Neural Correlates of Episodic Memory Formation in Audio-Visual Pairing Tasks

Chung-Yeon Lee (cylee@bi.snu.ac.kr)
Brain Science Program, Seoul National University
Seoul, 151-744, Republic of Korea

Beom-Jin Lee (bjlee@bi.snu.ac.kr)
Computer Science and Engineering, Seoul National University
Seoul, 151-744, Republic of Korea

Joon Shik Kim (jskim@bi.snu.ac.kr)
Cognitive Science and Brain Science Programs, Seoul National University
Seoul, 151-744, Republic of Korea

Byoung-Tak Zhang (btzhang@snu.ac.kr)
Computer Science and Engineering &
Cognitive Science and Brain Science Programs, Seoul National University
Seoul, 151-744, Republic of Korea

Abstract
Understanding episodic memory formation of real-world events is essential for the investigation of human cognition. Most studies have stressed on delimiting the upper boundaries of this memory by using memorization tasks with conditional experimental paradigms, rather than the performance of everyday tasks. However, naturally occurring sensory stimuli are multimodal and dynamic. In an effort to investigate the encoding and retrieval of episodic memory under more naturalistic and ecological conditions, we here demonstrate a memory experiment that employs audio-visual movies as naturalistic stimuli. Electroencephalography measurements were used to analyze neural activations during memory formation. We found that oscillatory activities in the theta frequency bands on the left parietal lobe, and gamma frequency bands on the temporal lobes are related to overall memory formation. Theta and gamma power of the frontal lobes, and gamma power of the occipital lobes were both increased during retrieval tasks. Furthermore, subjects’ memory retrieval performance on the query task was used to clarify our experimental results. Correlation between behavioral differences and neural activation was observed in the same regions. Our results extend the previous results of neurocognitive studies on memory formation via naturalistic stimuli, neural oscillations, and behavioral analysis combined.

Keywords: Memory formation; Naturalistic stimuli; EEG study; Neural oscillation; Reaction time.

Introduction
Memory processing is one of the most prominent features of human cognition. Particularly, understanding how the experience of an episode in our everyday life can be transformed into a long-term memory is a central issue in human memory research.

Episodic memory formation is a complex neurocognitive process that involves many interacting brain regions, and enables us to store contextual (spatial and temporal) information about individual events that can be later retrieved. In contrast, semantic memory consists of isolated facts that are decontextualized and not organized into a specific experience.

Research in cognitive neuroscience thus far has focused on the human memory system, and much knowledge has been acquired via the neuropsychological examination of brain-lesioned patients (Milner, Squire & Kandel, 1998; Squire, 2004). Furthermore, noninvasive neuroimaging studies in the last decade have revealed numerous functional roles of particular brain regions related to memory phenomena (Freeman, Dennis & Dunn, 2010; Spaniol et al., 2009).

However, the vast majority of experimental protocols used to study the neural mechanisms of episodic memory formation (Schacter & Addis, 2007; Vissers et al., 2008) deal with well-controlled experimental setups in which conditional static stimuli (e.g., single words or still images) are presented for memorization. They are typically dissimilar from what the human brain encounters in everyday life, since naturally occurring sensory stimuli are continuous and multimodal. (Bartlett, 1932; Jacobs & Shams, 2010; Tulving, 2002).

In an effort to investigate episodic memory encoding and retrieval under more naturalistic and ecological conditions, we performed a memory experiment employing audio-visual movies to mimic natural stimuli.

Movies are suitable for use as naturalistic stimuli because they reflect aspects of experiences in our daily lives by fusing multimodal sensory perception with emotional and cognitive overtones (Eisenstein, 1947; Hasson et al., 2007; Morin, 2005). In fact, cinematic materials have been used to explore memory since the early days of cinema (Boring, 1916), but only recently have some neuroimaging studies used audio-visual movies as natural stimuli for the examination of brain activation induced by memory.
operations (Ben-Yakov et al., 2011; Furman et al., 2007; Green, Li & Bavelier, 2011; Hasson et al., 2007; Milton et al., 2011; Sestieri et al., 2011).

