

ELECTROPHYSIOLOGICAL POTENTIALS IN THE HIPPOCAMPUS
DURING RECOGNITION MEMORY

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ABSTRACT

Neural circuits within the medial temporal lobe, including the hippocampus, support recognition memory. Patients and animals with circumscribed hippocampus damage experience significant episodic memory deficits but their general intellectual abilities remain intact. The present thesis sought to determine whether electrical field potentials generated in the hippocampus during a recognition memory task are influenced by stimulus repetition. Electroencephalography (EEG) is a non-invasive technique used to measure the voltage changes on the scalp in regards to a specific cognitive event. Event related potentials (ERP) is a post-hoc analysis of recorded EEG and allows the voltage changes to be time-locked to the occurrence of an event. EEG/ERP analysis was used to measure the voltage change in normal, healthy college students in a recognition memory task. When visual stimuli are presented repeatedly certain ERP components that are associated with recognition memory are attenuated, although some discrepancies exist in the literature. Beamforming spatial filtering analysis is a source estimation technique that allows inferences to be made about the locations of generators of the evoked potentials that are recorded at the scalp. In the current study, a repetition effect was observed for pictures and words at select electrode sites. Pictures and words previously seen (“Old”) had significantly decreased peak amplitude compared to pictures and words that had not been seen before. Although stimulus repetition clearly attenuated electrophysiological signals recorded on certain regions of the scalp, beamforming analysis of the hippocampus showed that these changes were not accompanied by similar changes in the field potentials generated within the hippocampus. Interestingly, however, pictures and words produced markedly different hippocampal field potentials.

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Finally, to my parents, thank you for the love, sacrifice, and understanding throughout the years.

DEDICATION

This thesis is dedicated to my late grandfather, Wilson Harrell George. It was you who ignited my interest in the brain. Never forgotten and always loved.

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Electrophysiological Potentials in the Hippocampus during Recognition Memory

Recognition occurs so quickly and automatically that in everyday life we generally give little thought to how the brain accomplishes it. This thesis project will measure bioelectric signals generated in the medial temporal lobe, a group of brain structures known to be crucial for recognition memory, that are generated during the first few hundred milliseconds after a stimulus is observed and determine whether those signals are related to the cognitive processes involved in recognition memory.

Recognition Memory

Mandler (1980) defined episodic recognition as making the judgment that an item has been previously encountered. Mandler argued that recognition involves a sense of knowing that the item has been previously encountered and then a search for insight as to the contextual information that is associated with the item.

Many researchers discuss recognition memory as two separate parts: familiarity and recollection. There is an on-going debate on whether these two separate components of recognition memory exist independent of one another (i.e., dual processes) or if a single process can account for both familiarity and recollection. The present study, however, is not designed to investigate the dual process question. Rather, the focus of the present study is on the patterns of electrophysiological activity that occur in the hippocampus during the early cognitive processes involved in recognition memory.

Amnesia and the Medial Temporal Lobes

Numerous studies have linked the medial temporal lobes to recognition memory. These studies range from neuroimaging (for a review, see Rugg and Yonelinas, 2003), brain damaged humans (Scoville 1954; Scoville and Milner, 1957; Zola-Morgan, Squire and Amaral, 1986;

Manns, Hopkins, Reed, Kitchner, and Squire, 2003), and animal lesion studies (Meunier, Bachevalier, Mishkin, & Murray, 1993; Suzuki, Zola-Morgan, Squire, & Amaral, 1993; Mumby & Pinel, 1994). Scoville (1954) was one of the first to report severe anterograde amnesia in a patient (H.M) after a bilateral medial temporal lobe resection was performed to control seizures. H.M.'s lesions encompassed the hippocampus and surrounding cortex as well as the amygdala and surrounding cortex, bilaterally (Scoville 1954; Scoville and Milner, 1957). This classic case has served as a basis for a multitude of memory studies.

Since the classic studies of H.M., several other researchers have presented cases ranging in severity of medial temporal lobe damage and memory deficits. Zola-Morgan, Squire, and Amaral (1986) reported the first case of anterograde amnesia resulting from damage limited to the hippocampus. The patient in this study showed stable and long-lasting impairment resulting from damage limited to the hippocampus. Manns, Hopkins, Reed, Kitchner, and Squire (2003) compared seven patients with bilaterally damaged hippocampi to healthy controls on a number of recognition tasks. Results showed that the hippocampal damaged patients were impaired on all recognition tasks as compared to the healthy control subjects. Other human lesion studies have confirmed the link between the medial temporal lobes and recognition memory (Reed, Steffanacci, Hamann, & Squire, 1997; Rempel-Clower, Zola, Squire, & Amaral, 1996). What can be noted from most of these studies is that humans with medial temporal lobe damage show varying specific deficits that impair memory while sparing general intellectual ability.

Animal Lesions

Animal lesion studies have shed more light on the relationship of the medial temporal lobe and recognition memory. Animal studies permit a more detailed investigation of this relationship because lesion locations are precise and controlled. It is known from these studies

that surgical removal of the perirhinal cortex in both rats and monkeys results in recognition memory deficits (Meunier, Bachevalier, Mishkin, & Murray, 1993; Suzuki, Zola-Morgan, Squire, & Amaral, 1993; Mumby & Pinel, 1994). Recognition memory impairment varies as a result of varying degrees of medial temporal lobe damage, specifically the hippocampal circuitry.

There literally are thousands of published animal studies that have replicated memory impairments found in human subjects with temporal lobe damage. What remains unknown, however, is precisely how the hippocampus circuits encode, store, and retrieve memories.

Medial Temporal Lobe Structures

The medial temporal lobe consists of the hippocampus, subicular complex, perirhinal cortex, entorhinal cortex, and the parahippocampal area. Opposing views exist as to what structures are significant for certain memory components but as previously suggested the hippocampus circuit plays a significant role in recognition memory. Rugg and Yonelinas (2003) review a multitude of recognition memory studies, finding several links between recognition and the medial temporal lobe. Meunier et al. (1993) and Buffalo et al. (1999) found that on delayed non-matching to sample tasks primates were significantly impaired by lesions limited to the perirhinal cortex. To summarize this point, the perirhinal cortex seems to be associated with familiarity-based recognition (Brown & Aggleton, 2001) while lesions limited to the hippocampus impair recollection on complex association tasks (Eichenbaum, 2000).

Single cell recordings from medial temporal lobe structures in animals have also provided evidence to support the relationship between the medial temporal lobe, particularly the hippocampus circuitry, and recognition. As reviewed by Brown and Aggleton (2001), numerous studies show a suppression of neural activity to previously encountered visual stimuli. Neural activity enhancement is less frequently observed in animal research. Brown and Aggleton

summarize several studies that show neural signal suppression associated with the perirhinal cortex and less often in the hippocampus. Xiang and Brown (1998) recorded neural responses from the perirhinal, entorhinal, and hippocampus of monkey's brains during a visual recognition memory task. Suppression of neural activity in the entorhinal and perirhinal cortices was found with very little evidence of suppression in hippocampal neurons.

With a few exceptions, single cell recordings are rarely used in human research. However, through the advancement of technology, techniques have been developed that allow powerful inferences to be made about the location of these signals. By using these techniques, we can non-invasively look at the place single cell recording studies show activity. These techniques are the electroencephalogram (EEG), event related potentials (ERP), and beamformer spatial filtering analysis.

Electroencephalogram (EEG)

Electroencephalogram (EEG) records electrical activity from the scalp that is generated by the excitatory and inhibitory post-synaptic potentials (EPSP's and IPSP's) of neurons. EEG can only measure electrical potentials from organized layers of neurons in which the apical dendrites are perpendicular to the cortex. The EEG signal is derived from neuronal interactions; however, the location of this signal on the scalp is not simply an indicator of the cortical generator of this electric activity. A major issue with EEG data is the problem with conductance and the spread of the signal across a conductor. The electrical activity of the brain that is measured at the scalp passes through several compartments. Each compartment (white matter, gray matter, cerebrospinal fluid, skull and skin) has its own conductance and geometric shape. Fortunately, research on algorithms that permit one to calculate the distribution of the potentials

and to localize the generators of potentials has progressed rapidly over the past several years (Zani and Proverbio, 2003).

The electrical activity is derived by non-invasively attaching electrodes to the surface of the scalp and to an amplifier, which in turn yields a pattern of voltage variation over time. The variation that is recorded is known as the EEG. For a normal EEG, the amplitude of the signal varies from -100 to +100 μV ; the frequency ranges can reach 40Hz or more (Rugg and Coles, 1995).

The electrical activity that is generated in the brain and recorded from the scalp is a raw composite of billions of post-synaptic potentials. That is to say, there are many generators of electric activity as well as many different cognitive processes that may be occurring at any given time. These cognitive processes range from attention to sensory stimuli, basic regulatory processes, bodily movements, breathing, etc. In fact, EEG data provides so much information that it is impossible to decode specific neuro-cognitive processes that are embedded in the raw signal. In a review presented by Zani and Proverbio (2003), the EEG is described as representing fluctuations of spontaneous electrical brain activity that is varied by the state of general activation that the person is in, whether this be a sleep/wake cycle or other various stages of arousal. In order to attribute the activity occurring in the brain to specific internal or external processes, a technique known as event related potentials can be used.

Event Related Potentials

Event related potential (ERP) is a technique that allows the recorded electrical activity to be linked to certain neuro-cognitive processes. ERPs are an average of the electrical activity recorded by the EEG as a response to a particular type of event (sensory, cognitive, and motor)

that is repeated under experimental control. The ERP represents brief changes of potentials synchronized and time-locked to an event of interest (Zani and Proverbio, 2003).

An event related potential is a post-hoc analysis of the recorded EEG-activity. After the EEG has been recorded, an epoch of the EEG is defined which is time-locked to the presentation of the stimulus. Typically, this epoch encompasses about 2 s, beginning 200ms before the presentation of the stimulus and ending 1800ms later. The voltage changes that are present during this epoch may reflect a relation to the brain's response to the stimulus. These voltage changes represent the ERP components (Rugg and Coles, 1995).

ERP Components

The ERP component is a feature of the extracted waveform, either a peak or a trough. The measurement of the component is its amplitude (μV) and latency (ms). The amplitude can either be the relation of peak to peak or in relation to the baseline, depending upon the specific electrophysiological question being addressed. The latency is measured by the temporal relationship to the presentation of the stimulus. It is always a possibility that ERP components are overlapping; that is, the component is being generated by several different sources within the brain (Rugg and Coles, 1995).

Several problems arise when considering ERP components. Since there is the possibility of several generators that produce the distribution of electricity at the scalp, there is also the possibility of several sets of latent components that sum together to make the ERP signal (Luck 2005). Slotnick (2005) summarizes a point made by Helmholtz (1853) that while exact cortical source configuration yields distinct scalp topography, a number of cortical source configurations can yield the same voltage at the scalp. The problem is finding the configuration of the sources by looking at the topographic spread of voltage from the scalp; it is an ill-defined

mathematic problem with no one solution. This has been called the *inverse problem*. However, a solution has been developed that relies on certain constraints; this is known as the *forward solution*.

The forward solution involves two factors. First, the voltage that is recorded from the scalp travels through a multi-layered three-dimensional space, so a theoretical model of the electrophysical properties of the head is used in the analysis. The model that is used to represent the head consists of three concentric spheres, each with its own distinct conductance. Second, there are only certain configurations of neurons that can be recorded from the scalp, so the source configurations must model the possible anatomic neural configurations. The forward solution uses these given constraints to interpret the electrophysiological potentials recorded at the scalp.

ERP Components of Recognition Memory

The ERP components that will be considered in this study have been common within recognition memory studies. Rugg and Coles (1995) provide an extensive literature review of these components.

P100

The P100 is a typical sensory component found in all sensory modalities. It is associated with a series of deflections in the ERP that are related to the transmission of sensory information from the peripheral sensory system to the cortex and/or the arrival of that information in the cortex (Luck 2005). The P100 (or P1) reflects the processing of visual stimuli in the visual cortex. It is somewhat of a later sensory component than other modalities (e.g., auditory which can be on the order of 10s of ms) because the neurons in the sensory relay nuclei

(e.g., the lateral geniculate nucleus) are configured in such a way they create a closed field that does not reach the scalp (Rugg and Coles 1995).

N170

At occipito-temporal sites around 170ms post-stimulus a negative waveform is evoked by face, objects and words. Simon, Petit, Bernard, and Rebaï (2007) show that word repetition produces a larger N170 amplitude in the left hemisphere than non-repeated words. However when the same words were presented in different fonts, this amplitude difference was not observed.

