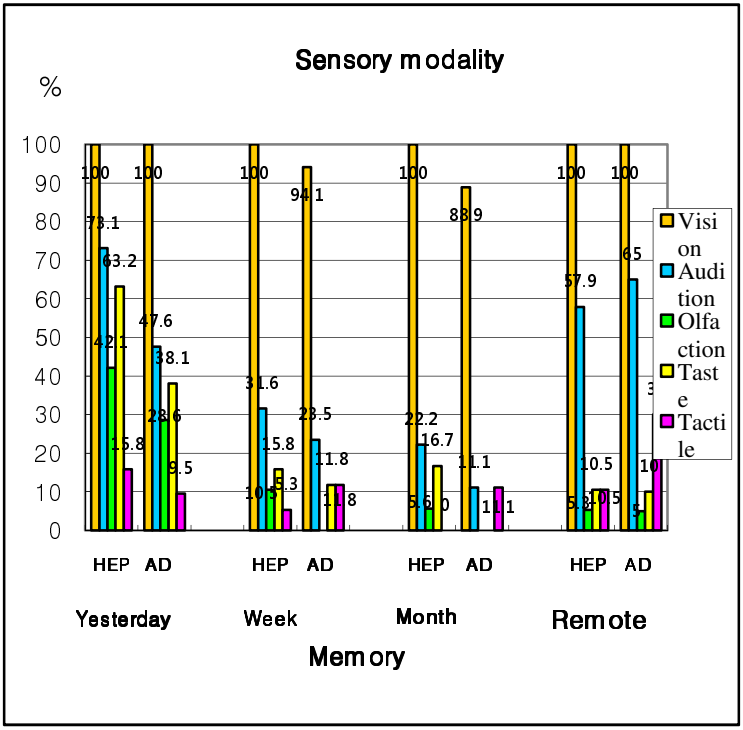

Figure 2-15. Frequency for Sensory modalities in Alzheimer's disease and Healthy elderly people.

HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

As shown in Table 2-16, there are no significant frequency differences between two groups. Considering sensory modality as a feature of the retrieval of episodic memory, vision is markedly recalled in yesterday, week, month and remote of memory. Secondly, the audition is recalled especially in yesterday and remote memory. Interestingly,

olfaction and tactile sensation recall well in memory of yesterday, but they decreased considerably in memory of remote (See Figure 2-15).

2.4. Factorial Analysis

A two-way ANOVA was used for factorial analysis. Post-hoc test was performed by Scheffe and Duncan. ANOVA is performed in Number of Image between sex, group and four different categories of memory (yesterday, week, month, and remote), in latency and following between group and memory.

2.4.1. Number of Images

As in Table 2-17, there are significant effects in Number of Image between sex and group, and between sex, group and memory. ANOVA is designed as 2x2 (sex x group) and 2x4 (group x memory)

Table 2-17 Tests of Between-Subjects Effects in Number of Image

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.
Corrected Model	1176.924	15	78.462	40.910	.000
Intercept	2695.238	1	2695.238	1405.316	.000
SEXGROUP	150.280	2	75.140	39.179	.000
SEXGROUP * memory	32.211	6	5.368	2.799	.013
Error	276.176	144	1.918		
Total	4110.000	160			
Corrected Total	1453.100	159			

a R Squared = .810 (Adjusted R Squared = .790)

Table 2-18 shows results of the ANOVA post-hoc test (Scheffe) from two groups and from the different genders in memory of week. Table 2-18 indicates that there are significant mean differences from the two groups, but not from sex difference in the homogeneous group in the four different memories.

Table 2-18 Mean difference between sex and group

(I) SEX GROUP	(J) SEX GROUP	MD (I-J)	SE	Sig.
Female control	**Male control**	.2278	.31815	.916
	Female AD	1.8136*	.30255	.000
	Male AD	2.3000*	.30967	.000
Male control	**Female control**	-.2278	.31815	.916
	Female AD	1.5859*	.31123	.000
	Male AD	2.0722*	.31815	.000
Female AD	**Female control**	-1.8136*	.30255	.000
	Male control	-1.5859*	.31123	.000
	Male AD	.4864	.30255	.463
Male AD	**Female control**	-2.3000*	.30967	.000
	Male control	-2.0722*	.31815	.000
	Female AD	-.4864	.30255	.463

Based on observed means.
* The mean difference is significant at the .05 level.

Consequently, four different groups are subset homogeneously in two groups from the group difference without reference to sex difference, as in Duncan and Scheffe (See Table 2-19).

Table 2-19 Homogeneous subsets of Number of image in different sex and group

	SEXGROUP	N	Subset 1	2
Duncan	**Male AD**	40	2.9000	
	Female AD	44	3.3864	
	Male control	36		4.9722
	Female control	40		5.2000
	Sig.		.119	.464
Scheffe	**Male AD**	40	2.9000	
	Female AD	44	3.3864	
	Male control	36		4.9722
	Female control	40		5.2000
	Sig.		.486	.910

Means for groups in homogeneous subsets are displayed. Based on Type III Sum of Squares The error term is Mean Square(Error) = 1.918.

a Uses Harmonic Mean Sample Size = 39.799.

b The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed.

c Alpha = .05.

2.4.2. Latency

Table 2-20 is shown the results of ANOVA in latency. ANOVA is designed as 2x4 (group x memory) in latency. There are no significant effects between groups and between memories.

Table 2-20 Tests of Between-Subjects Effects in Latency

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.
Corrected Model	970.915	7	138.702	1.451	.190
Intercept	10645.628	1	10645.628	111.367	.000
GROUP	11.959	1	11.959	.125	.724
GROUP * Memory	530.498	3	176.833	1.850	.141
Error	12713.524	133	95.590		
Total	24568.131	141			
Corrected Total	13684.439	140			

a R Squared = .071 (Adjusted R Squared = .022)

Table 2-21 reports a mean difference between four different categories of memory as the Scheffe post-hoc test. There are no significant mean differences between memories in both groups. It means that latency is not influenced by time of the past.

Table 2-21 Mean difference between sex and group

		AD Patients			Controls		
(I) Memory	(J) Memory	MD (I-J)	SE	Sig.	MD (I-J)	SE	Sig.
Yesterday	Week	-3.1145	3.42754	.843	-2.4333	2.48035	.810
	Month	3.0200	3.87144	.894	-6.8973	2.63113	.088
	Remote	3.2705	3.38548	.817	-.7863	2.40438	.991
Week	Yesterday	3.1145	3.42754	.843	2.4333	2.48035	.810
	Month	6.1345	3.90827	.487	-4.4640	2.72950	.451
	Remote	6.3850	3.42754	.333	1.6469	2.51165	.934
Month	Yesterday	-3.0200	3.87144	.894	6.8973	2.63113	.088
	Week	-6.1345	3.90827	.487	4.4640	2.72950	.451
	Remote	.2505	3.87144	1.000	6.1110	2.66065	.165
Remote	Yesterday	-3.2705	3.38548	.817	.7863	2.40438	.991
	Week	-6.3850	3.42754	.333	-1.6469	2.51165	.934
	Month	-.2505	3.87144	1.000	-6.1110	2.66065	.165

Interestingly, and only in control group, the memory of yesterday and week is subset in a homogeneous group according to Duncan, but not to Scheppe (See Table 2-22).

Table 2-22 Homogeneous subsets of Latency in different sex and group

		AD Patients		Healthy elderly people		
		N	Subset	N	Subset	
	Memory		1		1	2
Duncan	Remote	21	6.6595	19	6.0142	
	Month	13	6.9100	18	6.8006	
	Yesterday	21	9.9300	16	8.4475	8.4475
	Week	20	13.0445	13		12.9115
	Sig.		.116		.378	.088
Scheffe	Remote	21	6.6595	19	6.0142	
	Month	13	6.9100	18	6.8006	
	Yesterday	21	9.9300	16	8.4475	
	Week	20	13.0445	13	12.9115	
	Sig.		.391		.077	

Means for groups in homogeneous subsets are displayed. Based on Type III Sum of Squares The error term is Mean Square(Error) = 53.436 (HEP), Mean Square(Error) = 120.345 (AD).

a Uses Harmonic Mean Sample Size = 16.154 (HEP), 18.005(AD).

b The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed.

c Alpha = .05

2.4.3. Episodic Memory Retrieval on the Following day

Table 2-23 shows the results of ANOVA in latency. ANOVA is designed as 2x2 (Sex x group), 2x4 (group x memory) in following.

Table 2-23 Tests of Between-Subjects Effects in the Following day

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	12.789	15	.853	8.981	.000
Intercept	52.701	1	52.701	555.126	.000
GROUP	10.672	1	10.672	112.412	.000
DAY	.100	3	3.340E-02	.352	.788
SEX * GROUP	.106	1	.106	1.120	.292
GROUP * DAY	.306	3	.102	1.074	.363
SEX * GROUP * DAY	.711	3	.237	2.496	.063
Error	11.772	124	9.493E-02		
Total	86.167	140			
Corrected Total	24.561	139			

a R Squared = .521 (Adjusted R Squared = .463)

There are significant effects between groups and but not between memory of yesterday, week, month, and remote. Retrieval of the following day is performed to measure the anterograde memory. On the following day, the subject was tasked to recall the events before day of the interview. Therefore, there are no significant correlations between retrieving the recent memory and old memory. Consequently, four different groups are subset homogeneously in two groups from the group difference without reference to sex difference, as in Duncan and Scheffe.

2.5. Discussion

Over the years there have been many studies (Grober & Kawas, 1997; Bukner et al., 1998; Düzel et al., 1999; Smith et al., 2004) concerning the encoding, storage, and retrieval of episodic memory using methods of varying quality. This study attempts to gain new insight into the symptoms of early stage Alzheimer's disease by comparing episodic memory retrieval between AD patients and healthy elderly people. Tulving (1987) suggested that episodic memory is retrieved in our brain as an image as if we were replaying a picture or a movie (Fink et al., 1996). Episodic memory is encoded together with an experienced event with visual, auditory and olfactory input. What distinguishes the approach in this current study is that it investigates and analyzes the images of episodic memory that the subjects recalled themselves from their own experienced events in free recall conditions.

This study demonstrates significant impairment in the ability to recall the images of episodic memory in patients in the

early stages of AD compared to that of normal elderly volunteers. This impairment is made evident through Number of Image, recall ability and the ability to retrieve images recalled during the test on the following day of the interview. These results are consistent with the findings from previous studies (Grosse et al., 1991; Greene & Hodges, 1996; Thompson et al., 2003). These deficits, observed in patients with Alzheimer's disease, may contribute to social and behavior impairment.

In experiment 1, there are significant effects in the number of the images as a function of the retrieval ability of episodic memory between two groups. AD patients especially had great difficulty recalling in time order the images retrieved from the memory of yesterday, and of the general events of daily life.

As findings from previous studies suggest (Hodges et al., 1990; Thompson et al., 2003), AD patients had more problems in remembering the memory of yesterday (anterograde memory) than in the memory of remote events (retrograde memory). They particularly had great difficulty in recalling the memory of a week and a month, which also had significant effects statistically. After all, their memories which were encoded or saved after onset of the disease would have been destroyed. In the memory of yesterday, patients could remember some particular event, but had difficulty remembering daily life events and recalling in time order. Almost all patients recalled remote memories well. As suggested in many studies (Hodges et al., 1990; Cowles et al., 2003; Thompson et al., 2003), patients with AD have great problems in encoding, storing and retrieving new information. With consideration to their ability to retrieve saved information before onset, their ability of retrieval is impaired

later than that of encoding and storage. This finding is also supported by certain neuro-imaging studies (Fink et al., 1996; Buckner & Koutstaal, 1998), which report that the temporal lobe, hippocampus and peripheral-hippocampal areas play a very important role in explicit memory and that impairments in those areas occurs in the brains of AD patients (De Leon et al., 1989; George et al., 1990).