In contrast to recent studies investigating memory processes with functional magnetic resonance imaging (fMRI) during the presentation of video stimuli, here we aimed to examine brain activation using electroencephalogram (EEG) recordings. Neural oscillations have been linked to various cognitive phenomena in humans. Although there is no exact mapping of neural oscillatory rhythms to specific cognitive processes, neural oscillations in a specific frequency range in each brain region may function as their own cognitive process (Başar et al., 1999; Bechtel & Abrahamsen, 2010; Kahana, 2006; Klimesch et al., 2008).

We focused in this study on gamma and theta oscillations because recent research has suggested a functional role of theta (4–8 Hz) and gamma (30–50 Hz) oscillations in episodic memory (Doppelmayr et al., 1998; Klimesch et al., 2001, 2008; Osipova et al., 2006). Other rhythms such as delta (1–4 Hz), alpha (8–13 Hz), and beta rhythms (13–30 Hz) have not been discussed because they have not been consistently reported as being related to episodic memory, and they correlate not only with episodic memory but also with semantic memory (Düzel et al., 2005; Hanslmayr, Spitzer & Bauml, 2009; Weiss & Rappelsberger, 2000).

A secondary aim of this study was to investigate memory retrieval in consideration of the subject’s behavioral factors. Because the human brain can be easily affected by numerous factors that disturb the expected neural response to experimental paradigms, there may not be a specific interpretation of the acquired neuroimaging results. To alleviate this problem, we designed a 2-way analysis of brain oscillation rhythms based on subjects’ memory retrieval task performance. Using this approach enables the results of our oscillatory analysis during memory formation to be supported by behavioral analyses.

Materials and Methods

Two goals were considered when constructing the task and methodology used in this study. First, a set of memory tasks was designed to look at 2 aspects of episodic memory: encoding and retrieval. Second, we obtained EEG data on the scalp while memory tasks were being performed by subjects in order to specify the anatomical locations of brain activations associated with episodic memory formation.

Subjects

Ten neurologically healthy subjects (mean age, 24.0 ± 2.7 years; 4 women) with normal or corrected-to-normal vision (mean eyesight in left and right eyes, 0.87/0.80) were recruited from Seoul National University (Seoul, Korea). Informed consent was obtained from all subjects in accordance with the guidelines of the institutional review board (IRB) at the Clinical Research Institute of Seoul National University Hospital.

Stimuli

The experimental stimulus used in the encoding session was an audio-visual movie containing an episode of a television sitcom (duration, 27 minutes). The spoken language in the movie was American English, and subtitles were not displayed.

We extracted 20 video clips (each of 5 seconds), taking into consideration the current of its story, and captured 40 subsequent still images from the movie. These short video clips served as retrieval cues in the retrieval session of the experiment, and the captured images were used in the query tasks.

To make the experiment more accurate, we also developed a software program capable of displaying stimuli, including movies and images, sequentially following fixed time as input by an experimenter. Additionally, the program records subjects’ responses and reaction times (RTs) during query tasks, so that these records could be used in EEG analysis. In the program, all the stimuli are 130 mm wide and 100 mm high, and were displayed with a black background on a 15-inch LCD monitor placed approximately 50 cm away from the subject.

Experimental Paradigm

The entire experimental procedure is depicted in Figure 1. The memory experiment program begins with a tutorial task consisting of a concise example set of whole experiments in order to allow subjects to become accustomed to the experimental procedure.

Following the tutorial, the encoding session starts, playing an episode of a television sitcom in its entirety. The subjects watched the movie without requiring any response. EEG measurement also began at this point. The EEG data were analyzed later by using the time stamps recorded by the program.

In the retrieval session, each subject performed video cue-based free recall tasks by imagining the scene immediately following the cue stimuli. Finally, as for the query task, 2 images contained in the cue video were presented in a random order. The subject was asked to decide whether the order of presentation is correct or incorrect, and press the “O

![Image](image_url)
(correct)” or “X (incorrect)” button on a small keypad.