P300

The P300 is the most studied ERP component. This is due in part to its size (5-20 μ V) and because how easy it is to elicit the component. The standard paradigm for the P300 is known as the 'oddball paradigm.' A series of events are presented to a subject, and the events are composed of two classes. One type of event is occurs less frequently than the other—hence the name oddball. Subjects are usually required to respond in some way to the rarer of the two events. The ERP components for the oddball stimuli usually consist of a positive deflection, that is maximal over the parietal/central area, and that has a latency of 300 ms up to 900 ms (Rugg, 1995). Donchin and Coles (1988) have proposed that this effect reflects a process of context of memory updating by modifying the current model for the environment due to the incoming information.

N400

The N400 component is sensitive to deviance to abstract attributes of the eliciting stimulus, such as meaning. Kutas and Hillyard (1980) were the first to observe the N400 in a now classic paradigm. Subjects were required to read a series of sentences comprised of about

seven words. Some sentences ended in semantically inappropriate but syntactically correct words, others with the final word printed in a larger font size than the preceding words, while other sentences were normal (they ended with appropriate words and the font was kept constant). Semantically deviant final words elicited a negative deflection with a latency of about 400 ms (the N400). Physically deviant words elicited the classical P300 (latency ~560 ms). Neither component showed up for the normal sentences.

Source Estimation using a Beamforming Algorithm

The beamformer technique recently has been developed for applications involving EEG signal source estimation. The methods used in the beamformer analysis are developed for RADAR signal analysis. Beamformer analysis uses both spatial and temporal filters to separate the signal and interference at the receiver. The data that is collected from EEG recordings does not have enough detectors to sufficiently represent it; however, the spatial and temporal information is available to support the EEG waveform. Beamformer analysis allows a beam of interest to be formed that accounts for the geometric shape of the electrode array and head (brain); this provides a characterization of the signal at the location of interest (Van Veen and Buckley, 1988). *A priori* judgments of regions of interest have been determined from animal lesion studies and will provide the target brain regions that are the focus of my analyses in this thesis.

Present Study

The goal of this study is determine whether ERPs generated in the medial temporal lobes reveal electrophysiological signatures of recognition memory. Previous researchers have studied recognition memory using several different manipulations (repetition, depth of processing, oddball paradigm, etc.). Some of these previous studies have also used neuroimaging techniques

to further examine the link between brain activity and recognition (Ally and Budson 2007; Van Petten and Senkfor, 1996; Curran, 2000). Several of these studies have provided a theoretical framework of spatial and temporal locations of the regions of interest. However, the analyses thus far has been dependent either on topographical measures, focusing exclusively on the distribution of potentials across the skull, or questionable source localization techniques, therefore, the interpretation of how different brain regions contribute to the ERP components is severely limited. While functional magnetic resonance imaging (fMRI) allows for precise three-dimensional location of the sources, there is a considerable temporal setback with this technique. EEG and ERP analysis allow continuous recordings of the electrical activity. Since EEG is recorded in real time, it is possible to examine the electrophysiological activity in millisecond resolution (Rugg and Coles, 1995)

The current study will use beamformer spatial filtering methods and focus an analysis on the hippocampus (ROI) bilaterally and use the primary motor cortex area bilaterally as a control. Previous animal lesion studies as well as amnesic and fMRI studies have provided guiding information about critical regions of interest associated with recognition memory. This study aims to address whether the repeated presentation of visual stimuli (pictures and words) changes the amplitude and latency of electrical signals in these structures. Beamformer spatial filtering analysis will allow the virtual placement of activity sensors within these structures. It is hypothesized that the primary motor cortex should not reflect activity that is associated with the recognition memory. Also, in order to test the validity of the beamformer analysis, a separate analysis of the response itself will be used as a proper control for the beamformer technique. It is hypothesized that during the response phase of testing, the primary motor cortex will be activated just prior to button presses.

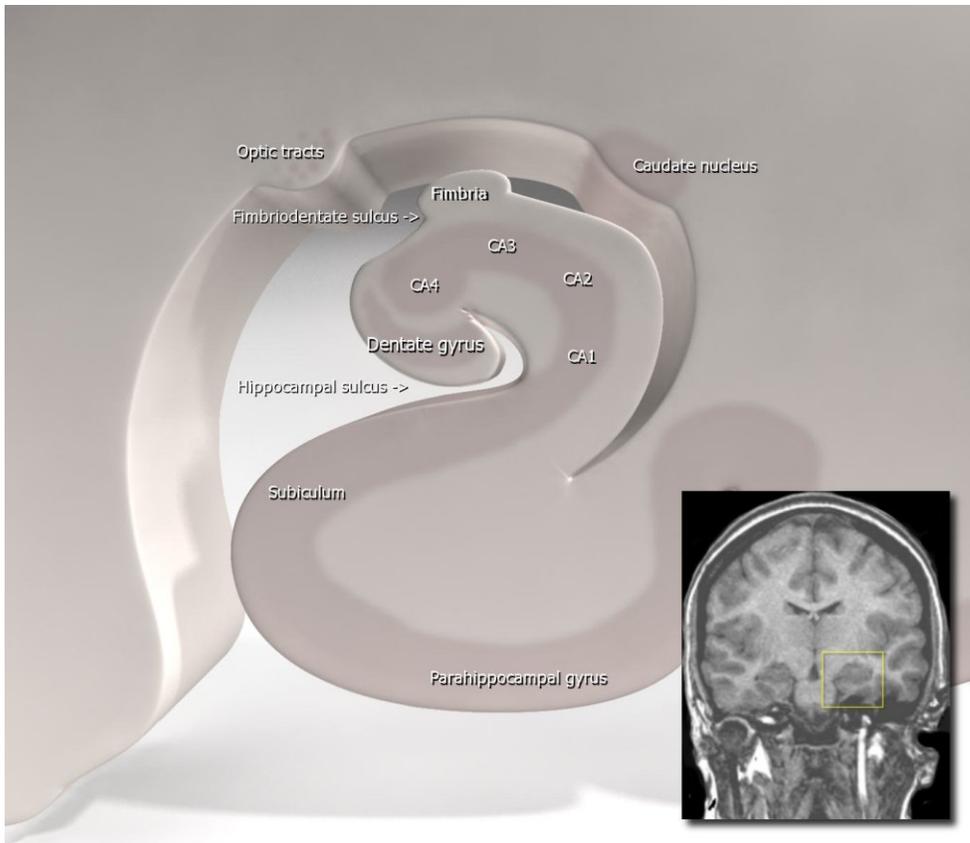


Figure 1. Coronal section of right hippocampus that is appropriately labeled with its subregions.

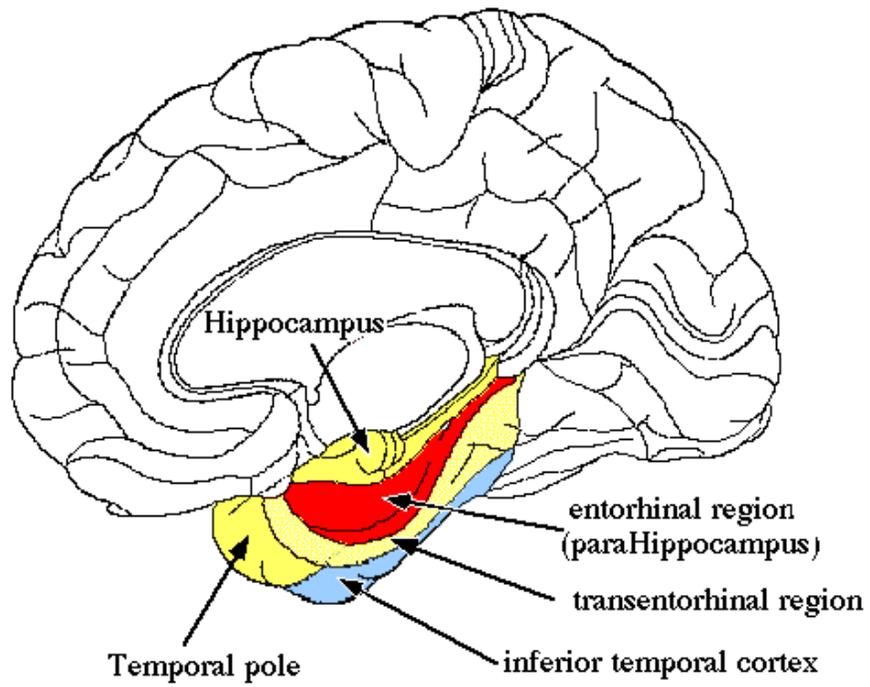


Figure 2. Illustration of location of the hippocampus and surrounding structures

Repetition Effect

A consistent finding from several recognition studies is that the repetition of stimuli produces more positive-going ERPs than novel stimuli (see review Rugg, 1995). Several researchers have studied this positive ERP modulation in repetition studies involving words and other stimuli in indirect tests (Bentin and Peled 1990; Rugg 1990, 1998; Van Petten et al., 1991). A typical study requires the subject to respond to occasional ‘target’ (e.g. non-words) items against a background of ‘non-targets’ (e.g. words). ERPs associated with the repetition of items are more positive going than ERPs associated with the first presentation of an item (for a review, see Rugg 1995). This positive going ERP modulation has been named the *ERP repetition effect*. Smith and Halgren (1989) examined recognition memory and the repetition effect in patients who had left or right-sided anterior temporal lobectomy and also in controls. The repetition effect was shown in the ERPs of the controls and the right-sided anterior temporal lobectomy, but this effect was not seen in the left-sided patients. Smith and Halgren noted that there were two components of the ERP wave form that were enhanced by the repetition of the stimuli. One component of the ERP wave form, N400, attenuated to the old items; that is, the negative component at 400 ms became more positive. Also, a late, positive component (associated with the P300 ERP component) was enhanced (became more positive). The modulation of these two components has been replicated in other studies (Besson et al. 1992; Joyce et al. 1998).

While this repetition effect seems reliable in studies involving words, it has not been the case for studies that have used pictures as stimuli. In fact, several studies suggest that the positive going shift that is associated with repetition of words is the opposite for the repetition of visual objects. That is, the repetition of pictures produces a negative going shift (Rugg et al.,

1995; Van Petten & Senkfor, 1996; Penney et al. 2001). Rugg, Soardi and Doyle (1995) found the ERP elicited by repetitions of structurally possible objects to be negative going. Possible explanations of this reverse ERP effect that is found in picture repetition studies are involvement of different cortical cells than those used during word repetition tasks, and also, reduction of neural activity for tasks involving visual stimuli (Penney, Mecklinger, & Nessler, 2001).

Stimulus repetition also produces systematic effects on behavioral responses. Namely, repetition of stimuli has been shown to improve both accuracy and reaction time. This improvement has been referred to by researchers as repetition priming (see Schacter et al. 1993). In the present study, we will employ stimulus repetition as a tool for analyzing relationships between ERP components and memory.

METHODS

Participants

Participants for both experiments were undergraduate students at the University of North Carolina, Wilmington. Participants were general psychology students who fulfilled a course requirement by volunteering to participate in the experiments. All participants signed informed consents before beginning the experiment and the study protocol was reviewed and approved by the Institutional Review Board before the study began.

A total of 30 participants (17 female, 13 male) were initially included in this study. Participants ranged between 17- 46 years, mean= 19.6, male age mean=18.77, female age mean= 20.24. There were 3 left-hand dominant individuals and 27 right-hand dominant. Each individual participated in both the picture and word experiments. The experiments were counter-balanced, half of the participants began with the picture experiment and half began with the word experiment.

Materials

Data acquisition was made possible by a 64 channel, high resolution analogue to digital ActiveOne® amplifier system and ActiveView® real-time software. Both are produced by BioSemi® (www.biosemi.com). Post-analysis was completed in EMSE Suite®—a modular biosignal data analysis program specifically designed to handle and integrate EEG/ERP and MRI data (<http://www.sourcesignal.com>). Stimuli were presented with Presentation® which is produced by Neurobehavioral Systems® (www.neuro-bs.com).

The ActiveTwo® head cap is a form fitting cap developed at the Behavioral Brain Sciences Center, University of Birmingham, United Kingdom. It is made of elastic and is fitted with custom made plastic electrode holders. The electrodes are not integrated into the cap—they must be physically inserted. Sixty four electrode holders are arranged according to the international 10/20 system (refer to figure 3). SignaGel® Electrode Gel is a highly conductive past used to form an electrical connection between the electrodes and the subjects scalp



Figure 3. Attaching electrodes to the ActiveTwo® head cap.