Remembering time (when) and place (where) is fundamental in episodic memory. In the test, patients with early stage AD had some remarkable difficulty recalling the time of their events and in arranging retrieved images in time order. According to findings from previous studies concerning the early stages of AD, patients often experienced losing their sense of direction and familiarity in places they had been too often. In the test, subjects were tasked to talk about the details of the retrieved images and also their context. The patients had more difficulty answering details related to retention of the memory of yesterday than of remote. And they had much more difficulty in memory of week and month.

The present study differs from previous studies in that it investigates features of retrieval of episodic memory by comparing a patient group with a control group. In the experiment, the color, movement, and position of the images, and the subject's perspective of the image is examined. Such a method may seem unorthodox as it has not been utilized often in previous research concerning episodic memory, but at the same time it should not seem too unfamiliar, considering how we remember our own past. Generally, our control group speaks for the features of the retrieval of episodic memory. The healthy elderly people recalled clear colors of the images and their images were moving like a movie in memory of yesterday. In the retrieval of remote memories, when they

recalled impressive events, they still reported such images, but also recalled some stationary and black & white images. The patients with AD had no great different features of the images in remote memories, but there were significant differences compared to controls. They recalled the color of images but in many cases, they recalled in stationary images, like pictures. In the memory of yesterday, almost all healthy elderly people recalled the panoramic images surrounding the subjects. Almost all healthy elderly people explained the image, reproducing the event as if they were within the image. This phenomenon was rarely found in the patients with AD. However, it cannot be said that recalling as an actor or observer is necessarily good either way, because both of these perspectives were featured in both AD and control groups. The patients also had some difficulty in performing and understanding this test, or it may depend on the context of the event.

This study also investigates the context of retrieved images for the reason of which episodic memory is related to a particular event. The control group took on different attitudes for the memory of yesterday and remote events. In the memory of yesterday, healthy elderly people remembered mostly daily life events, such as meeting people, work events, and human relationships. With remote memories, they retrieved mostly the Korean War, the death of family members and other such impressive events. The patients with AD had great difficulty recalling daily life events and they recalled more the events concerning their health and medication.

Episodic memory could be of a particular event experienced in the past. This memory is encoded together with emotion through the different sensory modalities, and then retrieved with the emotion of the event as well as the particular sensory

modality. For this reason, this study measures which emotion is retrieved more in the retrieval of episodic memory. Happiness was more salient in all four categories of memory and also in the patient and control groups. Hargrave and her colleagues (2002) suggested also that happiness is retrieved the most among the six different emotions. This result may look as if it suggests that patients with AD in early stages have no problem recognizing emotions according to the context of the retrieved image. However, the question is whether the patients are emotionalized themselves or not during the recall of episodic memory. Several studies suggested (Cadieux & Greve, 1997; Hargrave et al., 2002; Bucks & Radford, 2004) that early stages of AD are associated with impairments of emotional processing. This will be discussed in experiment 2.

As mentioned, episodic memory is retrieved with visual images, and therefore it is within its nature to recall vision. As shown in Figure 2-16, retrieval of sensory modalities came up with similar results between the two groups. In particular, vision and audition were retrieved more in all four different categories of memory. It says that these two sensory modalities are more important in encoding and retrieval and that we use more of them for long-term memory. Interestingly, olfaction and taste are retrieved well in the memory of yesterday, but not of remote events. These two sensory modalities are encoded by a different chemical process from that of vision and audition. A study (Schab & Crowder, 1995) demonstrated that we could not remember and recall the smell and taste of food correctly without any cue. They said that we recognize them.

There were some limits in distinguishing false memory in the experiment, because some patients recalled false memory

spontaneously during their recall of daily life events, and some of them also were pessimistic about their performance in the test because the patients with early stage AD still had good enough mental cognitive ability to recognize they were ill. More time was needed for these patients than the controls in helping to understand and perform this test, because they had to be more active for this test than for any other neuropsychological test they may have previously taken. The healthy elderly group however understood the test easily.

Experiment 2
The Report of the Experiment on Emotional Intensity of Episodic Memory

2.6. Introduction and Aim

Expressing and recognizing emotion is important in the context of social communication. In the case of AD patients, emotion processing profoundly affects the quality of their interaction with others. It is well established that emotion enhances episodic memory, that components of autobiographical memory is associated with emotion inevitably because this memory is a quality of our most recollective experience to a varying degree. Indeed, a close functional relationship between memory and emotion is supported by a number of lines of evidence that include enhanced learning for events with strong emotional valence (Bower, 1992) and preferential recall for emotionally laden autobiographical events (Holmes, 1970; Brewer, 1988).

The aim of this experiment is to investigate emotional intensity during episodic memory within different categories of memory (yesterday, week, month, and remote) by comparing healthy elderly people and AD patients. In the experiment the voice intonation of the subjects is estimated by valuators.

In general, the emotional intensity of AD patients is expected to be lower than that of healthy aged people. Remote memory is expected to be better than the other categories of memory, because remote episodic memories are related to particular and/or impressive events in the subject's life.

2.7. Method and Procedure

All 40 subjects both from the control group and patient group are measured for the emotional state of their voice by 8 different valuators (3 Europeans and 5 Koreans).

The experimenter selected 4 different episodes of a subject's retrieved memory from each category (yesterday, month, week, and remote). The most emotionally considered part is selected in each category by the experimenter considering the context. For example, during the remote memory part, the valuators heard a part of the retrieval of the Korean War. Since three of the subjects have not witnessed the Korean War, the most "emotion related" piece was selected the most emotion related piece for those cases. Before each piece (30s), the valuators heard the normal voice, which was recorded during a talk about everyday life of the subjects for about 10s. All 8 valuators listened to exactly the same parts of the recorded subjects' retrievals, and were tasked to estimate how each voice related to emotion. They had to select between 0, 1, and 2, whereas 0 means unrelated to emotion, 1 related and 2 highly related. All subjects speak Korean, therefore the three European valuators could not understand the context but tried to estimate the emotional relatedness of the speakers. For the Korean valuators in general it was difficult to grasp the complete context of the spoken parts because of their short duration.

In the statistical analysis, the t-test, two-way ANOVA and the Scheffe and Duncan as the post-hoc test were used for the verification of the mean difference between two groups, utilizing SPSS 11.0.

2.8. Results

As it can be seen from the result of the t-test between the two groups shown in Table 2-24, there were significant effects within memory for yesterday (p = .000 < .001, by two-tailed), within memory for the week (p = .002 < .01, by two-tailed), within memory for the month (p = .002 < .01, by two-tailed), within memory for the remote (p = .000 < .001, by two-tailed). The research hypotheses are supported: in the episodic memory of all four categories, the emotional intensity (the level of episodic memory related to emotion) of the patient group is significant compared to the unaffected aged group (see Fig.2-16).

Table 2-24 Voice involved emotion

	GROUP	N	Mean	SD	SE	P
Yesterday	HEP	19	1.2171	.42866	.09834	**
	AD	21	.5179	.31393	.06970	
Week	HEP	19	1.2566	.44189	.10138	*
	AD	17	.6838	.58816	.14265	
Month	HEP	18	1.2431	.54650	.12881	*
	AD	8	.6719	.29834	.10548	
Remote	HEP	19	1.6447	.33141	.07603	**
	AD	20	1.0125	.44036	.09847	

* $p < .01$,* * $p < .001$

HEP (Healthy Elderly People) indicates Healthy controls

AD (Alzheimer's Disease) indicates the patients

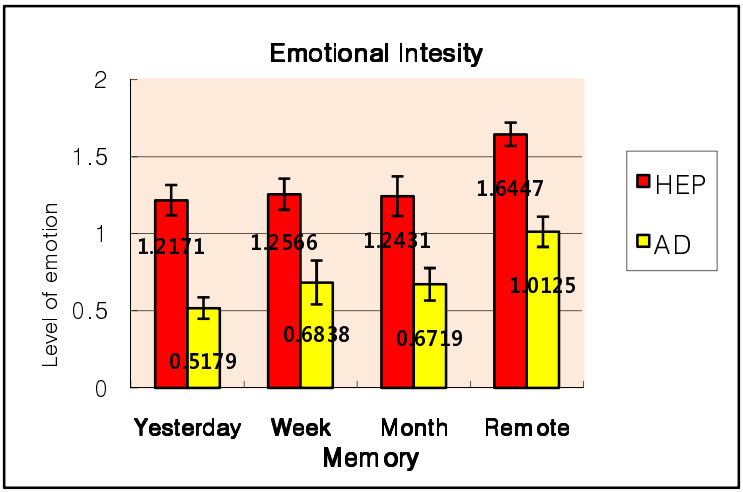

Fig.2-16. The emotional intensity compared with AD patients and normal-aging.
The intensity of emotion rages from 0 to 2 (0=unrelated, 1=related, and 2 high related)
HEP (Healthy Elderly People) indicates Healthy controls
AD (Alzheimer's Disease) indicates the patients

Table 2-25 Mean difference of Emotional intensity of yesterday in different sex and group

(I) SEXGROUP	(J) SEXGROUP	MD (I-J)	SE	Sig.
Male control	Male AD	.9167*	.16532	.000
	Female control	.3792	.16532	.174
	Female AD	.8826*	.16172	.000
Male AD	Male control	-.9167*	.16532	.000
	Female control	-.5375*	.16091	.020
	Female AD	-.0341	.15721	.997
Female control	Male Control	-.3792	.16532	.174
	Male AD	.5375*	.16091	.020
	Female AD	.5034*	.15721	.027
Female AD	Male control	-.8826*	.16172	.000
	Male AD	.0341	.15721	.997
	Female control	-.5034*	.15721	.027

Based on observed means, * The mean difference is significant at the .05 level.

The relatedness of the voice to emotion in AD patients is shown to be lower than in the control group. Regarding remote memory, AD patients related more with remote memory compared to memory of yesterday, the week, or the month, but are still lower in comparison with healthy elderly people.

Using ANOVA, mean differences between female and male subjects are compared. Mean differences of emotional intensity in the different categories of memory are also compared between two different groups. ANOVA was designed as 2 x 2 (sex x group) in entire subjects and 2 x 4 (sex x memory; yesterday, week, month, and remote).

Table 2-25 shows results of the ANOVA post-hoc test (Scheffe) from two groups and different genders in memory of yesterday. As it can be seen from Table 2-26, there are significant mean differences between control and patients, but not from genders.

Table 2-26 Homogeneous subsets of Emotional intensity of Yesterday in different sex and group

		N	Subset		
	SEXGROUP		1	2	3
Duncan	Male AD	10	.5000		
	Female AD	11	.5341		
	Female control	10		1.0375	
	Male control	9			1.4167
	Sig.		.834	1.000	1.000
Scheffe	Male AD	10	.5000		
	Female AD	11	.5341		
	Female control	10		1.0375	
	Male control	9		1.4167	
	Sig.		.997	.157	

Means for groups in homogeneous subsets are displayed. Based on Type III Sum of Squares The error term is Mean Square(Error) = .129.

a Uses Harmonic Mean Sample Size = 9.950.

b The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed. c Alpha = .05.

As it can be seen from Table 2-26, both groups of male AD and female AD are subset homogeneously and also male control and female control groups are subset in a group. Interestingly, according to Duncan, the control group is subset in two groups according to sex difference. This implies that there is a mean difference between the female control and male control groups as in Duncan.

Table 2-27 shows results of the ANOVA post-hoc test (Scheffe) from two groups and from the different genders in the memory of week. As it can be seen from Table 2-27, the male AD group has a significant mean difference between the male and female control groups, but the female AD group has no significant mean difference from any groups not also from sex.