The experiment constituted 20 rounds of the retrieval task.

EEG Measurement

Ongoing brain activity was recorded using Ag/AgCl electrodes mounted in a 128-channel Quik-cap, and a Neuroscan SynAmps amplifier (Neuroscan, El Paso, TX) in a dimly lit, soundproof, electrically shielded room at the Clinical Cognitive Neuroscience Center of Seoul National University Hospital. The ground electrode was located 10% anterior to FZ, with linked mastoids serving as references. Eye movements and blinks were monitored by a horizontal electrooculogram (hEOG) and a vertical electrooculogram (vEOG). Impedance was maintained at 5–10 kΩ or less. Throughout the experiment, EEGs were continuously obtained at a sampling rate of 1,000 Hz/channel.

EEG Data Analysis

EEG data analysis was performed using the EEGLAB toolbox (Delorme & Makeig, 2004) developed at the Institute for Neural Computation in the University of California San Diego\(^1\) using MATLAB 7.13 (MathWorks, Natick, MA). A baseline removal process was applied in order to eliminate some shift signals and to synchronize the zero levels of each channel. Eye movement artifacts were eliminated by excluding hEOG and vEOG components extracted by Independent component analysis (ICA). All signals were then band-pass filtered between 4.0 and 50.0 Hz in order to exclude unnecessary frequencies. Some electrodes on the prefrontal area (AF7, FP1, FPZ, FP2, and AF8) were excluded to reduce any remaining chance of including ocular artifacts. A fast Fourier transform (FFT) in the frequency domain on the artifact-free EEG record was then performed. Frequency bandwidths were divided according to the following divisions: theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (30–50 Hz). From the computed FFTs, overall power averages were computed for each bandwidth.

Experimental Results

Oscillatory Correlates of Memory Formation

2D brain maps showing the grand-average topographical distribution of theta and gamma frequency power during the 2 experimental conditions (memory encoding session and retrieval session) are presented in Figure 2(A).

First, we observed increased theta frequency activation on the left parietal lobe (C3 and CP1), and increased gamma activation on the temporal lobes (T7 and T8) during overall memory formation.

As seen in the topographical plots showing the difference between the encoding and retrieval sessions, theta and gamma power on the frontal lobes were more increased in retrieval sessions than in encoding sessions (indicated by

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\(^1\) http://sccn.ucsd.edu/eeglab

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**Figure 2**: Theta and gamma oscillatory activation during memory formation. (A) The first row indicates increased theta frequency power of the frontal lobes in the encoding task, and the second row indicates increased gamma frequency power of both the frontal and parietal lobes in the encoding task. Differences between retrieval and encoding tasks are depicted in the third column with ‘x’ markers which stand for locations showing the major differences. (B) Normalized theta and gamma frequency power values on the 8 topographical regions of interest (frontal left, FL; frontal right, FR; parietal left, PL; parietal right, PR; occipital left, OL; occipital right, OR; frontal center, FC; and occipital center, OC) shows quantitative differences between encoding and retrieval sessions. In the retrieval session, theta activations on the left and right frontal regions were increased. Gamma activations on the frontal and parietal regions were increased, although other regions were decreased.
positive values of the difference between encoding and retrieval in Fig. 2(A)). Some of occipital theta powers in the retrieval session were also increased, but they were not significant differences. Contrarily, theta powers on the occipital center regions were decreased in retrieval sessions. Occipital gamma power was increased during the retrieval session. Independent t-tests verified that both differences are statistically significant for theta ($F = 3.771; p < 0.005$) and gamma frequency powers ($F = 3.902; p < 0.001$).