Responses were made on a standard keyboard. Subjects were instructed to rest their hands on the keyboard with the right hand forefinger on the “/” key and the left hand forefinger on the “Z” key. Subjects were instructed to press the “Z” key if the stimulus had been previously seen in the study phase, and to press the “/” if the stimulus had not been previously seen in the study phase.

Electrode Layout

Electrode layout follows the standard international 10/20 system. Electrodes are labeled according to a standardized scheme that is composed of two parts. The first part is composed of a letter or short string of letters that corresponds to the underlying brain area. For example, Occipital electrodes are designated ‘O,’ and Central-Pariental areas with ‘CP’. The second part refers to the electrode placement relative to the midline. Electrodes found lying on the midline end in ‘Z;’ those left of the midline are assigned odd integers and those to the right have positive integers. The values increase the farther one moves away from the midline. Refer to Figure 4 for more detail.

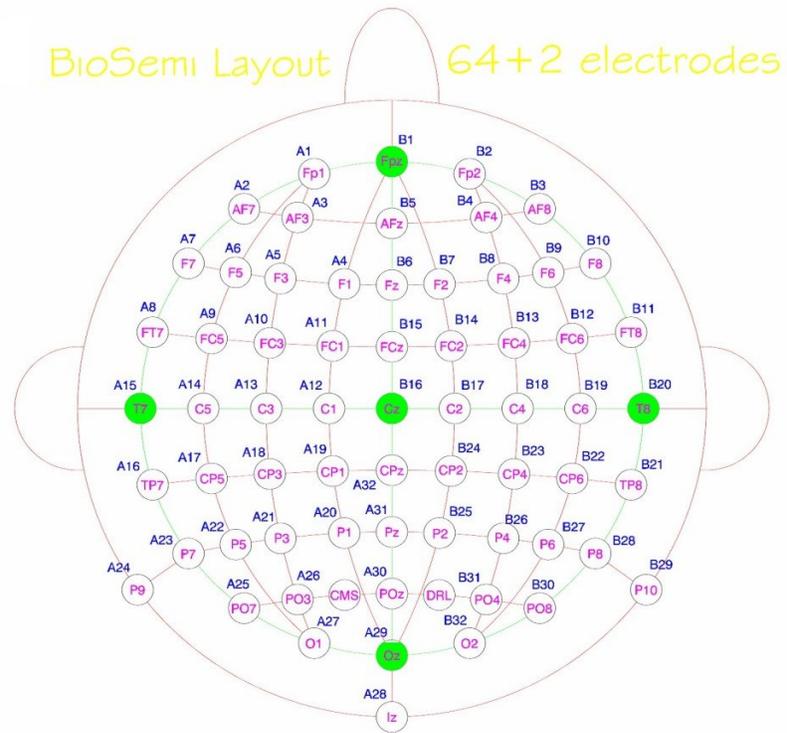


Figure 4. Electrode Layout according to the 10/20 system.

Stimuli

Experiment 1: Repetition for Pictures

The pictures that were used in Experiment 1 were used in a previous EEG experiment from our laboratory. Real world pictures of animals were collected from Google Images (www.google.com/images). All pictures had their background removed or replaced with a white background. Pictures range from coral and plant life to bugs to simple animals ranging from fish to mammals. In total, 120 different pictures were presented to each subject. The pictures were counter-balanced across each subject, such that pictures that were repeated for one subject could possibly be novel to another subject.

Experiment 2: Repetition for Words

Common used words were selected for use in the experiment. All of the words that were chosen to be included in the list were randomly selected by use of a random word generator found on the internet (www.watchoutforsnakes.com). Constraints were set such that the words were short and commonly used. All words were presented on a white background. A total of 120 words were presented. The list of words can be found in Appendix A.

Procedure

Experiment 1: Repetition Effect for Pictures

After the participant signed the informed consent, the researcher and assistant measured the circumference of the participant's head. The distance between the nasion and the inion were measured as well as the left periauricular point (LPA) and right periauricular point (RPA). The distance between the nasion and inion was divided in half and this was considered the position of the vertex (where the Cz electrode is positioned). The vertex was ensured position on the same line of the LPA and RPA.

Participants sat approximately 36” away from a 23” color monitor. Participants were shown how to initiate the stimulus presentation program and were instructed to remain as still as possible and blink as little as possible during the experiment. Each subject completed a practice session that consisted of 10 pictures. Subjects were told that the practice session would emulate the test session for each experiment (picture and word). The experimenter sat with the subject during the practice session to ensure that the subject was aware when to respond and when to remain still. Once the practice session was completed and the subject confirmed understanding the guided instructions then the experimenter closed the curtain to ensure the subject’s privacy and to decrease other distractors.

Study Session

Once the stimulus presentation program began, the participant read these instructions on the monitor:

Welcome to our experiment. Look at the center of the screen and study the pictures. Later, you will see more of these pictures again and you will be asked to recognize the studied pictures. Press the space bar on the keyboard to begin the experiment.

Test Session

After completion of the first part of the study, the participant was reminded that the test session would be similar to the practice session at the beginning of the experiment. The experiment then read the instructions:

Look at the center of the screen and study the images. When instructed, indicate whether the image was of the list previously studied. Press the Z key if the stimulus was previously seen. Press the / key if the stimulus was not previously seen. Press the space bar to begin.

The overall architecture of experiment 1 is a variation of the traditional “old/new” ERP paradigm (Rugg, 1995). A total of 60 pictures were shown during the study phase, each picture was presented for two seconds. Each picture was randomly shown three times during the study phase. The study phase included 180 trials (60 pictures randomly presented three times).

During the test phase, the pictures that were presented during the study phase were each presented once. In addition, 60 novel pictures were also presented. The test phase included a total of 120 trials. The test session began with a fixation point in the center of the screen “+” followed by the picture and then followed by a question mark “?”. The fixation point remained on the screen for one second and then the picture remained on the screen for two seconds. All three stimuli (fixation point, picture, and question mark) had a white background. In order to reduce movement artifacts, participants were instructed to remain motionless until the “?” appeared and to then make a response indicating whether the stimulus was presented previously (“old”) or “new.” The next picture in the series did not appear until a response was made.

Since participants were not allowed to respond until after the “?” cue, reaction time data is not informative since subjects were required to hold response until cued. Once a response was made, the next trial began. There was always a 2 second pause between the presentation of the stimulus and the response. These two seconds for each trial was what was used in the EEG analysis (discussed later).

Experiment 2. Repetition effect for words

The procedure for experiment 2 replicated the procedure of experiment 1. The only difference between experiment 1 and 2 was the stimuli presented. In experiment 2, common nouns were presented instead of pictures. A list of these words can be found in Appendix 1.

General Hypotheses

The experiments here are exploratory in nature. However, as a guiding framework the following hypotheses were developed.

Experiment 1. Repetition effect for pictures

In previous experiments, we have observed that participants respond faster and more accurately to stimuli viewed three times than to novel stimuli or those observed just once before. It has been previously shown in previous research that repeated stimuli produces an attenuated evoked potential as compared to an evoked potential produced by novel stimuli. That is, the repetition of stimuli results in a suppression of the peak amplitude of the signal. First, we hypothesized that peak amplitudes for select ERP components, including P300 and N400 (ERP components associated with the “old/new” paradigm) in the regions of interest will be suppressed as a function of stimulus repetition. Second, we hypothesize that peak amplitude latencies will shift toward shorter latencies as a function of repetition. It is expected that the event related potential difference at the scalp is generated in part by the hippocampus, so it is hypothesized that response amplitudes in the hippocampus would change as a function of stimulus repetition. Finally, we hypothesized that a lateralized effect for pictures, with dominance in the right hemisphere for both surface recordings of ERPs and hippocampal responses.

Experiment 2. Repetition effect for words

The effects of repetition of words are hypothesized to be identical to those predicted for pictures (Experiment 1) but the effect is expected to be lateralized such that repetition will produce larger ERP changes in left hemisphere for word repetition. It is also hypothesized that the N170 component will be elicited by the word experiment and show a repetition effect.

RESULTS

Data Analysis

Identical data analysis methods were used for experiments 1 and 2. The EEG recordings for each subject were processed using peak detection analyses from EMSE Suite EEG/ERP data analysis software. Beamformer analysis was performed on data files for each subject (two separate conditions for each subject) using the hippocampus and motor cortex, bilaterally. The analysis quantified peak amplitude, latency, and area under the curve for each region of interest within each condition for each subject.

The source files for each of the conditions and experiments for all subjects were saved. Peak detection analysis was performed on each file. Peaks were defined by previous “old/new” studies (Ally & Budson, 2007; Simon, Petit, Bernard, and Rebai, 2007) and labeled as the ERP components that were previously discussed. The peak detection analysis created a text file that included the peak latency, peak amplitude and area under the curve for the regions of interest that were previously defined.

Behavioral responses were classified as hits and false alarms. ERPs associated with each response type will be classified accordingly. Responses classified as false alarms and misses were not included in the event related potential data analysis. The first ERP analysis was based on ERPs collected on trials that were hits (positive yes response to stimuli previously seen) and correct rejections (correctly classifying “new” pictures with a “no” response) compare the peak amplitude and peak latency differences between the two conditions. Dependent measures t-tests were used to assess the differences in peak amplitude for ERP components in both the picture and word experiment.

Behavioral Results

Due to a sampling rate difference during the recording of the EEG, half of the collected data was not compatible. Therefore, the data that was collected at the same sampling rate was only included in the experiment. Also, two subjects had very poor recognition accuracies (below 70%) on both recognition tests and thus were not included in the analyses. Therefore, only data for 13 subjects was used in the following analyses.

Accuracy data is presented in a box-whisker diagram in Figure 5. The accuracy (both hits and correct rejections) for the picture experiment was significantly higher ($t=3.95$, $p<.01$) than for the word experiment. The accuracy for experiment 1 (pictures) was 90.2% and the accuracy for experiment 2 (word) was 78.3%.

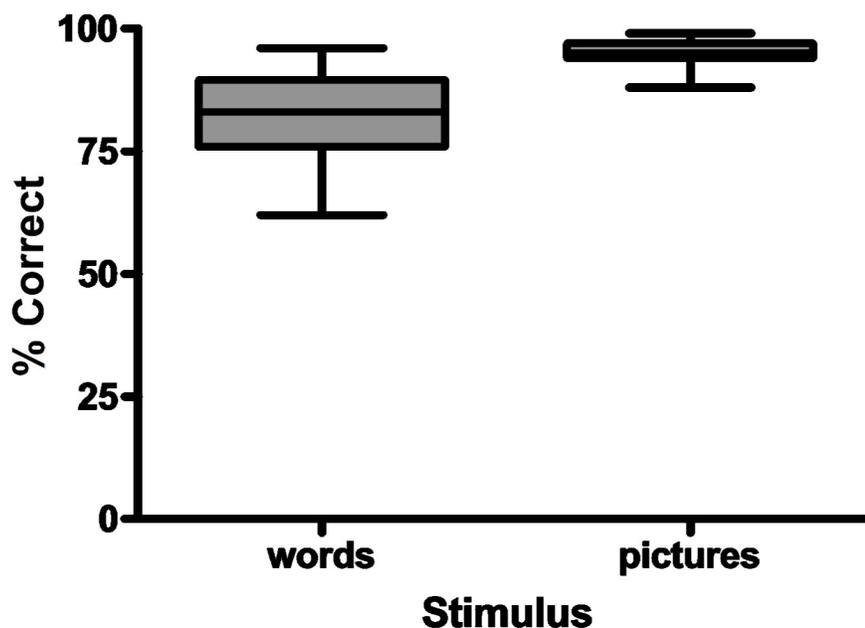


Figure 5. Accuracy data for both experiments is presented. Accuracy was significantly higher for pictures than for words ($t(11)=3.95, p<.01$).

Signal detection analysis was used to calculate the sensitivity (d') of the subject's decision for old and new stimuli in both the picture and word experiment. Figure 6 shows a box-whisker diagram of the calculated d' for the 13 subjects that were included in the analyses. d' was significantly greater for pictures than it was for words ($t(11)=-4.95, p<.01$). In cases where subjects had a perfect hit rate (60/60) and no false alarms (0/60) their scores had to be adjusted in order to carry out the signal detection analysis. This adjustment for hit rates was $1 - (1/60) = .98$ and for false alarms was $1/60 = .01$.