Table 2-27 Mean difference of Emotional intensity of Week in different sex and group

(I) SEXGROUP	(J) SEXGROUP	MD (I-J)	SE	Sig.
Male control	Male AD	.7837*	.25349	.037
	Female control	-.1181	.23111	.967
	Female AD	.3194	.23111	.597
Male AD	Male control	-.7837*	.25349	.037
	Female control	-.9018*	.24788	.010
	Female AD	-.4643	.24788	.337
Female control	Male Control	.1181	.23111	.967
	Male AD	.9018*	.24788	.010
	Female AD	.4375	.22495	.304
Female AD	Male control	-.3194	.23111	.597
	Male AD	.4643	.24788	.337
	Female control	-.4375	.22495	.304

Based on observed means.

* The mean difference is significant at the .05 level.

Therefore, Table 2-28 shows similar results that two AD groups are subset homogeneously and also both control groups have no reference to sex difference according to Duncan and Scheffe.

Table 2-28 Homogeneous subsets of Emotional intensity of Week in different sex and group

	SEXGROUP	N	Subset 1	2
Duncan	**Male AD**	7	.4107	
	Female AD	10	.8750	.8750
	Female control	9		1.1944
	Male control	10		1.3125
	Sig.		.062	.093
Scheffe	**Male AD**	7	.4107	
	Female AD	10	.8750	.8750
	Female control	9		1.1944
	Male control	10		1.3125
	Sig.		.308	.359

Means for groups in homogeneous subsets are displayed. Based on Type III Sum of Squares The error term is Mean Square(Error) = .253.

a Uses Harmonic Mean Sample Size = 8.811.

b The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed.

c Alpha = .05.

As it can be seen in Table 2-29, there are no significant mean differences between the four different groups which have been subdivided by sex and group. It may indicate that both healthy elderly people and AD patients were not involved in recalling episodic memory with emotion in memory of month.

Table 2-29 Mean difference of Emotional intensity of Month in different sex and group

(I) SEXGROUP	(J) SEXGROUP	Mean Difference (I-J)	SE	Sig.
Male control	**Male AD**	.3333	.29194	.730
	Female control	-.3194	.22901	.592
	Female AD	.4896	.29194	.439
Male AD	**Male control**	-.3333	.29194	.730
	Female control	-.6528	.29194	.203
	Female AD	.1563	.34352	.976
Female control	**Male Control**	.3194	.22901	.592
	Male AD	.6528	.29194	.203
	Female AD	.8090	.29194	.081
Female AD	**Male control**	-.4896	.29194	.439
	Male AD	-.1563	.34352	.976
	Female control	-.8090	.29194	.081

Based on observed means.
* The mean difference is significant at the .05 level.

Table 2-30 Homogeneous subsets of Emotional intensity of Month in different sex and group

	SEXGROUP	N	Subset 1	2
Duncan	**Male AD**	4	.5938	
	Female AD	4	.7500	
	Female control	9	1.0833	1.0833
	Male control	9		1.4028
	Sig.		.126	.286
Scheffe	**Male AD**	4	.5938	
	Female AD	4	.7500	
	Female control	9	1.0833	
	Male control	9	1.4028	
	Sig.		.081	

Means for groups in homogeneous subsets are displayed. Based on Type III Sum of Squares The error term is Mean Square(Error) = .236.
a Uses Harmonic Mean Sample Size = 5.538.
b The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed. c Alpha = .05.

Perhaps there were some significant effects between groups, because AD patients and controls were subset in each different groups without reference to sex by Duncan, but not from Scheffe (See table 2-30). However, it is very difficult to say the statistical results have effects because the size of subjects in male and female AD groups is too small to have statistical data.

Table 2-31 Mean difference of Emotional intensity of Remote in different sex and group

(I) SEXGROUP	(J) SEXGROUP	Mean Difference (I-J)	SE	Sig.
Male control	Male AD	.7361*	.18253	.004
	Female control	-.0903	.17791	.967
	Female AD	.4609	.17404	.090
Male AD	Male control	-.7361*	.18253	.004
	Female control	-.8264*	.17791	.001
	Female AD	-.2753	.17404	.484
Female control	Male Control	.0903	.17791	.967
	Male AD	.8264*	.17791	.001
	Female AD	.5511*	.16919	.024
Female AD	Male control	-.4609	.17404	.090
	Male AD	.2753	.17404	.484
	Female control	-.5511*	.16919	.024

Based on observed means.
The mean difference is significant at the .05 level.

Table 2-31 shows mean differences of emotional level of memory of the remote in different sexes and groups. There are no significant mean differences caused by sex differences. All significant effects are shown between AD patients and controls, but interestingly, between the male control group and female AD group, no significant mean difference was found.

However, in the Duncan post-hoc test, the significant mean difference between those groups was found out because those groups were subset in different homogeneous groups.

Table 2-32 Homogeneous subsets of Emotional intensity of Remote in different sex and group

			Subset		
	SEXGROUP	N	1	2	3
Duncan	Male AD	9	.8611		
	Female AD	11	1.1364		
	Female control	9		1.5972	
	Male control	10		1.6875	
	Sig.		.127	.611	
Scheffe	Male AD	9	.8611		
	Female AD	11	1.1364	1.1364	
	Female control	9		1.5972	1.5972
	Male control	10			1.6875
	Sig.		.494	.096	.966

Means for groups in homogeneous subsets are displayed. Based on Type III Sum of Squares The error term is Mean Square(Error) = .150.

a Uses Harmonic Mean Sample Size = 9.682.

b The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed.

c Alpha = .05.

Interestingly in the Scheffe post-hoc test, the female AD and control groups were subset in a homogeneous group and overlapped in each different groups (See Table 2-32). This means that in the Scheffe test, there was some significant correlation between those two groups.

Table 2-33 Mean difference of Emotional intensity in Memory

		AD Patients			Controls		
(I) Memory	(J) Memory	MD (I-J)	SE	Sig.	MD (I-J)	SE	Sig.
Yesterday	Week	-.1664	.13935	.701	-.0395	.14083	.994
	Month	-.1542	.17746	.860	-.0250	.14277	.999
	Remote	-.4960*	.13345	.006	-.4274*	.14083	.034
Week	Yesterday	.1664	.13935	.701	.0395	.14083	.994
	Month	.0121	.18313	1.000	.0145	.14277	1.000
	Remote	-.3296	.14090	.153	-.3879	.14083	.065
Month	Yesterday	.1542	.17746	.860	.0250	.14277	.999
	Week	-.0121	.18313	1.000	-.0145	.14277	1.000
	Remote	-.3418	.17868	.311	-.4024	.14277	.056
Remote	Yesterday	.4960*	.13345	.006	.4274*	.14083	.034
	Week	.3296	.14090	.153	.3879	.14083	.065
	Month	.3418	.17868	.311	.4024	.14277	.056

Based on observed means.

* The mean difference is significant at the .05 level.

As shown in Table 2-33, there is a significant mean difference between memory of yesterday and remote. These results tell that the subject is more involved emotionally during the retrieval of episodic memory than remote (See Figure 2-17).

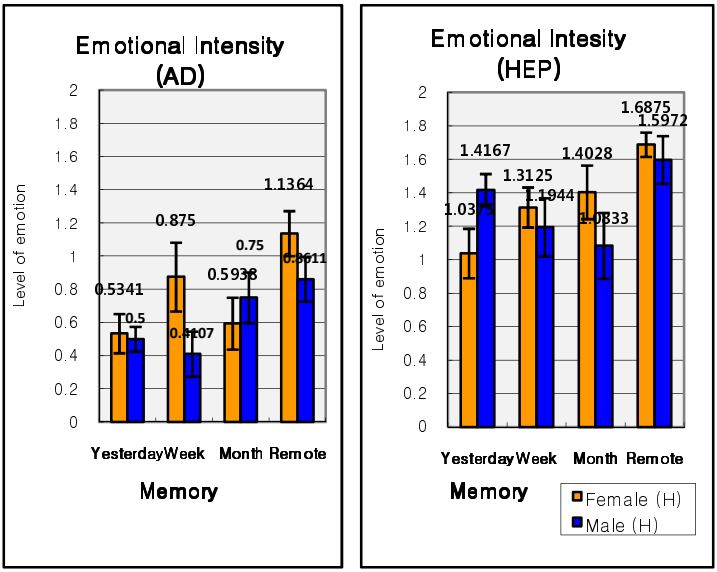

Figure 2-17. The emotion intensity compared within female and male healthy elderly people and within female and male AD patients. The intensity of emotion rages from 0 to 2 (0=unrelated, 1=related, and 2 high related) F=Female subjects, and M=Male subjects

HEP (Healthy Elderly People) indicates Healthy controls, AD (Alzheimer's Disease) indicates the patients

In the Duncan post-hoc test (See Table 2-34), the memory of yesterday, week, and month are subset in a homogeneous group and the memory of remote is subset alone in a group. This indicates that emotion is involved more when the subject retrieved retrograde memory than anterograde memory. In the Scheffe post-hoc test, the memory of week and month belong in both groups.

Table 2-34 Homogeneous subsets of Emotional intensity in Memory

		AD Patients			Healthy elderly people		
		N	Subset		N	Subset	
	Memory		1	2		1	2
Duncan	Yesterday	21	.5195		19	1.2195	
	Month	8	.6738		18	1.2444	
	Week	17	.6859		19	1.2589	
	Remote	20		1.0155	19		1.6468
	Sig.		.334	1.000		.796	1.000
Scheffe	Yesterday	21	.5195		19	1.2195	
	Month	8	.6738	.6738	18	1.2444	1.2444
	Week	17	.6859	.6859	19	1.2589	1.2589
	Remote	20		1.0155	19		1.6468
	Sig.		.783	.220		.994	.054

Means for groups in homogeneous subsets are displayed. Based on Type III Sum of Squares The error term is Mean Square(Error) = .182 (AD), Mean Square(Error) = .188 (HEP) .

a Uses Harmonic Mean Sample Size = 14.212 (AD), and 18.740 (HEP).

b The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed.

c Alpha = .05.

2.9. Discussion

The present study examining emotional expression (prosody/vocal intonation, tone and speech speed) during emotional episodic memory retrieval in early AD has generated several important results pertaining to AD specifically and to four different memories (yesterday, week, month, and remote). In the experiment, eight valuators measured how much the subjects expressed emotion during the retrieval of emotional episodic memory. Afterwards, the mean difference was compared between the AD patients group and control group.

The results reported significant mean differences between two different groups. This study shows that patients in the early stages of AD are impaired in the ability to express emotions during emotional episodic memory retrieval compared to

healthy elderly adults.

Bucks and Radford (2004) reported that AD patients have deficit of ability in emotion and cognition tasks compared to healthy elderly adults. However, other studies (Koff et al., 1999; Lavenu et al., 1999) have argued that deficit in emotional processing is secondary to the cognitive impairments associated with AD. For example, Koff et al., (1999) indicated that AD patients do not have a primary deficit in the processing of emotion. The results concerning recognition of emotions in Experiment 1 expand on this fact. In Experiment 1, impairment in recognizing emotions was not observed in the AD patients. This supports several previous studies on emotional processing in AD, which reported that AD patients in early stages are not impaired in the ability to recognize and identify emotions.

As reported in a functional neuroimaging study of Fletcher et al. (1998a; 1998b), the prefrontal and parietal cortices and the hippocampus are involved in memory retrieval, in particular the hippocampus, parahippocampus and anterior temporal lobe. Fink et al. (1996) identified that the right anterior temporal lobe is involved in autobiographical memory retrieval. More precisely, Dolan et al. (2000) identified an anterior temporal pole activation that reflected the psychological set associated with emotional memory retrieval. According to these studies, another region activated during emotional memory retrieval is the left amygdala. The fact that the amygdala participates in emotional processing is evidenced by several studies (Zald & Pardo, 1997; Paradiso et al., 1999; Dolan et al., 2000; Iidaka et al, 2001). The pathology in these brain areas was associated with impairment of episodic memory retrieval, such as primary deficit in AD. Evidently, the findings in the present study demonstrated that

AD patients have difficulties in expressing emotion during emotional episodic memory retrieval compared to healthy elderly adults. More technical studies, using methods such as neuroimaging, are needed to glean evidence as to which brain regions of AD are exactly associated with this impairment and how are it neurologically involved. For now, it is important to emphasize here that it is a significant finding that this deficit is observed in early stages of AD.