**Analysis based on Behavioral Factors**

To clarify our finding regarding neural oscillations associated with memory formation, correlation between EEG and RT of the query task was analyzed. We classified the experimental results from 20 query tasks into 2 types: sustained RT and instant RT. Sustained and instant RT represent an RT that is longer and shorter, respectively, than the sum of the average and standard deviation of all RTs. Fig. 3 depicted RT histogram of one subject as an example. Theta and gamma oscillatory activations during the query task were then analyzed in consideration of the 2 different classes of responses on query tasks.

Interestingly, as shown in the topographical plots in Fig. 4, a correlation between neural activation and RT of subjects in query tasks were observed in the theta and gamma oscillations in some meaningful brain regions: increased theta power on the left parietal lobe, and increased gamma power on the right frontal and left occipital lobes during query tasks with sustained RT.

This indicates that memory formation, especially retrieval, is more activated when subjects make more effort on the query tasks. Additionally, this result supports the notion that regions with high theta and gamma power, including the left parietal lobe, right frontal lobes and left occipital lobes, are related to episodic memory retrieval.

As for other behavioral factors, the average correct response rate on the query task was 69.4% (about 14 questions were correct) and the average RT for each query task was 7.1 ± 3.3 seconds. However, there was no significant effect observed in the frequency power analysis of factors such as true/false sequential order of presented pictures in the query task, correctly/incorrectly answered tasks, or the correlation between RT and these factors.

**Discussion**

Recently, many functional neuroimaging studies using fMRI or positron emission tomography (PET) have shown that specific brain regions are significantly correlated with memory formation. For example, the temporal lobes have been long associated with memory retrieval (Nakamura & Kubota, 1996), and the medial prefrontal cortex (mPFC) and transverse occipital sulcus (transOcS) have been shown to play a significant role in subsequent memory retrieval (Hasson et al., 2007). Furthermore, neural oscillations in the gamma and theta frequencies have long been observed in cognitive tasks, such as those used to investigate episodic memory, and in focal lesion studies (Milner et al., 1985; Nyhus & Curran, 2010).

In consideration of using naturalistic stimuli, unlike traditional experiments that have consistently revealed memory effects for still images or words, we observed similar results in both the spatial and spectral domains. Moreover, our results link the frequency domain with each observed region (i.e., delta frequency on the frontal and left parietal lobe, and gamma frequency on the frontal and occipital lobes). This is similar to the results of several
studies that have shown greater gamma power in the posterior cortex for subsequently remembered items than for forgotten items (Hanslmayr et al., 2009; Osipova et al., 2006).

As for the individually different effects of the experimental stimuli, there is some evidence from previous studies showing the same effect in a previous experiment using similar movie narrative stimuli (Hasson et al., 2004; Wilson, Molnar-Szakacs & Iacoboni, 2008). Thus, a statistical evaluation showed that the observed brain activations in our results are significantly different from each other.

Our study has some limitations. It is not entirely unexpected that there was no significant correlation observed between correctly and incorrectly answered questions in the query task, because the subject might not care what the correct answer is at the time of the task. In addition, the paradigm of the query task is too ambiguous to determine which image has been shown earlier, because the presented images were both taken from the same scene. This problem could be addressed by choosing 2 images from different scenes, but such a paradigm might also evoke some semantic memory processes, with the subject cued by many possible different factors in the images or stories, such as actors’ clothes and the scenery of each scene. Instead, RT seems to be a more appropriate factor for behavioral analysis because RT will be longer when subjects make more effort to retrieve stored memories, and thus, the brain region related to retrieval memory will be more activated at that time.

Conclusion
In summary, we have demonstrated episodic memory formation using with an audio-visual movie as a naturalistic stimulus, and measured subjects’ EEG signals throughout the task in order to reveal the neural responses involved in episodic memory operations. We also developed a memory task program designed to obtain more accurate experimental results. We identified oscillatory activities related to memory formation in the spatial and spectral domains. Different oscillatory activities in the retrieval session were also observed. A correlation between RTs and oscillatory activation during the query task was observed in the same regions. We expect that our naturalistic and behavioral factor-based analysis approach for memory investigation could help extend the range of neurocognitive research.

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