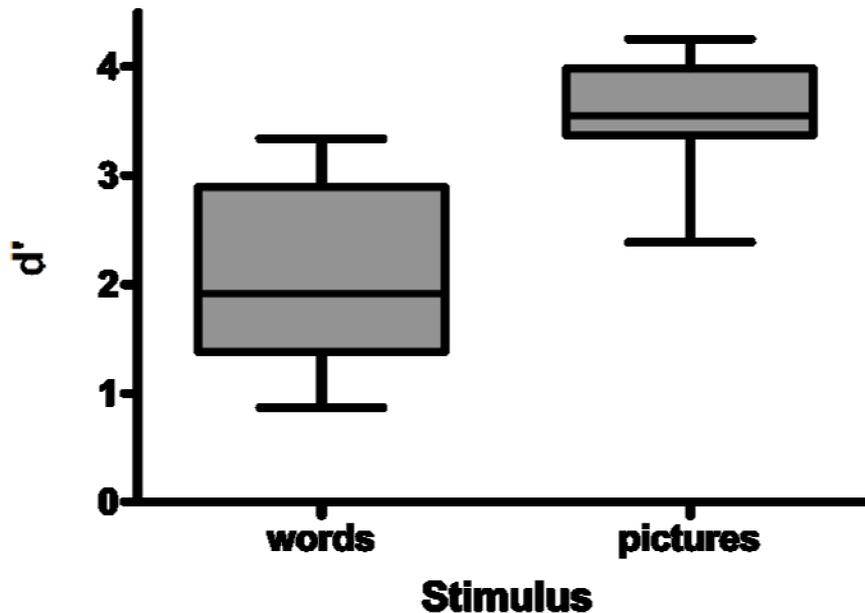


Figure 6. Signal detection analysis for both picture and word experiments revealed significantly larger d' for pictures than for words ($t=-4.95, p<.001$).

Electrophysiology results for Experiment 1

Grand Averages

The grand average event related potential was created by averaging a time epoch of 2 seconds (200ms pre-stimulus onset-1800ms post stimulus) across 60 trials for each condition (new and old). Thus, one grand average ERP was created for the novel picture condition and one grand average ERP was created for the old (3-repetition) picture condition.

The ERP components selected for statistical analyses were chosen on the basis of previous recognition memory experiments. In the picture experiment, peaks in the P100, N200, P300 and N400 were selected. ERP components were selected by defining a range of milliseconds in EMSE Suite ®. The most positive or negative point within the selected latency is defined as the peak. Statistical analyses of the components that were mentioned earlier were conducted to determine whether there was any difference between the peak amplitude and peak latencies of the ERP components. Dependent samples t-test was used to analyze the statistical difference in peak amplitude for the selected ERP components between the old and new conditions of the picture and word experiment.

All of the reported statistics from this experiment do not fall into the normal range of statistical significance. Thus, even though some of the observations that are highlighted in the results section failed to reach the conventional significance level of $p < .05$, it seemed judicious to err on the side of detecting potentially important effects by giving special attention to all effects that reached the $p = .2$ significance level, referred to below as “marginally significant.”

All electrode locations were analyzed, however, only certain electrodes were included in the project. Electrodes showing good clear evidence for the components of interest were used and had been previously used in our laboratory. There were a total of four electrodes that were used for the analysis (Af7, F8, P10, and Cpz); the electrodes were non-adjacent and

corresponded to certain scalp locations (i.e., Af7 is left, frontal; F8 is right, frontal; P10 is right, posterior temporal; and Cpz is located on midline of parietal). While the scalp location of these electrodes is given, it should be a reminder that the scalp location of the electrode doesn't necessarily pertain solely to the particular brain region.

Figure (5) illustrates the ERP for both novel and repeated conditions at electrode Af7. Electrode Af7 is located in the frontal left hemisphere. It can be noted that there is a significant difference between the amplitude of the waves around 300ms post-stimulus, the P300 ERP component ($t(11) = 2.6, p = .02$). Generally, P300 is a positive going wave that peaks around 300ms over the parietal electrodes. It can be noted that in Figure 5, it is clearly a negative waveform. However, it is expected that the increased positivity in the parietal and occipital regions during this time frame would produce negativity in the frontal region (i.e. electrode Af7) due to the dipolar nature of the field potential. The wave form shows that for the "old" condition, the amplitude of the wave is smaller than for the novel stimuli. This finding replicates the repetition effect that Rugg and other researchers have previously reported (Rugg et al., 1995; Van Petten & Senkfor, 1996; Penney et al. 2001).

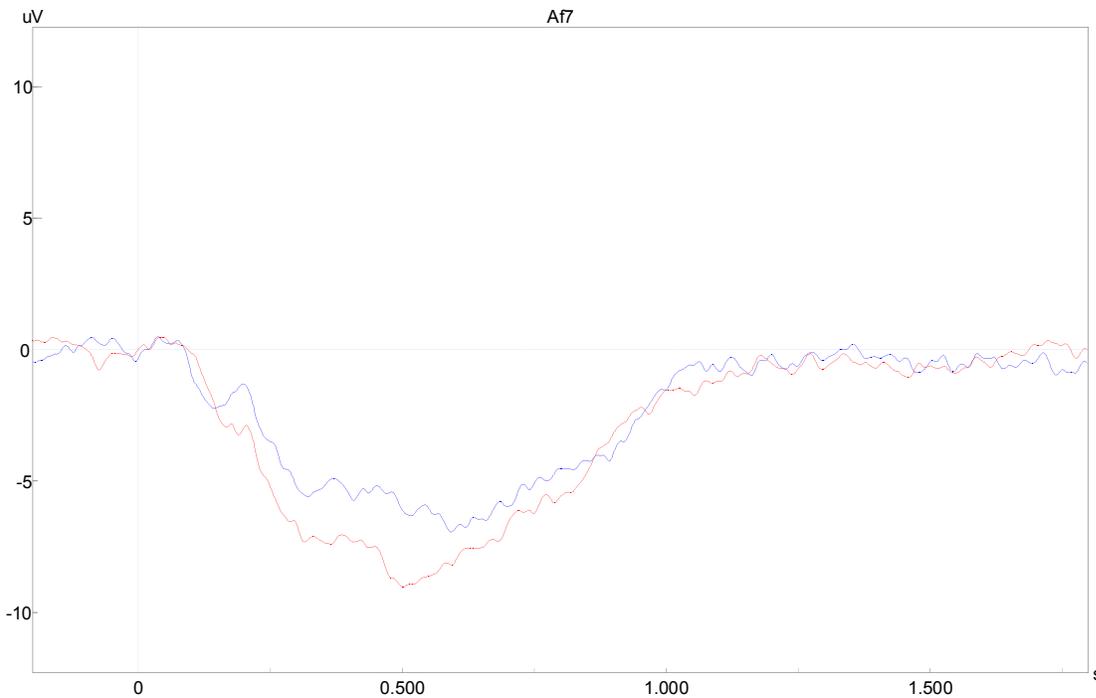


Figure 7. Event related potentials for “hits” (Old condition, represented in blue) and “correct rejections” (new condition, represented in red) for Experiment 1 (Pictures) at Electrode Af7. Peak amplitude difference at P100 is not significantly different, $t= 1.78$, $p=0.10$, however is within a reasonable margin of significance. Peak amplitude differences are significant for P300 ($t=2.6$, $p=0.02$) and N400 ($t=2.5$, $p=0.02$) components. As for peak latency differences, P100 ($t=-1.55$, $p=0.15$) is marginally significant.

Figure 8 shows the grand averaged ERP at electrode F8. Electrode F8 is located in the frontal, right hemisphere. It should be mentioned that the repetition effect that was shown in the previous figure (Figure 7) is not as distinct in Figure 8. This is consistent with previous data from our lab. In earlier findings, it was shown that the P300 repetition effect was not significantly found across all electrodes. It is worth mentioning that the peak amplitude difference for the N400 time frame is within the margin of significance ($t(11)=-1.73, p=0.10$).

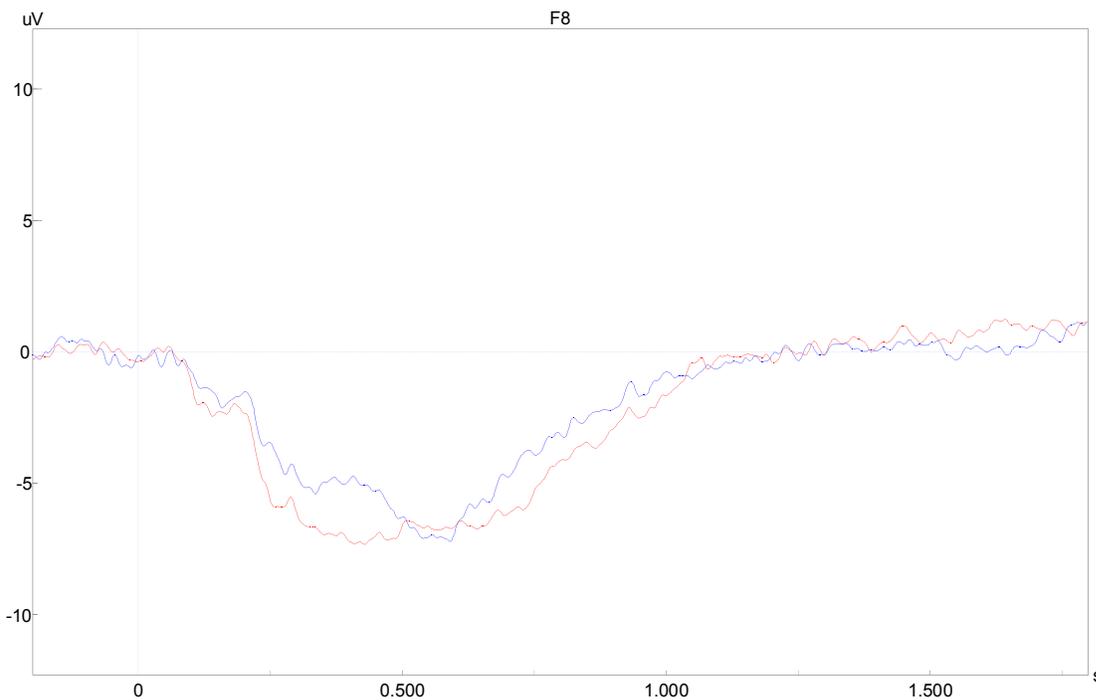


Figure 8. Event related potentials for “hits” (old condition, represented in blue) and “correct rejections” (new condition, represented in red) for Experiment 1 (Pictures) at Electrode F8. No significant peak amplitude differences for P100 or P300, however N400 did show a marginally significant difference ($t= -1.73, p=0.10$). There were no significant peak latency differences for any of the components between old versus new.

Both figure 7 and figure 8 have illustrated the grand averaged wave forms for frontal electrodes. Electrodes Af7 and F8 can be characterized by negative-going and shifting to become more positive-going. The opposite is true for the next two figures (Figure 9 and 10). These two figures are for electrodes that are located posterior to Af7 and F8. Figure 9 shows the waveform for both old and new conditions for the picture experiment at electrode P10. P10 is located in the right hemisphere, near the parietal, temporal, and occipital junction.

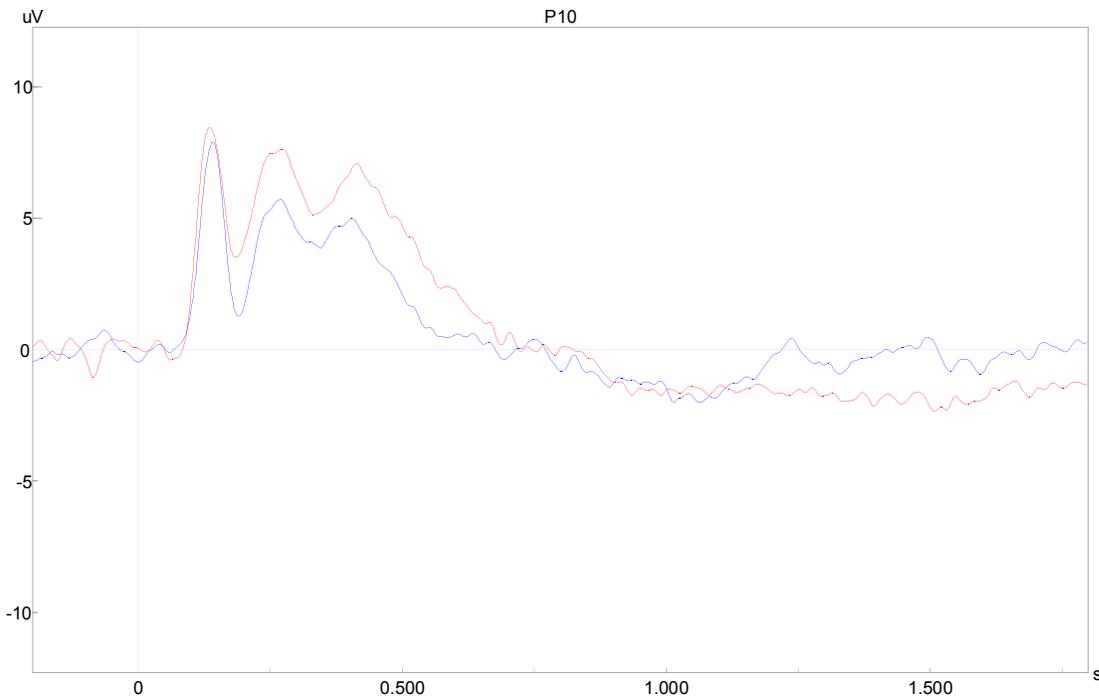


Figure 9. Event related potentials for hits (old condition, blue) and correct rejections (new condition, red) for Experiment 1 (Pictures) at Electrode P10. Peak amplitude difference was marginally significant for P100 ($t=1.92$, $p=0.08$). Peak amplitude difference was significant for P300 ($t=2.8$, $p=0.01$) and N400 ($t=3.8$, $p=.008$) components. Peak latency differences were marginally significant at P100 ($t=-1.78$, $p=0.10$) and N400 ($t=1.35$, $p=0.20$).