In the present study, sex differences in emotional intensity of episodic memory retrieval are analyzed, but there were no significant results in both groups. Herlitz et al. (1999) investigated sex differences in episodic memory, using verbal and visuospatial tasks. They reported results wherein women performed better on episodic memory tasks than men. In their study, women performed at a higher level than men on most verbal episodic memory tasks. This may to some extent explain the generally known superior ability of women in verbal production. Moreover, episodic memory tasks cannot fully measure the whole of episodic memory, including the content of autobiographical memory. Generally, in our everyday life, women express more of their emotions when they speak or in emotionally affecting situations (sad movies, etc.) than men. While this may because society is generous or liberal to women's emotional expression, the findings in this study demonstrate that men express their emotion as much as women when talking about their own past. The same phenomenon was observed in the pathological group. There are many ways of exhibiting emotion itself and recognizing the emotion of others. We can observe emotional expression not only through crying, laughing, and shouting, etc. but also through speech speed, prosody and voice intonation. The present study concentrated also on speech speed, prosody and

voice intonation for evaluating emotional expression in episodic memory retrieval. This is because cultural restraints usually come into play when men express their emotions. Men may cry or laugh according to emotion, but more frequently observable are changes in the speed or tone of speech. In this study, men had a clear tendency to speak softer or slower when recalling emotionally distressful memories. Taking this into account, men and women had no significant differences in expressing their emotions.

We also compared the emotional intensity between memory of yesterday and remote memory. Analysis of group data showed that the AD group was lower than the control group in emotional intensities of both memory of yesterday and remote memory. In both groups however, emotional intensity was concentrated more in the retrieval of remote events than of yesterday's events. This phenomenon is conspicuous in the AD patients group. These findings support previous findings wherein AD impaired anterograde memory more than remote memory in the early stages of AD.

All groups showed more emotional intensity retrieving remote memory than memory of yesterday. This phenomenon is clear in the AD patients group. Early stage AD patients had difficulty retrieving memory from time after the onset of their disease, but were capable of retrieving memory already stored. This gives additional evidence as to how loss of remote memory for early stage AD patients is less significant than loss of recent memory.

This study used a different approach from previous emotional processing studies in evaluating the expression of emotion in relation to episodic memory. In the present study, certain limits were manifested in the experimental design. As reported in the results, there were significant mean differences

between valuators. This problem may be caused by the size of the scale used and by the small group of valuators. Also, the experiment would be more sensitive if the subject's facial expressions, video-recorded during emotional episodic memory retrieval, had been evaluated. The results of the present study might be subjective because some people do not express their emotions well to others due to their own personality or environment pressures.

Expressing emotion in communicating in personal and social relationships is as important as perceiving and recognizing the emotional expression of others. As shown in this study, AD patients tend to have reduced emotional expression, which may be mistaken for depression. In the author's own clinical experience, AD patients in early stages do not express their emotions during intervention, and their relations often report of less talk or activity in their afflicted family member, showing symptoms similar to that of depression. Indeed, there are some cases where such patients are misdiagnosed as depressed. Some of the author's patients who participated in this study had themselves been initially diagnosed as depressed and undergone depression therapy for some time.

Ultimately, emotional intensity during the retrieval of episodic memory is a complex issue especially in early AD patient groups, and further investigations which are extensive, detailed and designed within the framework of the multiple trace theory are required.

Chapter III
CLINICAL CASE REPORTS

This chapter reports and describes 6 cases of episodic memory in health elderly people and in patients with Alzheimer's disease.
One female and two male outpatients were selected from KyungHee Medical Center. In the healthy elderly group, one male and two females were selected, with one of them having light symptoms of mild depression. All patients and controls participated in the experiment according to the procedure outlined in Chapter II.

3.1. Case 1: Patient HEC

3.1.1. Case Description

HEC was aged 55 years old at time of testing and is a right-handed woman with 12 years of formal education (See Tab.3-1). She is a housewife living with her husband and has two daughters, also living with her. She was referred to our service because of increasing difficulties in calculation, forgetfulness, depression and a mild personality change. There was no history of dementia or neurological disease in the family and the husband mentioned no previous head trauma or psychiatric disorder from alcohol abuse. She was visited by a neurologist a year ago, when she and her husband first suspected she had problems. At that time she was diagnosed as depressed, and was prescribed anti-depressives for one year. Despite this she developed memory impairment that increasingly became more serious. One day she was shocked

when she realized that a street she went to everyday was unfamiliar to her. However, she has no difficulty talking to her daughters or keeping house. Only social contacts and activities were reduced after the shock and she is accompanied by her husband every time she goes out.

Tab. 3-1 HEC's personal data

Subject's personal data	
Name of subject	HEC
Sex	Female
Age	55
Education	12
Group	Patient

3.1.2. Clinical Notes

The subject had some difficulty understanding the procedure of the test. Her face expressed perplexity because the questions of the test concerned her own life. She was calm and spoke with a low voice. She was worried and stressed about her disease. However, no neuro-clinical symptoms such as slowing of behavioral or verbal ability were observed.

3.1.3. Psychopathological Assessment

The subject showed symptoms of depression when thinking about her disease. She was anxious for her family, believing she was going to be a burden to them, in particular to her two daughters. Her husband reported that she cried often from fears of onset.

Aside from unwillingness to go out and reduced social contact, she did not show substantial changes in personality.

3.1.4. General Neuropsychological Assessment

Towards determining mental cognitive ability, the subject was administered two formal neuropsychological tests. Her MMSE-K score was 23. However, her K-DRS score was 106. Results of both tests indicated that she has some problems of cognitive ability and that she is a typical dementia patient (See Tab. 3-2).

Tab. 3-2 HEC's neuropsychological test results

K-DRS and MMSE-K							
	Attention	**Initiation perseveration**	**Construction**	**Categorization**	**Memory**	**Total**	**MMSE**
Score	25	28	2	31	20	106	23
%	2.7	14.9	4.1	10.8	13.5	1.4	

3.1.5. Episodic Memory Retrieval

HEC's response time for each memory tasks and total duration of test are reported on Table 3-3.

Tab. 3-3 HEC's response time and total duration

Time				
Total Duration	**Latency Yesterday**	**Latency Week**	**Latency month**	**Latency Remote**
27:31	35'50"	33'40"	03'38"	01'33"

The amount of the retrieved episodic image of HEC demonstrated on Tab. 3-4.

Tab. 3-4 HEC's Number of retrieved episodic memory images

	Number of Image				
	Total	**Yesterday**	**Week**	**Month**	**Remote**
Testing day	12	6	3	1	2
Following day	11	5	3	1	2

The subject recalled the episodic image slowly with a long interval between each image. She had no great difficulty in retrieving the episodic events concretely, but she was confused when asked to remember the events in time order and could not reproduce the events coherently or systematically. She also could not recall the context and details of the event which happened a month ago, even though she retrieved the event itself (Tab.3-5).

She seemed to be suffering from depression as well, because she was anxious and fearful of her disease during the interview. She recalled episodic images in as much quantity as healthy elderly people. However, her recalled episodic images in her memory of yesterday were like photographs, while controls reported images that were like short movies (See Tab.3-5).

Tab. 3-5 HEC's context of the retrieved episodic memory image

	Yesterday	**Week**	**Month**	**Remote**
Emotion	**Happy, fear** She had a happy image of cultivating some fruits from her garden and playing with her	**Fear, happy** She was worried about losing her passport, but she was	**Fear**	**Sadness**, She was sad about leaving her best friend.

	dogs. She was worried about her disease.	glad to find it in a bag.		
Sensory modality	**Vision, olfaction, audition.** She recalled a visual image of her garden and the smell of the fruits and the sound of her dogs.	**Vision** She recalled only visual images.	**Auditio n** She recalled the sound of guns from a movie.	**Vision, audition touching** She recalled a visual image of her friend and the feeling of her hug and the sound of an airplane.
Color or Black & White	**Color** She recalled the color of each fruit and of her husband's clothes .	**Color** She recalled the color of the bag and sofa.		**Color** She clearly recalled the color in the image.
Moving or Stationary	Stationary	Stationary		Moving
Subject's position in image	**1st**	**1st**		**1st**
Object	Husband, dogs, tomatoes, corn, garden and house	Passport, husband, sofa, curtain, bag		Best friend, airport.
Context	Taking care of the garden, cleaning, dogs	Losing and finding the passport, checking	Watchin g a movie	Best friend leaving
Event related	**Both**	**Related**	**Related**	**Both**
Time order	**Failed** She could not recall the events of yesterday in time order.			
Details	**Failed**	**Pass**	**Failed**	**Failed**

Etc.	She recalled images slowly, but could remember in detail.	She could not recall the details of the image or the context of the movie.	She recalled some images unrelated to events, but could not recall when.

3.2. Case 2: Patient CJC

3.2.1. Case Description

In August 2004, CJC was a 63 years old right-handed man with 16 years of education (obtained an undergraduate degree, see Table 3-6). He lives with his wife in a small city in eastern Korea. At the time of the testing he was retired, but up to a couple of years ago he worked as teacher in a high school.

Tab. 3-6 CJC's personal data

Subject's Personal data	
Name of subject	C. J. C.
Sex	Male
Age	63
Education	16
Group	Patient

He came to the hospital because of difficulty in remembering recent events. He sometimes forgot appointments with colleagues and also had trouble recognizing them. However, his daily life was not yet greatly affected by memory decline. He was able to do talk and write, to drive his car and to recognize friends and relatives, and had no problem finding his way around. According to him, there was no history of

dementia or neurological disease in his family and his wife mentioned no previous head trauma, psychiatric disorders or alcohol abuse. He seemed to be depressed at the time of testing. His wife mentioned that he became depressed since recognizing his memory problem. In all probability it was caused by several episodes of memory loss.
CJC underwent a detailed neuropsychological assessment and received standard and experimental tests exploring the specific aspects of his decline of episodic memory.

3.2.2. Clinical Notes

He had no great difficulty understanding questions during intervention. However, the questions had to be repeated many times. He also needed time to answer simple questions. He spoke with notable slowness. He had no other pathological behavior such as slow movement or trembling hands.

3.2.3. Psychopathological Assessment

Since the onset of his symptoms, CJC's wife had noted that he had a tendency to become more anxious and depressed compared to his previous self. Also during testing, he became more anxious when he failed or could not respond properly.
Deterioration of social activity or changes in attitude was not observed, but his speaking speed slowed.

3.2.4. General Neuropsychological Assessment

Formal neuropsychological tests, namely the Mini-Mental State Examination Korean version (MMSE-K) and a standard dementia test, K-DRS (Choi, 1998), devised to explore attention, initiation preservation, construction, categorization and memory, were administrated. Results of these assessments are reported in Table 3-7.

Tab. 3-7 CJC's neuropsychological test results

K-DRS and MMSE-K							
	Attention	**Initiation perseveration**	**Construction**	**Categorization**	**Memory**	**Total**	**MMSE**
Score	34	37	6	38	15	130	24
%	14.3	100	100	100	2.9	68.9	

3.2.5. Episodic Memory Retrieval

The subject CJC used relatively slow speech, but his speed matched controls when he reproduced episodic images from remote memory. The table 3-8 reports the total duration of the test interview and latency of CJC.

Tab. 3-8 CJC's response time and total duration

Time				
Total Duration	**Latency Yesterday**	**Latency week**	**Latency month**	**Latency Remote**
25:18	11'76"	34'74"	09'97"	14'35"

He could not distinguish between the images of yesterday and some days ago, implying some overlapping. He seemed tense and unstable when reporting images of yesterday, week and month ago memory, but returned to a comfortable state when remembering his remote past. His quantity of the recalled episodic images for each categories and total is described on Tab.3-9.

Tab. 3-9 CJC's Number of retrieved episodic memory images

	Number of Image				
	Total	**Yesterday**	**Week**	**Month**	**Remote**
Testing day	15	7	2	1	5
Following day	0	0	0	0	0

He reported that all of his reported images had no colors, and images flashed by like a slide show rather than a moving film. This patient also could not remember particular events of yesterday, only their general occurrence. He could not arrange the events in order of occurrence or reproduce any concrete emotion at the time (See Tab.3-10)

Tab. 3-10 CJC's context of the retrieved episodic memory image

	Yesterday	**Week**	**Month**	**Remote**
Emotion	The patient remembered he went to Catholic mass and a restaurant with his family, but he could not retrieve his actual feelings in the images.	**Happiness** The patient recalled 2 images. One was weekly mass and another was visiting his godson who is blind. He said he was happy when he visited his godson because his godson was healthy.	The patient recalled an image of a monthly meeting at his church. But he could not remember how he felt during the meeting.	**Fear and sadness** The patient recalled 5 images. He retrieved 2 images about the Korean War. One was about being a refugee and enemy troops. He clearly remembered his fear. He remembered his sister's husband

				dying, and feeling sad.
Sensory modalities	**Audition, vision** The patient remembered the sound of the choir at mass and that there were many people in the restaurant but he could not remember the taste of the food and which food he ate.	**Vision** The patient could remember the figure of objects and his godson, but could not recall any other senses.	**Vision** The patient recalled the image of the church where he went and of a priest.	**Vision, audition, sensor soma** The patient saw enemy troops and his old house, and he recalled the sound of airplanes and bombing. And he could remember how cold it was when he went to school.
Color or Black & White	**No Color** The patient could not remember the color or figure of the church or the restaurant clearly. The patient said the image is not B&W exactly but is not clear.	**B&W** The patient said his images are like B&W photos. He could remember the figure of the meeting room and his godson but could not remember the color.	**B&W** The patient could not remember the color of the church. He likened his image to a B&W photo.	**Color and B&W** The patient said he could see the color of the enemy's clothes and of the airplane clearly, but his old house was like a B&W photo.

Moving or Stationary	**Stationary** The patient said that the images did not move but were like still photos. He could not see the movement of family members in the pictures.	**Stationary** The patient said he saw the images like a photo album.	**Stationary** The patient could not see any movement in the picture.	**Moving and Stationary**. He said when he remembered the K-war it was like watching a movie. But his old house was not remembered so.
3D or 2D	**3D** When the patient explained the detail of the images, he indicated the positions of the each object by hand as if he was in the images.	**2D** The patient said his images were like photos. He did not explain the images like the images of yesterday.	**2D** The patient explained the figure of the church, drawing with his finger before his face.	**3D and 2D** He explained the K-war as if he was in the war.
Subject's position in image	**1st** The patient said he could see his body, but not his face.	**3rd** He said he could see himself in the meeting.	**3rd** He indicated himself in the image.	**1st and 3rd**
Object and person	The patient saw **the choir, a bulletin, a missal, the communion, and his son** in his	The patient recalled the figure of **the meeting room of the church and the face of his godson.**	**The church and the priest**.	**Snow, the enemy troops, his old house, airplane, and his father.**

	images.			
Context	**Mass, and the restaurant** The patient retrieved two images. One was of mass and the other was the restaurant where he went with his family for lunch.	**Meeting and godson.** The patient remembers his weekly meeting of the church and visiting his godson.	**Monthly meeting**	**K-war, refugees, his old house and the street on the way to school, and his sister's husband dying.**
Event related	**Related**	**Related**	**Related**	**Related**
Time order	**Failed** He could not remember what he did yesterday in sequence.	**Failed** He could not remember what he did in the meeting or his godson's house in sequence.		
Details	**Failed** He had difficulty rememberin g the details of the images and he could not remember what he ate for lunch or dinner or what the	**Failed** He could not remember the topic of the meeting or what he had talked to his godson about.	**Failed** He could not remember the topic of the meeting or when exactly it was held or who was there with him.	**Pass** He described every detail of his images and what his father said.

	priest said at mass.			
Etc.	He took a long time recalling these images and spoke slowly. He was not sure about everything he said. He confused things of yesterday with that of some days ago. This was confirmed by his wife.	His speech speed was slow, and he was also tense.		His speech speed became normal with respect to NAG. He was also relaxed and active in answering questions.

3.3. Case 3: Patient HGB

3.3.1. Case Description

Mr. HGB was a 69 year-old retired high school teacher attending medical care for AD. He lives with his wife in Seoul (See Tab. 3-11). He came to the hospital after forgetting an important appointment which he made and couldn't remember making.

Tab. 3-11 HGB's personal data

Subject's Personal data	
Name of subject	H.G.B.
Sex	Male
Age	69
Education	16
Group	Patient

However, he had no problems recognizing friends and familiar relatives or going to hospital sessions or driving. He still goes out alone without company and never loses his way. Reviewing his clinical history, there was no history of dementia or neurological disease in his family and no head trauma, psychiatric disorder or alcohol abuse. He was very active in therapy, and looked cheerful. A year ago he had a surgical operation for prostatitis.

3.3.2. Clinical Notes

The subject had a good understanding of the questions, and gave clear responses. No other pathological behaviors such as slow speech and movement or trembling of hands were observed. He became anxious once he found some difficulties chronologically ordering retrieved events.

3.3.3 Psychopathological Assessment

HGB's wife said he had no great mood changes since the onset of the disease, considering that he has had problems before retrieving memory events chronologically. No symptoms pertaining to depression or anxiety disorder were observed during the test, nor was there deterioration of social

activity or changes in attitude.

3.3.4. General Neuropsychological Assessment

The MMSE-K and KDRS were administered. The subject's MMSE-K score was 29/30 and total KDRS score was 137. Results of the serial assessments of KDRS are reported in Tabl 3-12. These results indicate that HGB showed no sign of general mental impairment or of dementia. Moreover, he obtained high scores in both neuropsychological tests compared to the healthy subjects' scores.

Tab. 3-12 HGB's neuropsychological test results

K-DRS and MMSE-K							
	Attention	**Initiation perseveration**	**Construction**	**Categorization**	**Memory**	**Total**	**MMSE**
Score	36	36	6	36	23	137	29
%	77.1	95.7	100	80	80	100	

3.3.5. Episodic Memory Retrieval

The subject reacted quickly to memory of yesterday, and had no trouble remembering, but he took more time retrieving remote memory (See Tab.3-13).

Tab. 3-13 HGB's response time and total duration

Time				
Total Duration	**Latency yesterday**	**Latency week**	**Latency month**	**Latency Remote**
25:46	01'87"		06'57"	17'88"

On the following day after the test, he could not recall all the images he reported on testing day and confused the interview test with the neuropsychological test done previously (See Tab. 3-14).

Tab. 3-14 HGB's Number of retrieved episodic memory images

	Number of Image				
	Total	**Yesterday**	**Week**	**Month**	**Remote**
Testing day	14	6		1	7
Following day	8	3		0	5

While recalling an image of a week ago without much trouble, he realized for himself that the image he was describing happened a month ago. He could not retrieve the exact place of the event, and he needed a long time to recall the related images between events. As with the other patients, he became more active during the recall of remote memory events (See Tab. 3-15).

Tab. 3-15 HGB's context of the retrieved episodic memory image

	Yesterday	**Week**	**Month**	**Remote**
Emotion	**Happiness, delusion, fear** The subject had a happy image of watching a game, an image that they were not his members in a club, and a fearful image of the dentist.		**Happiness** He had a happy image of meeting old friends.	**Happiness, fear, sadness** He had some happy images of his childhood, obtaining a scholarship, his wedding, and some fearful and sad images of evacuation and

				his brother dying.
Sensory modality	**Vision, touch, taste, audition.** He had a vision of gambling, felt that the doctor put something in his mouth, and recalled the sound of the TV and the taste of lunch.		**Vision** He had a vision of the station where he waited for his friends.	**Vision, audition** He retrieved the sound and the vision of crying from his brother dying.
Color or Black & White	**All his images are B&W**		**B&W**	**Both** He had a color image of his brother dying.
Moving or Stationary	Moving		Stationary	Both Same as above
Subject's position in image	**1st**		**1st**	**3rd**
Object	Disinfectant, nurse, air conditioner, Korean playing cards, club friends			Pine cone, letter of brother's death, dead brother, the church, his roommate

Context	Dentist, club meeting, watching TV, lunch.		Meeting old friends	Playing with a pine cone, brother's dying, K-war, wedding, scholarship
Event related	**Both**		**Related**	**Both** One image is not related to event
Time order	**Failed**			
Details	**Pass** He retrieved every detail		**Failed** He could not remember the main menu of the lunch and where they went, but he retrieved his friends well.	**Pass** He retrieved in detail.
Etc.	Not his thoughts		He had a long latency in retrieving things.	He had good memory of remote

3.4. Case 4: Control KYJ

3.4.1. Case Description

In October of 2004, KYJ, a 65-year-old right-handed woman with 9 years of formal education, participated in this study as a volunteer (See Tab. 3-16).

Tab. 3-16 KYJ's personal data

Subject's Personal data	
Name of subject	K. Y. J.
Sex	Female
Age	65
Education	9
Group	Control

The subject lives with her husband and daughter in one of Korea's major cities, and is a housewife. There was no history of dementia or neurological disease in the family and no previous head injury, psychiatric disorder or alcohol abuse.

3.4.2. Clinical Notes

At the examination, certain difficulty in understanding and performing the test of episodic memory retrieval was observed. During the test, the subject was inactive, cynical and spoke in a low voice. Her expression was dark and she was inattentive.

3.4.3. Psychopathological Assessment

She reported that she had a tendency to become more depressive, anxious, irritable and overall apathetic. Her sleeping time increased, and at the same time she saw reductions in speech, social contact and appetite.

3.4.4. General Neuropsychological Assessment

She was tasked in two formal neuropsychological tests with one test evaluating depression. Her MMSE-K score was 28 and K-DRS score 135 as shown Table 3-17. She is at normal levels on both tests. However her attention score is lower than average. It may be caused by depression, leading to

administering a BDI (Back's Depression Inventory). As expected, her score in BDI was over 17.

Tab. 3-17 KYJ's neuropsychological test results

K-DRS and MMSE-K							
	Attention	**Initiation perseveration**	**Construction**	**Categorization**	**Memory**	**Total**	**MMSE**
Score	35	37	6	35	22	135	28
%	37.1	100	100	57.1	57.1	100	

3.4.5. Episodic Memory Retrieval

The latency of recalling episodic images of each category of memory types and the total duration of KYJ are represented on the table 3-18.

Tab. 3-18 KYJ's response time and total duration

Time				
Total Duration	**Latency yesterday**	**Latency Week**	**Latency Month**	**Latency Remote**
13:18	01'45"	37'80"		00'73"

The number of the recalled episodic images by KYJ is reported on Tab 3-19.

Tab. 3-19 KYJ's Number of retrieved episodic memory images

	Number of Image				
	Total	**Yesterday**	**Week**	**Month**	**Remote**
Testing day	15	8	2	0	5
Following day	12	6	1		5

The below table 3-20 is detailed the context of the episodic images reproduced from KYJ in each memory and in each element such emotion, sensory modality, and time order etc.