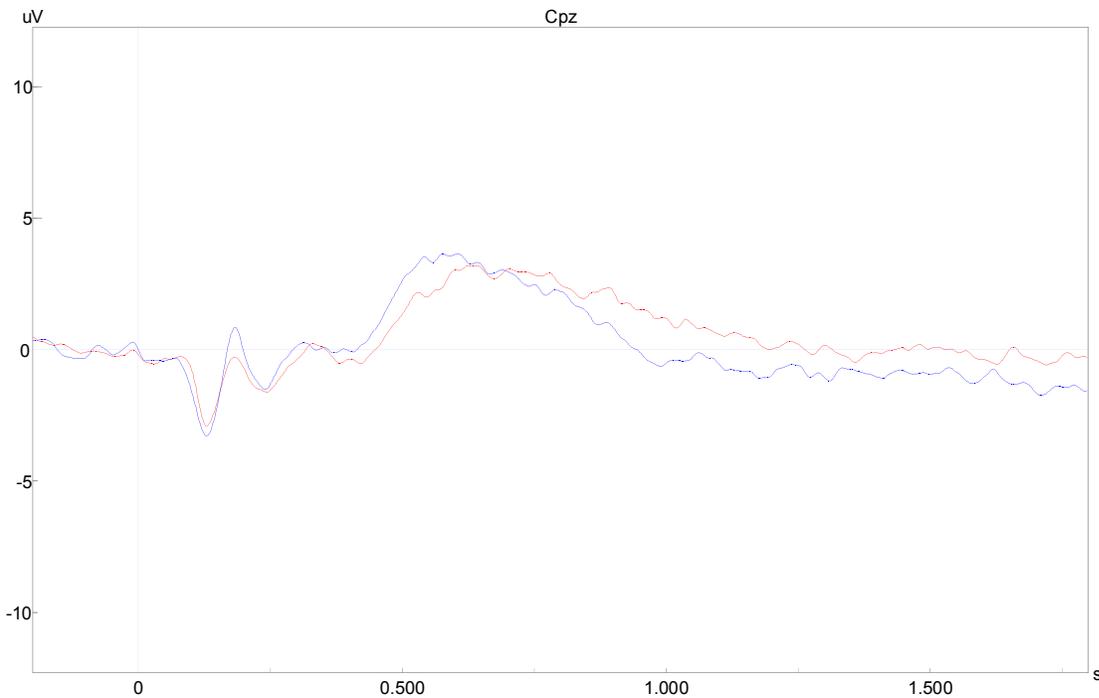


Figure 10. Event related potentials for hits (old condition, blue) and correct rejections (new condition, red) for Experiment 1 (Pictures) at Electrode Cpz. There were no significant peak amplitude differences for either P100 or P300, however, N400 proved to be within the margin of significance ($t=-1.78$, $p=0.11$). No significant differences were found for peak latency of any of the components.

As observed by other researchers, not all electrode sites show the repetition effect (Rugg et al. 1998). Some sites were more sensitive to the repetition while other sites seem to remain unaffected by the additional exposure to the stimuli. Statistical analysis of the peak amplitudes of the electrode sites that did show this repetition effect revealed to be significantly different. Figure 11 shows the grand average wave form for old and new conditions for all electrode sites.

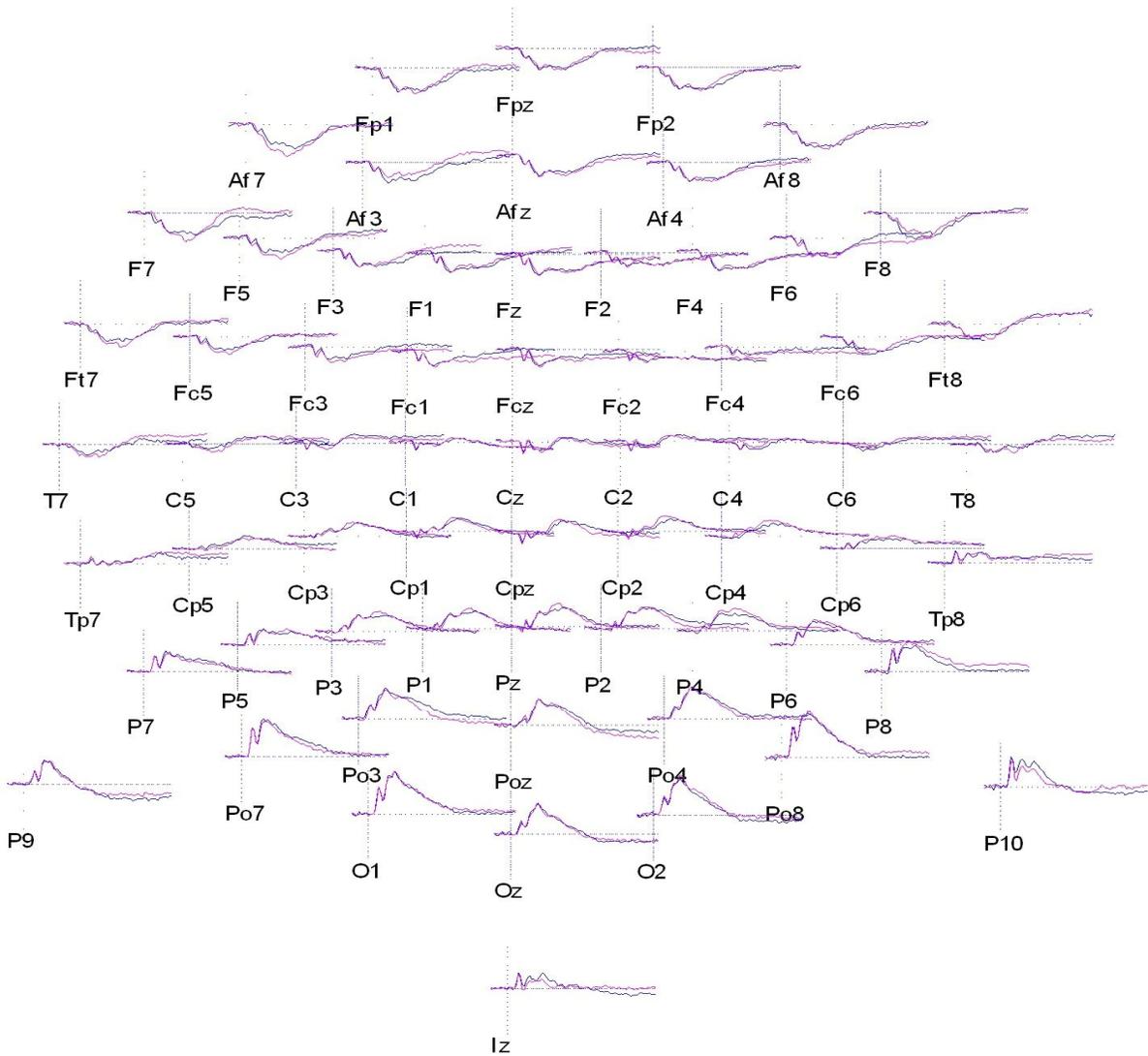


Figure 11. Grand averaged ERPs for old (hits, blue) and new (correct rejections, red) conditions in picture experiment.

Electrophysiology results for Experiment 2

The grand average ERP files for Experiment 2 (words) were identically compiled in the same manner as Experiment 1. Figure 12-15 represents the ERP for old vs new conditions at electrodes Af7, F8, P10, and Cpz, respectively. There is a visually identifiable repetition effect at ~170ms post stimulus for electrode F8 and P10. N170 is an ERP component that is associated with word recognition is believed to represent face, object and word processing discrimination in the ventral stream (Simon, Petit, Bernard and Rebai, 2007).

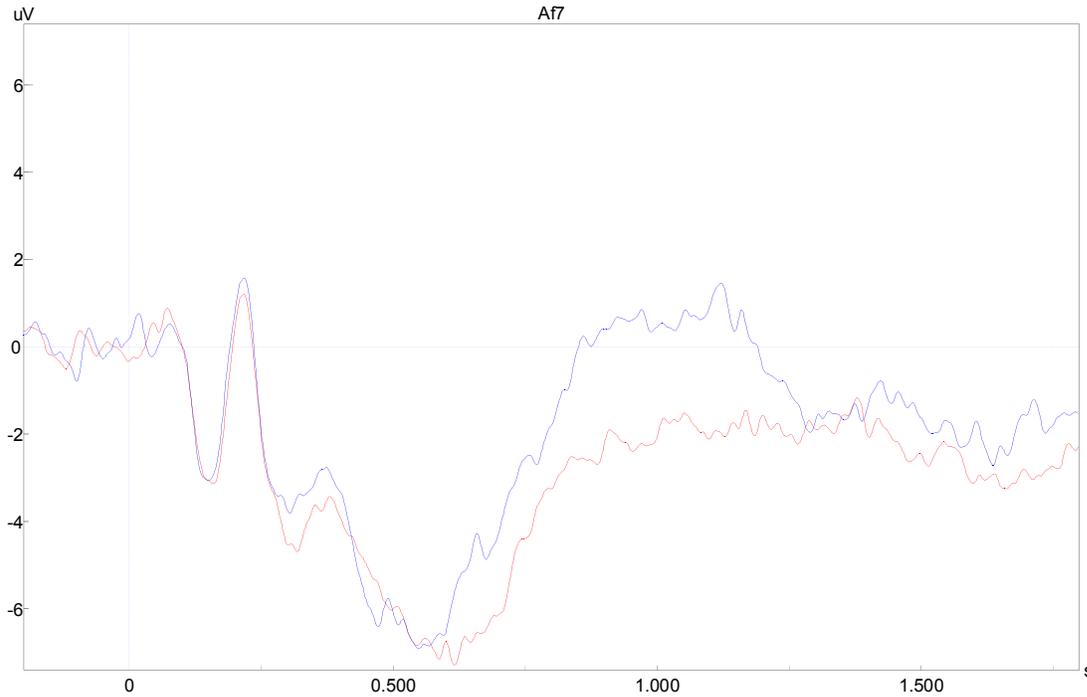


Figure 12. Event related potentials for hits (old condition, blue) and correct rejections (new condition, red) for Experiment 2 (Words) at Electrode Af7. No significant peak amplitude differences or peak latency differences were found at any of the ERP components.