Tab. 3-20 KYJ's context of the retrieved episodic memory image

	Yesterday	**Week**	**Month**	**Remote**
Emotion	**Happiness** She met her sisters after a long separation. Some images are not related to emotion.	Nothing She recalled 2 images, but they were not related to emotion.	Rejected	**Happiness, anger** She recalled a very happy memory about summer vacation in childhood. During the war it was very chaotic, but it was fun for her. She retrieved that she had suffered for her husband.
Sensory modality	**Vision** She recalled her sister's face, her new sofa and an Indian plant.	**Vision** She recalled an image of the dentist and a nursery		**Vision, audition, taste** She saw the beach, and heard the sound of cannons and

		school.		airplanes. She recalled also salt and watermelon.
Color or Black & White	**Color** She retrieved the color of sister's clothes and various objects.	**Color**		**Both**
Moving or Stationary	**Both** The familiar meeting is static, but her sister is moving.	**Both** Intervention of dentist is moving image, but the other is not.		**Both** The image of the beach is static but the war is like a movie.
Subject's position in image	**Both** She could see herself in image of the meeting.	**1st** She could not see herself in the image.		**Both**
Object	Sisters, sofa, medicine, bus, school, Indian plant, fruits	Artficial tooth, dentist.		Watermelon, sister, father, special cover
Context	Familiar meeting, working out, buying medicine and fruit, cleaning, meeting older sister	Service in a nursery school, taking an artificial tooth		Summer vacation, evacuation, meeting father, an inclination to gambling
Event related	**Both** 3 images are related to events, the others not	**Related**		**Related**

Time order	**Pass** She could describe each image in sequence.	**Pass** She described in sequence between images		**Pass**
Details	**Pass** She recall every detail in the image	**Pass**		**Pass**
Etc.	She was a little apathetic.	She was apathetic and depressive.		She was active to answer.

3.5. Case 5: Control KJM

3.5.1. Case Description

At the time of the test, the subject was a 61 year-old man living with his wife and has two married sons (See Tab. 3-21). One of them is living in another city. He has graduated university, and works in the industrial sector.

Tab. 3-21 KJM's personal data

Subject's Personal data	
Name of subject	K.J.M.
Sex	Male
Age	61
Education	16
Group	Control

He actively volunteers at his local Catholic church. In

testing he was very active and reacted positively. He does not smoke and is only a social drinker. He was never hospitalized long-term and has never had any kind of operation, nor any neurological or psychiatric disorder including head injury.

3.5.2. Clinical Notes

During the test the subject did not exhibit any particular clinical symptoms which might be related to mental disease. The tone of his voice and speech speed was adapted. He had good understating of the procedure of the test. There were no observed symptoms relating to dementia or memory disorder.

3.5.3. Psychopathological Assessment

He was relaxed, and not under stress. He was able to express emotions easily. He wished to maintain his content life and good health. He seemed to be successful overall in coping with stressful situations. He had no problems sleeping. His appetite was normal. His social contacts and other activities were also normal.

3.5.4. General Neuropsychological Assessment

Two neuropsychological tests, MMSE-K and K-DRS, were used. As shown in the following Table 3-22, his MMSE score was 29 and K-DRS total score 133. The scores of both tests are marked in normal level. All subcategories of K-DRS are marked normally. There were no pathological results suspecting depression or dementia.

Tab. 3-22 KJM's neuropsychological test results

K-DRS and MMSE-K							
	Attention	**Initiation perseveration**	**Construction**	**Categorization**	**Memory**	**Total**	**MMSE**
Score	36	34	6	35	22	133	29
%	70.3	43.2	100	51.4	48.6	45.9	

3.5.5. Episodic Memory Retrieval

The latency of recalling episodic images of each category of memory types and the total duration of KJM are represented on the table 3-23.

Tab. 3-23 KJM's response time and total duration

Time				
Total Duration	**Latency Yesterday**	**Latency Week**	**Latency month**	**Latency Remote**
28:40	12'79"	01'27"	13'20"	04'23"

The number of the recalled episodic images by KJM is reported on Tab 3-19.

Tab. 3-24 KJM's Number of retrieved episodic memory images

Number of Image					
	Total	**Yesterday**	**Week**	**Month**	**Remote**
Testing day	22	8	6	3	5
Following day	20	7	6	2	5

The below table 3-25 is detailed the context of the episodic images reproduced from KJM in each memory and in each element such emotion, sensory modality, and time order etc.

Tab. 3-25 KJM's context of the retrieved episodic memory image

	Yesterday	Week	Month	Remote
Emotion	**Fear, anger** He was angry about unfair work conditions faced by his colleagues.	**Fear, joy** He had a joyful image of meeting an old friend, and some fearful images of his son's house.	**Happiness** He had happy images of going to a monastery.	**Fear, surprising, joy.** He had some fearful images of the premature birth of a grandson and a fun image of evacuation.
Sensory modalities	**Vision/sensor** He recalled the feeling of the injection.	**Vision, audition** He recalled an image of an old friend and the voice of his son on the telephone.	**Vision** He recalled the view of the monastery.	**Vision, audition**
Color or Black & White	**Color** He recalled the colors of each object.	**Color** He recalled the colors of each object.	**Color**	**Both**

Moving or Stationary	**Moving**	**Moving**	**Stationary**	**Both**
3D or 2D	3D	3D	2D	Both
Position of image	Panoramic	Panoramic	Down	Panoramic/ Down
Subject's position in image	**1st**	**1st**	**1st**	**Both**
Object	Nurse, syringe, account book, icon	President, son, friend	Tree, priest, tomb, and friends	Car, hospital, relatives, grandson.
Context	Vaccination, meeting, prayer, mass	Medicine, visiting a friend. Visiting son's friend	Visiting the tomb of his wife's father and monastery	Accident, evacuation, k-war, hard labor
Event related	Both	Both	**Related**	**Related**
Time order	**Pass** He could recall the images in time order.			
Details	**Pass** He recalled the context of the lecture and of the conversation during the meeting.	**Pass** He recalled the context of the conversation in detail.	**Pass** He recalled exactly when, where, and why he went there, etc.	**Pass** He reproduced the image vividly.

3.6. Case 6: Control HKJ

3.6.1. Case Description

The subject is 61 years-old and female (See Tab. 3-26). She has been single all of her life and lived alone for a long time. She graduated a French university majoring in architecture. She works as an architect.

Tab. 3-26 HKJ's personal data

Subject's Personal data	
Name of subject	H.K.J.
Sex	Female
Age	61
Education	16
Group	Control

She volunteered for this research in order to examine her cognitive abilities. She is a non-smoker and does not drink alcohol. She was actively attentive during examination. There were no long-term diseases such as hypertension or diabetes in her clinical history. The subject has never undergone surgical operation or therapy in neurology or psychiatry.

3.6.2. Clinical Notes

This was her first psychological assessment, and she participated actively. She had the best understanding of the procedure out of all the subjects. She expressed her emotions easily and had no difficulties retrieving her own past. No clinical symptoms related to dementia of memory or cognitive

ability was observed during the test.

3.6.3. Psychopathological Assessment

Recently, she was stressed by an excessive workload and problems with personal relationships connected to work, but she has adapted well in coping with such situations. Also recently, her sleeping time has increased and she begins to easily tire. She does not avoid social contact. No symptoms of nervousness, depression or anxiety were observed during the interview.

3.6.4. General Neuropsychological Assessment

She was administered two neuropsychological tests like the other subjects. Her score of MMSE-K was 28 and K-DRS score 140 (See Tab. 3-27). She scored above normal levels, the only one among the subjects to obtain full marks. She has excellent cognitive abilities for her age group.

Tab. 3-27 HKJ's neuropsychological test results

K-DRS and MMSE-K							
	Attention	**Initiation perseveration**	**Construction**	**Categorization**	**Memory**	**Total**	**MMSE**
Score	37	37	6	39	25	144	28
%	100	100	100	100	100	100	

3.6.5. Episodic Memory Retrieval

The latency of recalling episodic images of each category of memory types and the total duration of HKJ are represented on the table 3-28.

Tab. 3-28 HKJ's response time and total duration

Time				
Total Duration	**Latency yesterday**	**Latency Week**	**Latency month**	**Latency Remote**
24:24	00'54"	01'06"	01'35"	01'57"

The number of the recalled episodic images by HKJ is reported on Tab 3-29.

Tab. 3-29 HKJ's Number of retrieved episodic memory images

	Number of Image				
	Total	**Yesterday**	**Week**	**Month**	**Remote**
Testing day	26	10	4	3	9
Following day	26	10	4	3	9

The below table 3-30 is detailed the context of the episodic images reproduced from HKJ in each memory and in each element such emotion, sensory modality, and time order etc.

Tab. 3-30 HKJ's context of the retrieved episodic memory image

	Yesterday	Week	Month	Remote
Emotion	**Happiness** She had a happy image of having lunch with a choir member.	**Fear, Happiness** She had 2 stressful images of a meeting at work, and 2 happy images of having a picnic.	**Happiness** She had some calm images of staying at a beach.	**Fear, happiness, sadness** She had happy images of childhood, embarrassing images of bed-wetting, and sad images of her mother.
Sensory modality	**Vision, taste, audition, olfaction** She recalled the sound of the choir, the taste and the smell of lunch and the sound of the people around her.	**Vision, olfaction, audition** She recalled the refreshing scent and the panorama of the mountain.	**Vision** She saw foreigners and the sea and the white beach.	**Vision, audition** She recalled her mother was looking at her continuously, and the sound of bombing.
Color or Black & White	**Color** She had colorful images.	**Color** She recalled the color of the mountain.	**Color**	**Color**
Moving or Stationary	**Moving** She saw the movement of people.	**Moving** She had moving images.	**Moving**	**Moving** All her images were like a movie.
3D or 2D	3D	3D	2D	Both

Position of image	Panoramic	Panoramic	Front of the face	Panoramic
Subject's position in image	**1st** She could see her body herself, but not her face.	**1st**	**1st**	**Both** In some images, she looked little.
Object	Offering-basket, a choir-member, salad, beef, rice	Herb, lunch box, and friend	Foreigner, sea, beach	Vest, basket, photo, ship, airplane, mother
Context	Meeting, mass, cleaning, watching TV, cleaning house	Meeting, work place picnic, lunch	Visiting his brother	K-war, mother, photographing, leaving for France, bed-wetting
Event related	**Both** She recalled the things she did in everyday life.	**Related** All images were related to a particular event.	**Related**	**Related**
Time order	**Pass** Images in sequence.			
Details	**Pass** The context of the lecture, the number of members, position of each person, the conversation, the reason to for meeting	**Pass** She recalled when, why and what she did in the image.	**Pass**	**Pass** She recalled which dream she had, and its historical background story.

3.7. Analysis and Discussion

This study considers autobiographical images. In this chapter, three AD subjects, one mild depression subject, and two healthy elderly subjects reported autobiographical images, which were further analyzed qualitatively and in detail. The early stage AD and depression subjects will be compared with the two healthy control subjects in order to determine the neuropsychological mechanisms of episodic memory disruption.

- *Emotion*

All three patients had deficit of retrieval concerning anterograde memory, such as memory of a week and a month. CJC was not emotionalized when recalling an event that happened a month ago, but he reproduced clear episodic images from retrograde memory of events taken place before the onset of the disease. His emotions were also engaged to the same level as health controls when he re-experienced them. This fact was also identified by diverse studies (Hodges et al, 1990; Graham et al., 2004; Hargrave et al. 2004). Interestingly, some patients of all subjects in the experiment were not emotionalized when they retrieved remote episodic memory, describing the event as if reporting a historic fact. Considering this finding, we can suspect that decline of emotional expression in the early stage of AD can bring about impairment in episodic memory.

Dolan and his colleagues (2000) investigated whether neural systems known to be involved in episodic memory retrieval also subserve retrieval of emotional episodic memory by using functional imaging materials. They identified an anterior temporal pole activation that reflected the

psychological association with emotional memory retrieval.