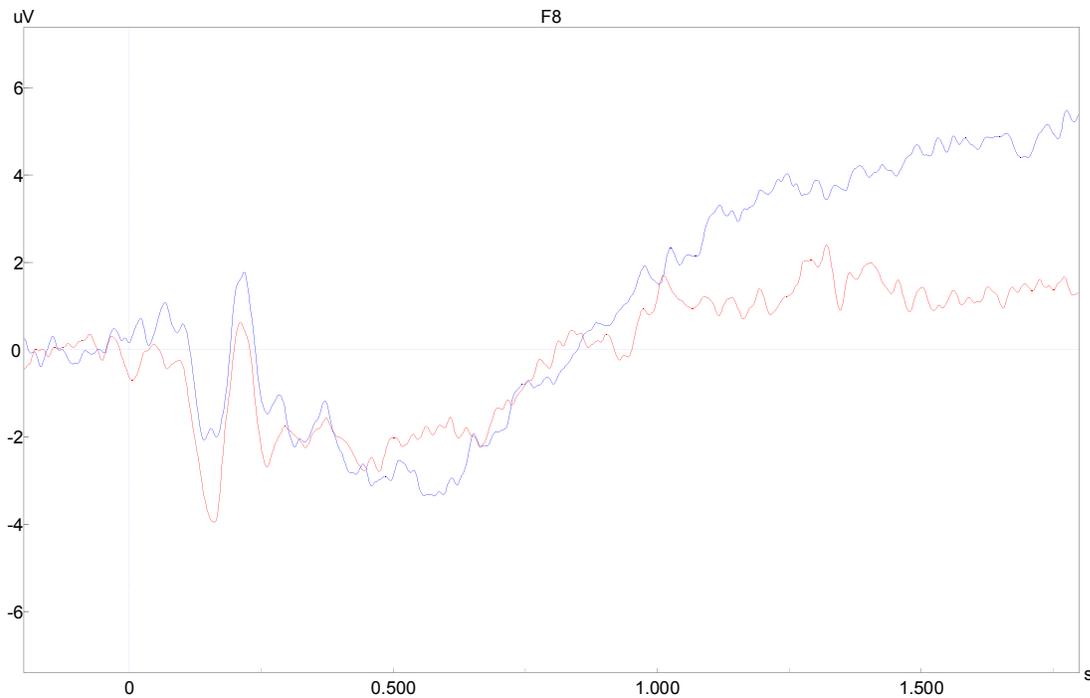


Figure 13. Event related potentials for hits (old condition, blue) and correct rejections (new condition, red) for Experiment 2 (Words) at Electrode F8. The peak amplitude difference for P100 ($t=-1.34$, $p=0.20$) was within the margin of significance. A significant difference in peak amplitude was found for N170 component ($t=-3.09$, $p=0.01$). A marginally significant peak latency difference was found for P100 ($t=1.6$, $p=.13$).

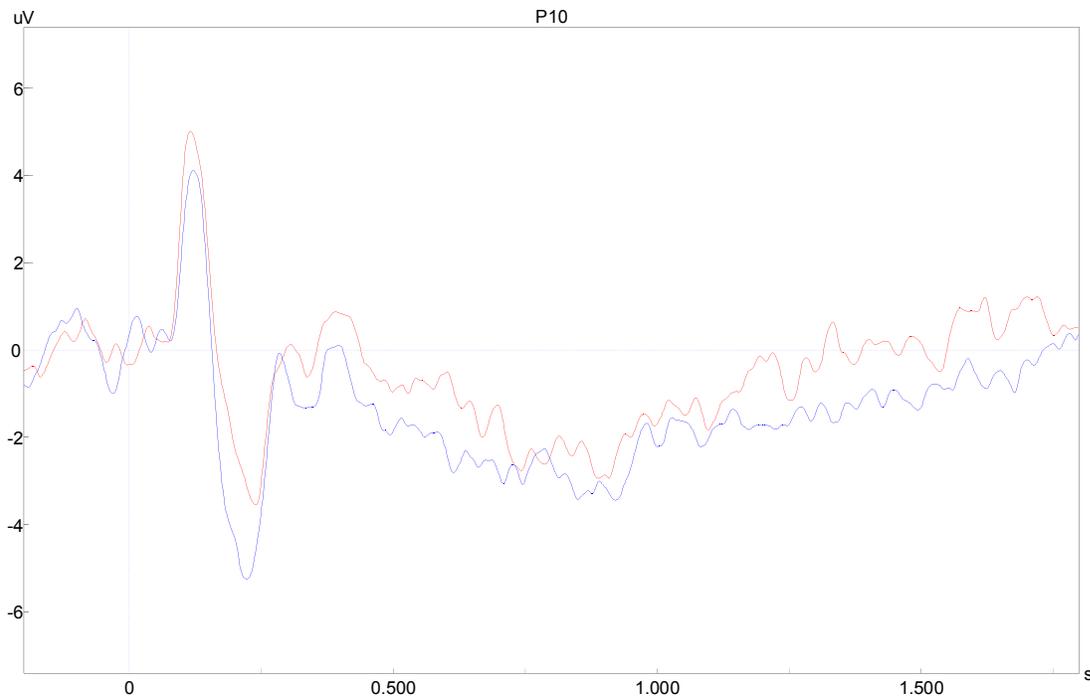


Figure 14. Event related potentials for hits (old condition, blue) and correct rejections (new condition, red) for Experiment 2 (Words) at Electrode P10. There was a significant peak amplitude difference for N170 ($t=2.21$, $p=.04$) and a significant peak latency difference for N400 ($t=-2.87$, $p=0.01$).

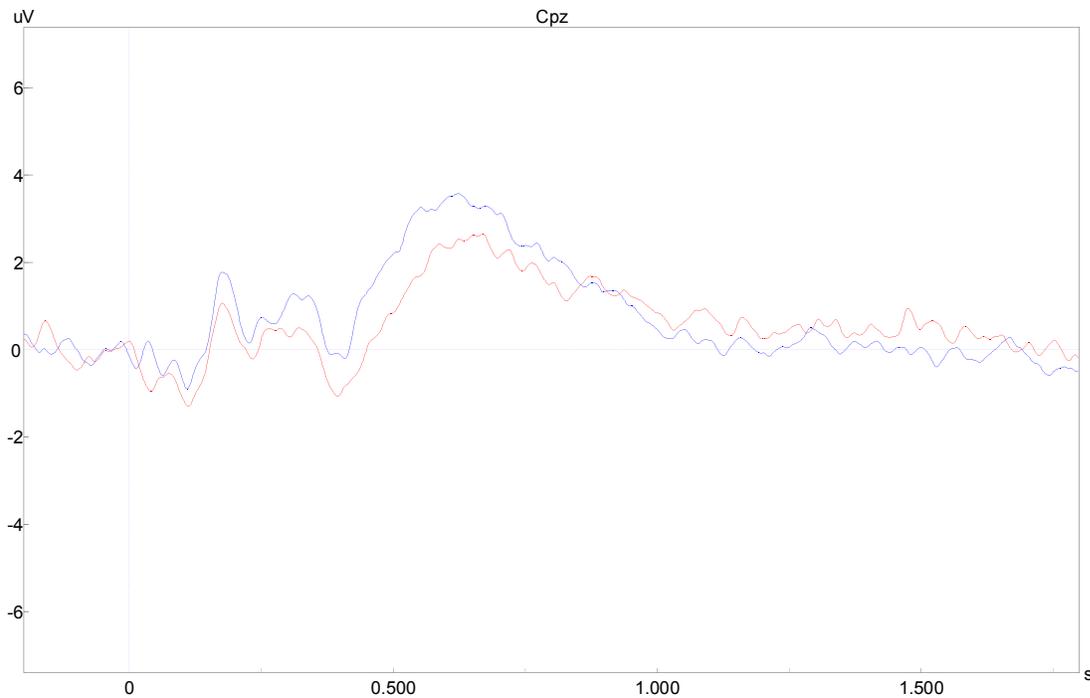


Figure 15. Event related potentials for old condition (blue) and the new condition (red) for Experiment 2 (Words) at Electrode Cpz. Peak amplitude difference of P100 was within the margin of significance ($t=-1.8$, $p=0.08$) while the remaining ERP components did not show any significant difference in peak amplitude. Peak latency differences for the ERP components were non-significant.

Figures 16-19 show the stimulus difference between the “old” picture and “old” word condition in several different electrode locations. It should be noted that there are distinct differences in the waveforms when comparing picture versus word.

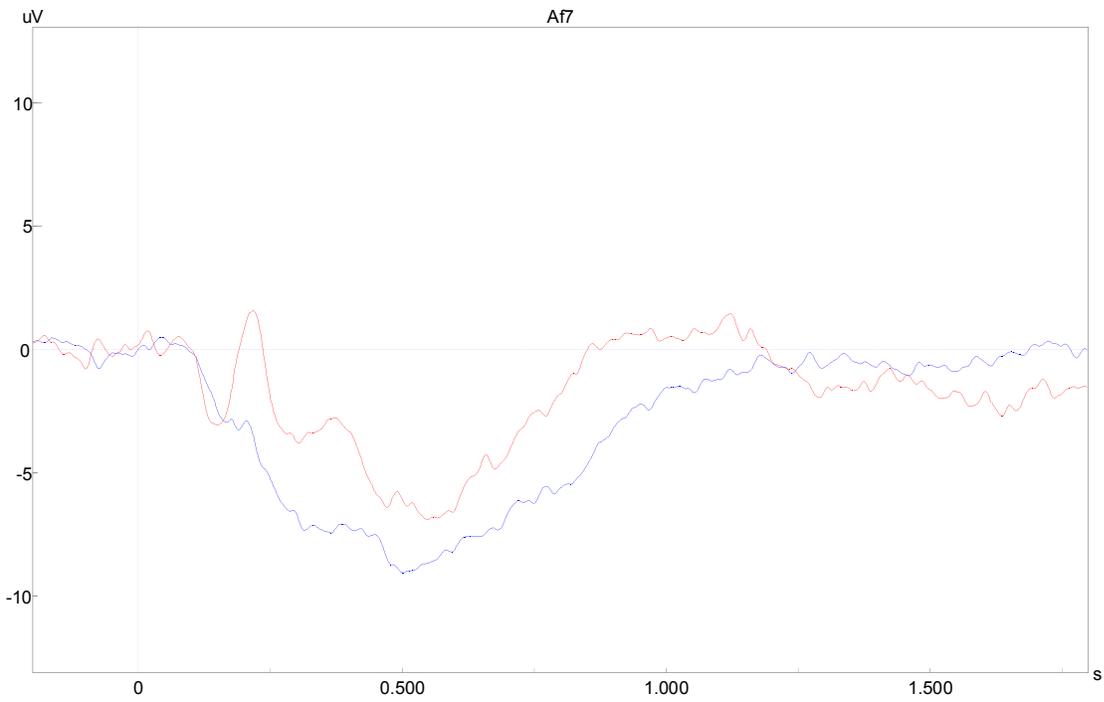


Figure 16. Grand averaged ERPs of picture (blue) and word (red) for the old condition at electrode Af7.

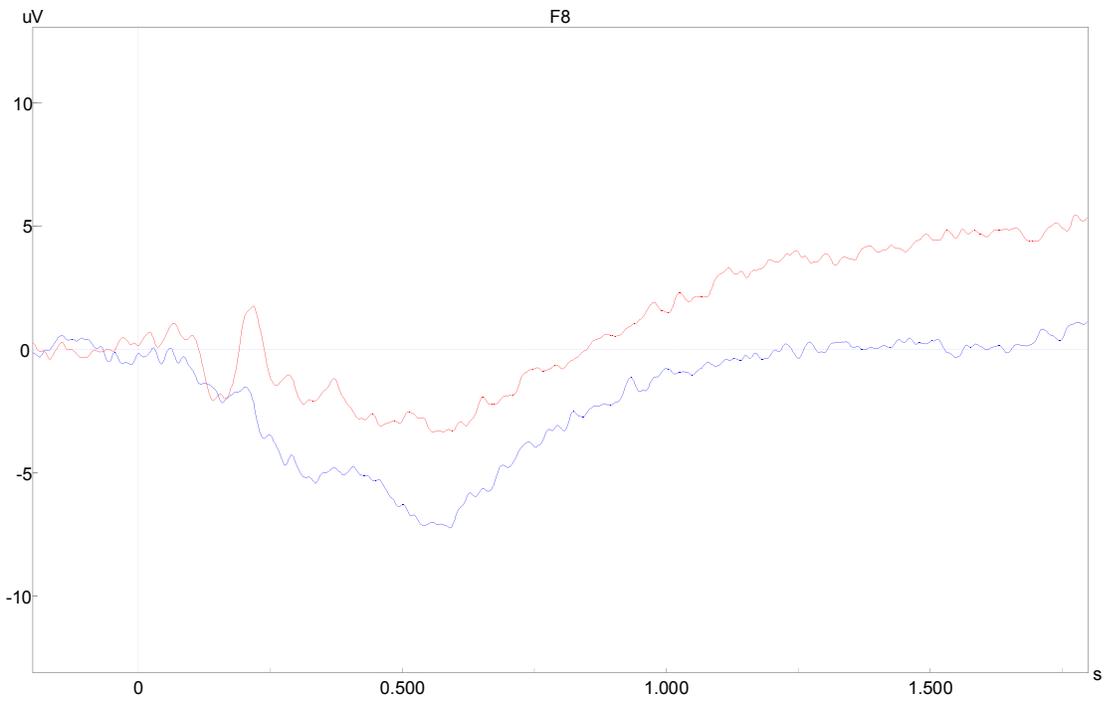


Figure 17. Grand averaged ERPs of picture (blue) and word (red) for the old condition at electrode F8.

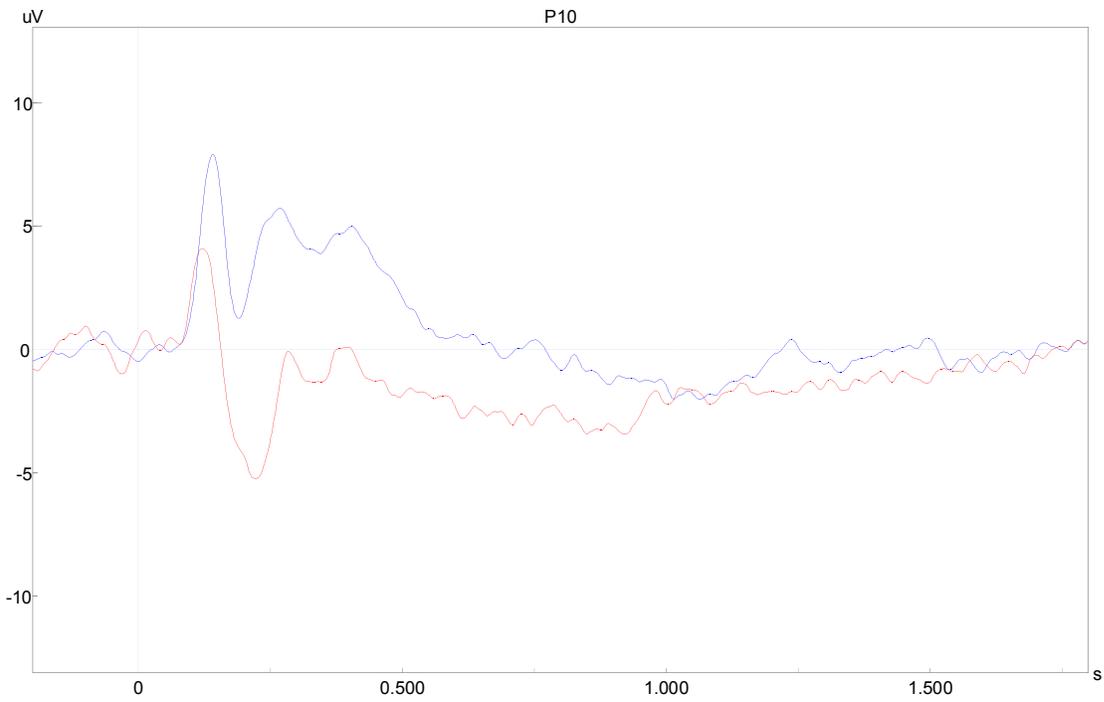


Figure 18. Grand averaged ERPs of picture (blue) and word (red) for the old condition at electrode P10.

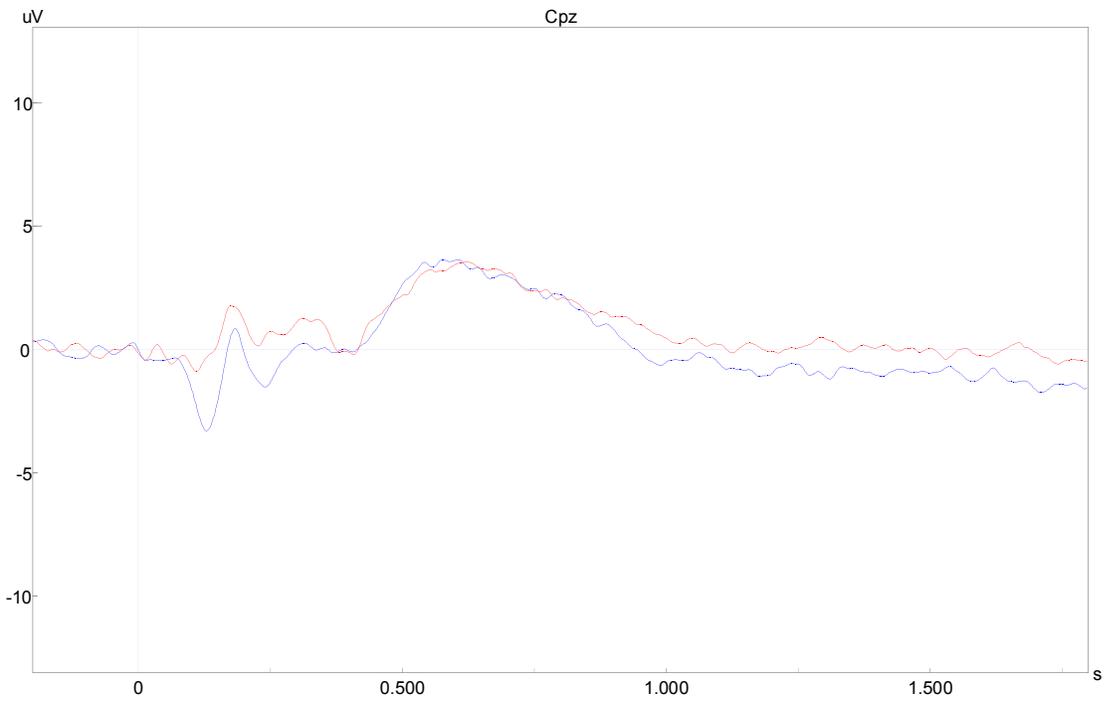


Figure 19. Grand averaged ERPs of picture (blue) and word (red) for the old condition at electrode Cpz.

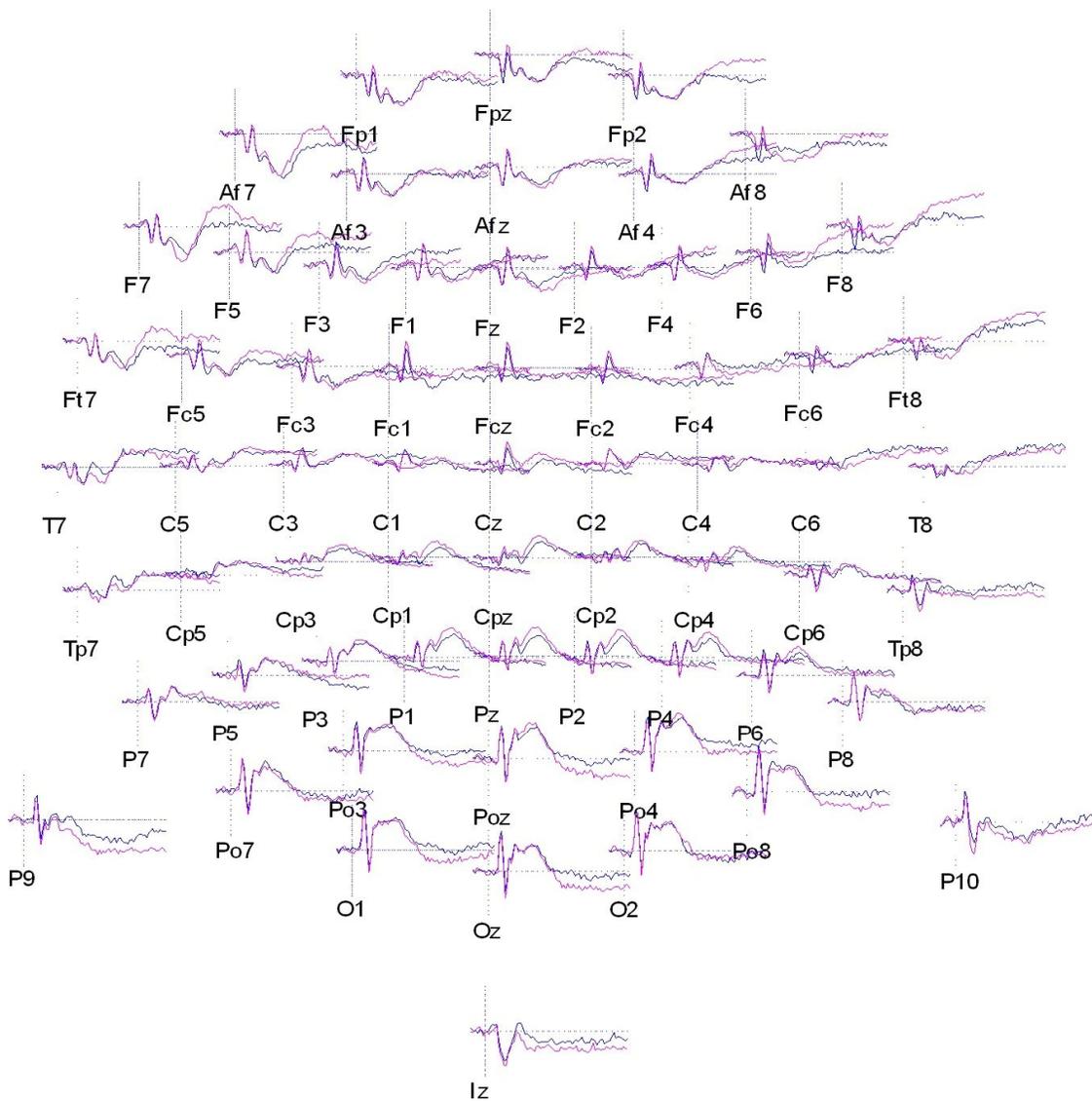


Figure 20. Grand averaged ERPs from word experiment for all electrodes for old (blue) and new (pink).

The grand average ERPs for all four conditions (old picture, new picture, old word and new word) are represented in Figure 22. This figure is included to show the distinct ERP differences between stimulus type. There is a difference in the wave form between picture and word experiments and also a difference between the grand averaged wave forms for old versus new.

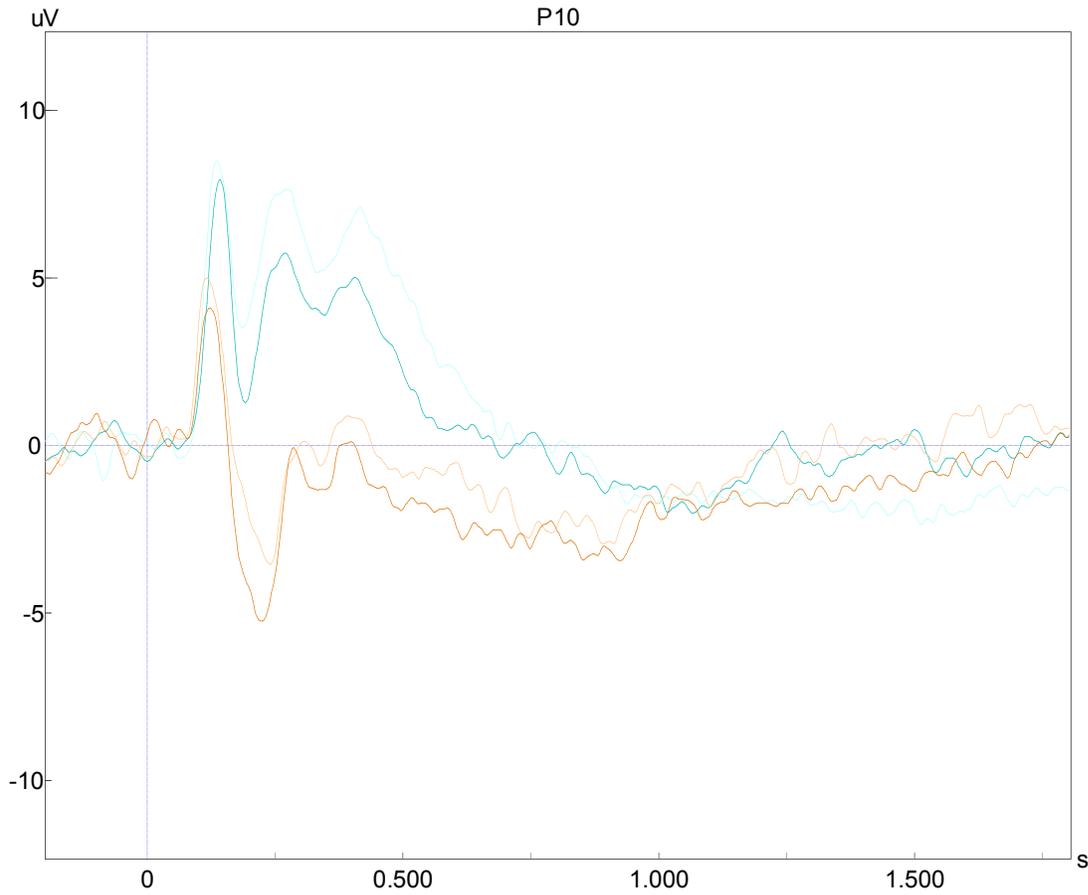


Figure 21. Grand averaged ERP waveform for all four conditions at electrode P10. “New” picture condition (light blue) and “old” picture condition (blue) have a similar wave form however differ distinctly for “new” word condition (light orange) and “old” word condition (orange).