Tab. 3-31. Analysis of the retrieved episodic memory images

		Emotion	Colorful/ B&W	Moving/ Stationary	Event related	Details	Time Order
Yester Day	HEC	H, F	Color	Stationary	Both	Failed	Failed
	CJC	None	Unclear	Stationary	Related	Failed	Failed
	HGB	H,D,F	B&W	Moving	Both	Failed	Failed
	KYJ	H	Color	Both	Both	Pass	Pass
	KJM	F,A	Color	Moving	Both	Pass	Pass
	HKJ	H	Color	Moving	Both	Pass	Pass
Week	HEC	H, F	Color	Stationary	Related	Pass	Unavailble
	CJC	H	B&W	Stationary	Related	Failed	
	HGB	-	-	-	-	-	
	KYJ	None	Color	Both	Related	Pass	
	KJM	H, F	Color	Moving	Both	Pass	
	HKJ	H, F	Color	Moving	Related	Pass	
Month	HEC	F	Rejected	Rejected	Related	Failed	Unavailble
	CJC	None	B&W	Stationary	Related	Failed	
	HGB	H	B&W	Stationary	Related	Failed	
	KYJ	-	-	-	-	-	
	KJM	H	Color	Stationary	Related	Pass	
	HKJ	H	Color	Moving	Related	Pass	
Rem Ote	HEC	S	Color	Moving	Both	Pass	Unavailble
	CJC	F, S	Both	Both	Related	Pass	
	HGB	H,S,F	Both	Both	Related	Pass	
	KYJ	H,S	Both	Both	Related	Pass	
	KJM	H, F, Su	Both	Both	Related	Pass	
	HKJ	H, F, S	Color	Moving	Related	Pass	

A=Anger, D=Delusion, F=Fear, H=Happiness, S=Sadness, Su=Surprising.
'-'means that subject did not recall any episodic memory image

- *Color/Moving image*

The three controls recalled episodic images, and managed to recall the color of each object in the images. They reported that the images were not like still photographs but moving images. The controls reproduced the episodic images of

yesterday, week, month, and remote similarly all in this manner.

However, the forms of the episodic images recalled by the three AD patients were more variable. HEC clearly recalled the colors in the images, saying her episodic images were like color stills cut off from each other, with the exception of her remote memory images. With CJC and HGB, retrieved images of memory of yesterday and week were unclear, and looked like faded black-and-white photos. However, HGB managed to recall moving images instead of stills. Interestingly, in remote memory retrieval, they would retrieve either colorful moving images or black-and-white images depending on the context of the remote episodic memory(See Tab.3-31). There were several studies (Cornoldi et al., 1989; Dror & Kosslyn, 1994; Cocude et al., 1997; De Beni et al., 2006; Gardini et al., 2006) which were concerned to autobiographical images and visual images, focusing more on the generation and the maintenance and transformation of the visual images, differently here concentrated on the features of the image.

- *Event related*

Generally, healthy elderly controls retrieved everything that happened yesterday, whether the incident was routine or particular. AD patients remembered particular events but not events unrelated to those events. They also could not remember routine events that took place in everyday life.

- *Details*

The three patients retrieved some episodic images, but could not recall details of each images. HGB could not remember when he went to the dentist, whether it was in the morning or the afternoon. HEC could not remember why she went to the

farm. CJC remembered participating in a meeting, but could not recall the context or attendees of the meeting. The confabulations were observed too on the patients during the interview test. There have been some studies found out this fact (Nedjam et al., 2000; Cooper et al., 2006)

KYJ, who is under mild depression, recalled fewer images compared to healthy elderly subjects, but reproduced exact details of each image. Raes et al. (2005) examined the relationship between emotional abuses such trauma and autobiographical memory specificity. They provided evidence for an association between emotional abuses and reduce memory specificity. Most subjects in study of Raes et al. (2005) are under depression and distressed. These types of people generally are cynical, apathetic and sometime irritable. Their problem of memory retention might be more related to the attention or concentration then the loss memory. Evidently, Bergouignan et al. (2006) found out that there is no global episodic autobiographical memory impairment in patients with remitted depression.

- *Time Order*

All three patients reported episodic images from memory of yesterday, but could not recall them in time order (See Tab.3-31). Two healthy elderly subjects and a subject with mild depression performed time ordering successfully without any difficulty.

Several previous studies (Johnson & Kesner, 1997; Storandt et al., 1998; Lawlor et al., 2004) found patients in the early stage of AD had impaired time order memory. This finding was reinforced in the present study as it too discovered patients in the early stage of AD had difficulty arranging retrieved episodic images in order of occurrence. Yasuno et al. (1999)

specifically investigated impairment in temporal order memory, and suggested it was caused by direct disconnection between the frontal lobe and hippocampus by disruption of the fornix. Several studies also revealed that the hippocampus is closely related to pathogenesis of AD in the early stage of AD, as well as to episodic memory. Tulving et al. (1994) indicated in a neuroimaging study that patients with frontal lobe damage have great difficulty remembering the temporal order of events. Kopelman (1989) also already discovered that the patients of Alzheimer's disease are impaired at anterograde temporal context memory likely the patients of Alcoholic Korsakoff.

The results are also supported by many studies of AD which discovered that patients in the early stage of AD have impaired anterograde memory. For example, HGB recalled and reproduced episodic images of memory of yesterday in as much quantity as healthy elderly controls, as well as performing just as well in neuropsychological tests K-DRS and MMSE-K. Nonetheless he had difficulty recalling events of yesterday in time order. Such outcomes also manifested in a test of retrieving the contents of an interview the following day of a test performance. Healthy elderly subjects retrieved objects or images in time order on the following day, even when not asked to recall in sequence. Although the number of AD patients who retrieved memories is inadequate for analysis, those who did retrieve did not do so in time order.

- *Number of Images and Images in the Following Day*

The most remarkable deficit observed in the early stage of AD is anterograde memory decline as showed Fig.3-1, an issue investigated in many studies (Greene & Hodges 1996a; Lawlor et al., 2004).

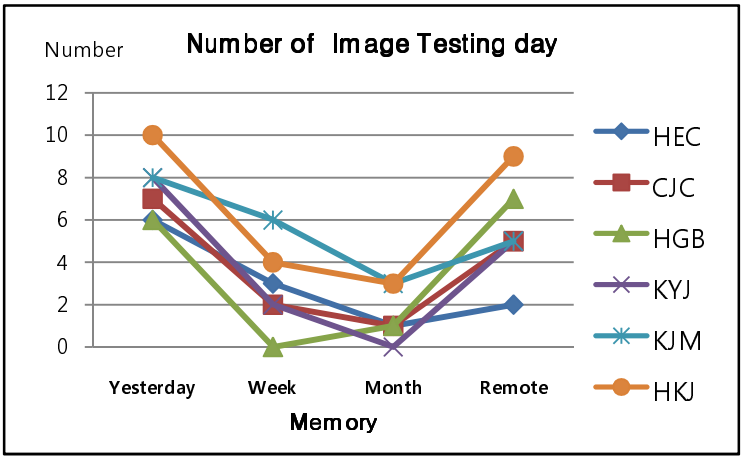

Figure 3-1. Number of the retrieved episodic image on the testing day

In the present study, all three AD patients were tasked to recall all episodic images retrieved on testing day on the following day of the interview test. As expected, they did not retrieve them as well as the controls. They were confused by the neuropsychological and interview test. As show from Fig.3-2, HEC recalled the images in as much quantity as the controls, but she did not reproduce them in sequence or in details. She had to be reminded to remember a significant amount of times. While HGB reproduced the images in detail and order, he nevertheless recalled less than HEC.

In retrieving remote memory, AD patients retrieved and reproduced episodic images at levels close to those of healthy elderly people. The impairment of retrieval of remote memory, encoded before the onset of the disease, has not been observed in the early stage of AD in several studies (Greene & Hodges, 1996b; Larsson et al., 1999; Leube et al., 2003). According to

present results however, AD patients were observed to not reproduce their remote memories as vividly in emotional quality as their healthy counterparts. Similarly, Steinvorth et al. (2005) observed that Medial temporal lobe structures play the significant role in re-experience autobiographical memories in remote past through reporting two cases of amnesic patients in MTL lesion

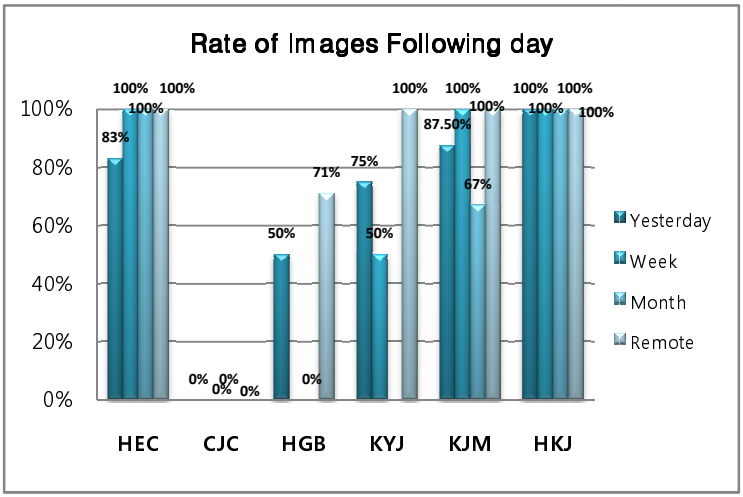

Fig. 3-2 Rate of images on the Following day

The second chapter presented evidence of deficit of the memory in AD by statistic level of significance. The clinical case report that comprises another approach in the current study suggests an interesting outcome. In the clinical case reports, practical problems observed and confronted in the actual clinical field provide a different perspective on the

problems discussed. For example, HEC may be diagnosed as AD according to the results of the neuropsychological test, but this patient was not diagnosed with the disease for more than a year. Instead, she was diagnosed and treated for her mild depression. She was able to remember things that happened yesterday as well as healthy controls, and she was only fifty years old. Her memory problems were taken to be light forgetfulness that comes with age. However, her deficit in episodic memory revealed otherwise.

HGB's case is the inverse of HEC's. This patient performed well in neuropsychological tests. His scores, in fact, were higher than the general score of healthy controls. He could not, however, recall order of occurrence or details in the interview test.

In the experiment, the interesting fact that some subjects of all subjects from experiment 1 recalled insignificant images which were not related to particular events and the images which they were not experienced in the past during the retrieval of remote especially has been observed. More precisely, some subjects did not copy the reality into the images. Probably such images might be their illusions and/or fantasy. They, in fact, reorganized the event in the images in the reproduction and even some of them did not recognized whatever they were projected from reality to images. Several studies (Schacter et al., 1997; Hyman, Jr. & Loftus, 1998; Hyman, Jr., et al., 1998; Johnson & Raye, 1998; Miller & Gazzaniga, 1998; Pezdek et al., 2006; Karpicke et al., 2008) defined this phenomenon or such metamemory as false memory and confabulation. Norman and Schacter (1997) investigated illusory memories of elderly people comparing younger adults. They reported that older people were relatively more susceptible to false recall and recognition

effect than youngers and indicated that elderly people have difficulties recollecting the true information in confusing perceived and imagined experiences. Several studies (Balota et al., 1999; Waldie & Kwong See, 2003) investigated the false memory effect in comparison between healthy older adults and AD's patients and indicated the patients group increased the susceptibility to false memory in effect. Such findings, in fact, were observed in the current experiment. Especially, some Patients had great difficulty maintaining the retrieved images. In the case of HGB, he had to recall the same images again in again for maintaining them and he became more incoherent and confused over time. And then we observed that one his image overlapped into another image or into the illusory memory. In the case of healthy elderly subjects, we observed such things rarely too, but they tried to eliminate the false image and may distinguish between illusion and reality. In the experiment, this fact was verified and evaluated in the 'details' questioning subject on the congruence of the event in the retrieved episodic memory, but it's not enough because the goal of the current study is not regard to verify false memory effect of AD patients. We believe, however, that it needs to investigate about this subject in depth for illuminating our future research of the episodic memory.

In the early stage of AD, the general symptoms of AD such as being unable to recognize family members or one's own street do not occur. Erroneous diagnosis is all too easy in the very early stages of AD. Healthy elderly subjects such as KMM and HNN performed the tests without any kind of difficulty or problems. They reproduced retrieved images concretely, in sequence, and with emotion, even when not tasked to do so.

Following the results of this study, evaluating the retrieval

ability of episodic memory from the patient's own past will be useful towards making a more accurate diagnosis of Alzheimer's disease.

Chapter VI
GENERAL DISCUSSION

Episodic memory is retrieved in our brain in the manner of a projected image of a picture or a movie (Fink et al. 1996), encoded together with the various characteristics an experienced event. It is reproduced together with these encoded and stored characteristics such as feelings, sound, and sensory modalities. The present study focuses on evaluating episodic memory using the introspection technique through analyzing the characteristics of the projected mental images of the subjects' own past.

Experiment 1 is designed to determine the effect and process of normal and pathological aging on cognitive skills in episodic memory by analyzing projected mental images. In Experiment 2, the subjects' voice intonations were observed by 8 valuators for evaluating the emotional intensity of episodic memory. The third chapter supports the results of Experiment 1 with further evidence, analyzing from a clinical viewpoint 3 patients with AD, 1 patient with mild depression and 2 controls

The current study shows significant impairment in the ability to recall the images of episodic memory in patients in the early stages of AD compared to that of normal elderly volunteers as several previous studies suggested (Grosse et al., 1991; Greene & Hodges, 1996; Thompson et al., 2003). Such impairment is quantitatively evident, with the number of retrieved mental images in the AD group significantly lower than controls as shown in the statistical analysis. Results also show qualitative differences, with some patients while recalling the same amount of the mental images of episodic

memory failing to logically recall the details of images (for example, exactly when and why they were in the image, as demonstrated in the case analysis in Chapter III).

Impairment in retrieving anterograde memory in patients with AD was observed in the Experiment 1, also in line with previous studies that suggested patients with AD have greater problems in encoding, storing and retrieving new information (Hodges et al., 1990; Thompson et al., 2003). During the test, several patients with AD failed in recalling the memory of a week and a month ago, which also had significant statistical effects. On the other hand, such patients would successfully recall the memory of remote events. In other words, memory encoded and stored after the onset of AD deteriorates, but memory that is set up before onset is not impaired, at least not in the early stage of AD. As revealed by certain neuro-imaging studies (Fink et al., 1996; Buckner & Koutstaal, 1998), the temporal lobe, hippocampus and peripheral-hippocampal areas play an important role in explicit memory, with impairment in those areas occurring in AD patients (De Leon et al., 1989; George et al., 1990).

There were several studies (Cornoldi et al., 1989; Dror & Kosslyn, 1994; Cocude et al., 1997; De Beni et al., 2006; Gardini et al., 2006) concerned with autobiographical images and visual images, focusing on the generation and the maintenance and transformation of visual images, an approach modified for this study to focus on the specific features of the image. In Experiment 1, we attempted to use this new method based on previous research concerning episodic memory. The present method is delineated to evaluate our episodic memory qualitatively, analyzing the color, movement, position of the images, the subject's perspective of the image, and the time order of images. Results show that controls successfully

recalled colorful and moving images in memory of yesterday. They still recalled such images when they retrieved impressive events in remote memory. However, they also recalled some stationary and black & white images in the retrieval of the remote past. In contrast, patients with AD did not recall colorful and moving images as the controls did in the retrieval of memory of yesterday. They also had great difficulty recalling mundane daily life events. This deficit also happened to a patient in the earliest stage of AD who can still attend hospital on his/her own as described in Chapter III. Impairment in arranging past events in order of occurrence has been discovered by several previous studies (Johnson & Kesner, 1997; Storandt et al., 1998; Lawlor et al., 2004). The present study also revealed that the patients in the early stage of AD had impaired time order memory. In Chapter III, a subject with mild depression was shown to recall fewer images compared to healthy elderly subjects, but reproduced exact details of each image. Their problem of memory retrieval might be more related to low attention resulting from cynicism, apathy and irritability than the memory loss that can be observed in patients with AD. Bergouignan et al. (2006) suggested that episodic autobiographical memory is not impaired in patients with remitted depression.

Episodic memory could be of a particular event experienced in the past. When we recall a particular event, we do not retrieve only the objective facts of the event, but also reproduce feelings, sentiments, and sounds etc., as such characteristics are encoded together with emotion through the different sensory modalities and then retrieved with the emotion of the event as well as with the particular sensory modality. This study measures which emotional and sensory modalities are retrieved more in the retrieval of episodic

memory. Results show that vision is always reported in the retrieval of episodic memory, as expected. This may be inevitable because all subjects were tasked to recall mental images. It is interesting to note that in Experiment 1, patients in the moderate or severe stage of AD said that they had no images and saw only a white blank when this test was administered to them. But they reacted actively when they recalled mental images of remote memories. These subjects often reproduced mental images with sound, with some of them even simulating that sound during the test. Vision and audition were the most used sensory modalities when retrieving episodic memory in both groups.

Several studies have suggested that the early stage of AD is associated with impairments of emotional processing (Cadieux & Greve, 1997; Hargrave et al., 2002; Bucks & Radford, 2004). In the results of Experiment 1, almost all subjects recalled more happy events in all four categories of memory in both groups. Hargrave and her colleagues (2002) have already suggested that happiness is retrieved the most among the six different emotions. This result may look as if it suggests that patients with AD in early stages have no problem recognizing emotions according to the context of the retrieved image. However, these results come from analysis of context. In other words, it does not measure how the subjects were involved emotionally during the actual retrieval of the episodic memory. For this reason, in Experiment 2, emotional intensity was measured examining the emotional expression (prosody/vocal intonation, tone and speech speed) by 8 valuators who measured how much the subjects expressed emotion during the retrieval of an emotional episodic memory. The results reported significant mean differences between two different groups. This indicates that patients in the early stages

of AD are impaired in the ability to express emotions in the retrieval of the episodic memory. Several neuro-imaging studies have identified brain areas which are involved to emotional memory retrieval (Fink et al., 1996; Fletcher et al. 1998a; 1998b; Dolan et al., 2000). The pathology in these brain areas was associated with impairment of episodic memory retrieval, such as primary deficit in AD.

In this experiment, some patients spontaneously recalled false memories during their recall of daily life events, in particular during the retrieval of remote. Several patients reported mental images from fantasy or illusory memory. Many previous studies defined this phenomenon or such metamemory as false memory and confabulation (Schacter et al., 1997; Hyman, Jr. & Loftus, 1998; Hyman, Jr., et al., 1998; Johnson & Raye, 1998; Miller & Gazzaniga, 1998; Pezdek et al., 2006; Karpicke et al., 2008). In fact, we too observed such findings in the current experiment. Several patients had difficulty maintaining the retrieved images, and their images overlapped with other images or with illusory memory. We also observed such phenomenon in the controls from time to time, but they tried to eliminate the false image and distinguished between illusion and reality. We tried to falsify and evaluate this fact in the ‘details’ part, questioning the subject on the congruence of the event in the experiment.

In this study, a new method was used for evaluating episodic memory. Special consideration was made for the subjects, who were likely to find previous methods difficult or awkward. Interestingly, the healthy elderly people mentioned that this method was more user-friendly than the standard neuropsychological tests, for it was based on their own memories. It is also a useful method for those patients who need regular administration of neuropsychological tests, for

this method has no learning effect.

Episodic memory is one of our most important and complex cognitive skills utilized in daily life. This study attempts to objectively evaluate episodic memory through a method that combines quantitative and qualitative measures. Impairment of episodic memory was shown to occur not only by such pathology of Alzheimer's disease, but also in the normal aging process. Additional studies shall attempt to utilize young subjects in order to further illuminate the progress of episodic memory deterioration.

SUMMARY

The current research attempts to examine and analyze cognitive skills in episodic memory through a new method which is assessed mental images of the subject's own past reproduced in the mind like projected pictures and movies.

Chapter I gives a theoretical perspective on episodic memory and Alzheimer's disease. The general concept of episodic memory including its definition from cognitive and neuroanatomical aspects is described, and the features of previous experiments in episodic memory are presented. The theoretical concept of Alzheimer's disease is also presented in this chapter towards understanding the causes, diagnosis and prognosis of this disease.

Chapter II presents two empirical studies, one regarding the analysis and evaluation of the mental images produced in episodic memory and the other measuring the emotional intensity of the subjects reproducing their own pasts. The first experiment examines cognitive skill in episodic memory by analyzing the effects of normal aging and AD. 40 subjects participated within two groups: 21 patients with AD and 19 normal control patients, aged 55 to 70. All subjects retrieved their episodic memory of the previous day, week, month and a day remote from testing day. The retrieved mental images of the episodic memory were analyzed, focusing on their specific features. In the following day, subjects were tasked to recall again all the images that they retrieved in the previous day's test. This was done to observe impairment in anterograde memory. Results revealed that patients failed to arrange the retrieved images in time order and their images of the previous day were unclear in color and were stationary like

photographs, even when they reproduced the mental images at as much quantity as controls. In the early stage of AD, decline in the retrieval of recent episodic memory were shown to occur, and qualitative impairment happened earlier than quantitative.

In Experiment 2, the subjects' voice intonations were estimated by 8 valuators for investigating the impairments of the emotional intensity of episodic memory in AD compared to a healthy elderly group. The results showed that the emotional intensity of AD patients were evaluated lower than controls. This demonstrates that the ability to express emotions during emotional episodic memory retrieval is impaired in the early stage of AD.

The third chapter supports the results of Experiment 1 with further evidence, analyzing from a clinical viewpoint 3 patients with AD, 1 patient with mild depression and 2 controls. The fourth chapter concludes the study with a general discussion synthesizing the theoretical framework and all the results, providing a general perspective of the dissertation.

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Finally, I dedicate this dissertation to my parents. I do not know where I would be today without their unconditional trust and devotion.

Appendix I

Used Pictures as examples

Appendix II

Form of the questions using in interview

1. What is your first picture for yesterday? Or what kind of pictures do you remember for yesterday? And then?
2. What is your picture for last week excluding yes terday?
3. What is your picture for last month excluding ye sterday and last week?
4. What is your first picture for your entire life (ch ildhood, puberty and etc)?

1. Could you tell (explain, describe) me everything about the picture as much as possible?

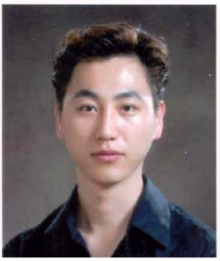
1. Does your picture have colors or not?
2. Is your picture moving or stationary?
3. Are you yourself in the picture or front of the p icture?
4. Is there a specific person or many?
5. Is there particular object in your picture?
6. Do you have deep pain?
7. Do you feel disgusted with this picture?
8. Are you happy or surprised? Or are you angry, a nxious or sad?
9. Is this picture positive/negative memory for you? Why?
10. Do you smell, hear, touch or taste something?
11. How do you feel to this smell, sound, touch and taste accompanying the picture?

12. Do you have pictures of sexual activity in your memory? (for yesterday, etc)

1. Is the picture front, behind, up, down, left or rig ht of you?
2. Do you have entire vision?
3. Is the picture moving like movie or is the pictur e itself moving?
4. How many details could you describe in the pict ure?

1. What are you doing in there?
2. Do you think why you are there?
3. Do you remember when?
4. Do you remember where?

1. Could you tell (describe) me everything about the picture of the day before yesterday that you have described me yesterday as much as possible?



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