Peak amplitude difference of N400 for the picture experiment was plotted as a function of each subject's response ("old" v "new") criterion as determined in the signal detection analysis. Figure 22 shows that the magnitude of the difference in the peak amplitude of the N400 evoked by novel versus familiar pictures increases as a function of individual subjects' response criteria such that the conservative criteria were associated with larger changes in the amplitude of the peak of the N400. Repetition produces a larger change in the N400 amplitude as subjects' criterion for responding "old" increases.

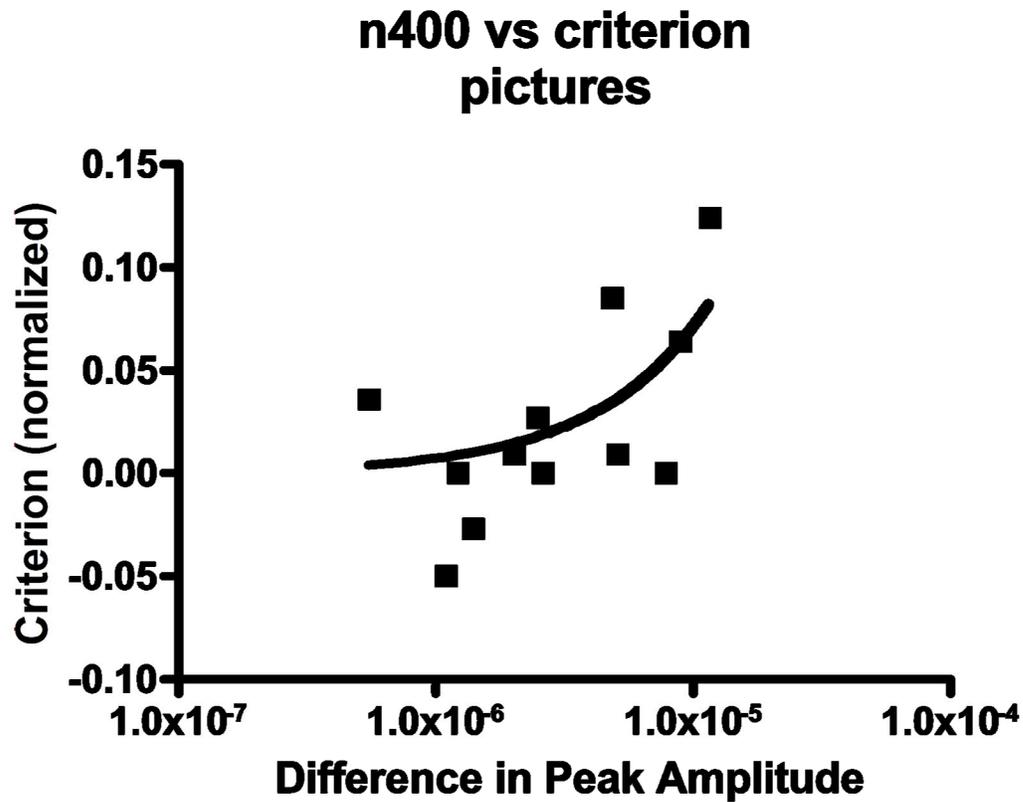


Figure 22. Differences in peak amplitude between old and new conditions for picture experiment for N400 component increases as criterion increases. Peak amplitude difference is recorded from the beamforming spatial analysis of the hippocampus ($r=.49$, $p<.05$).

Beamformer Spatial Filtering

The beamformer spatial filtering analysis that was discussed earlier was applied to the grand averaged ERP wave forms. The beamformer dipole file was created by using the EMSE Suite® software. The talarach coordinates for the hippocampus were chosen by using brain magnetic resonance images averaged over 100 individuals. Right hippocampus coordinates were 30, -24, -8; left hippocampus coordinates were -30, -24, -8; right motor cortex coordinates were 27, -26, 55; and the left hippocampus coordinates were -27, -26, 55. Figure 23 shows the beamformer source file at each region of interest for the picture experiment. It can be noted that there was a significant difference between the hippocampus and the motor cortex signal; however there is little difference in peak latency or in peak amplitude for repetition of the pictures.

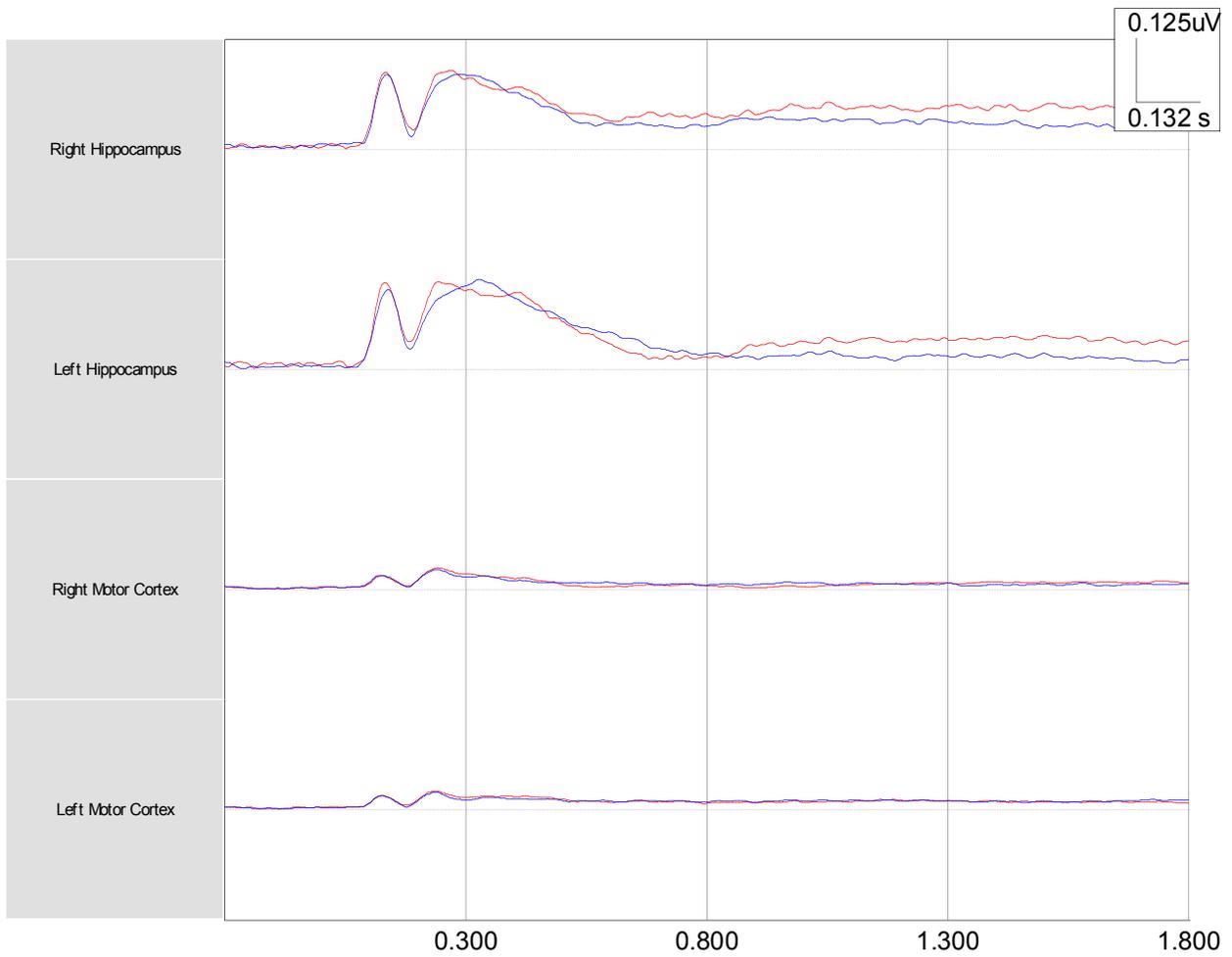


Figure 23. Beamformer signals at each region of interest for the picture experiment. “Old” pictures are represented in blue and “new” pictures are represented in red.

The beamformer analysis for the word experiment reveals a distinctly different waveform than was observed when pictures were presented. Figure 24 shows the two conditions for the word experiment (old v. new) at the four regions of interest.

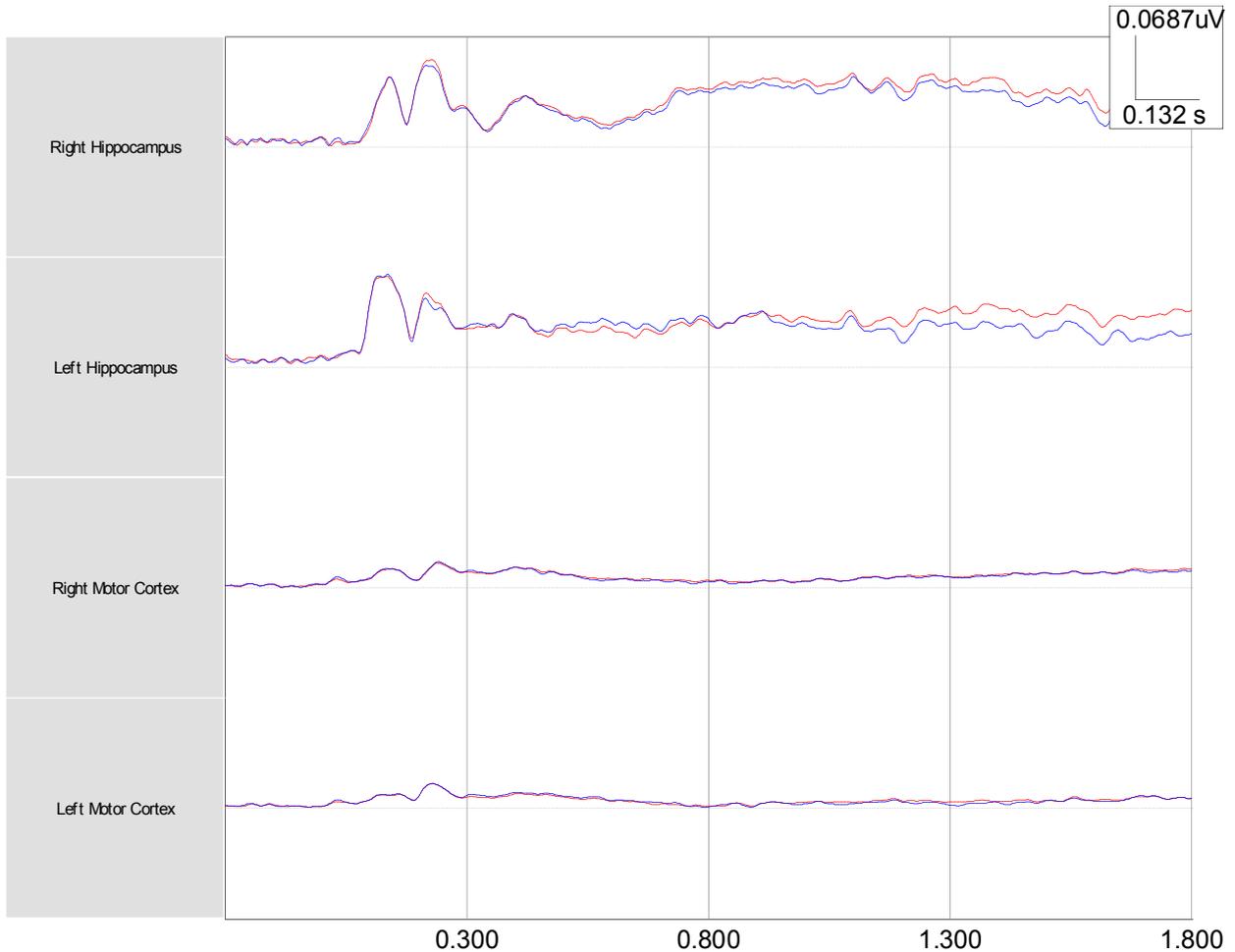


Figure 24. Beamform spatial filtering analysis of the word experiment for both “old” (blue) and “new” (red) conditions. There is a significant difference between the peak amplitudes for the hippocampus regions of interest compared to the motor cortex regions of interests. There is no significant difference between the peak amplitudes of conditions (old v. new) at any of the regions of interest.

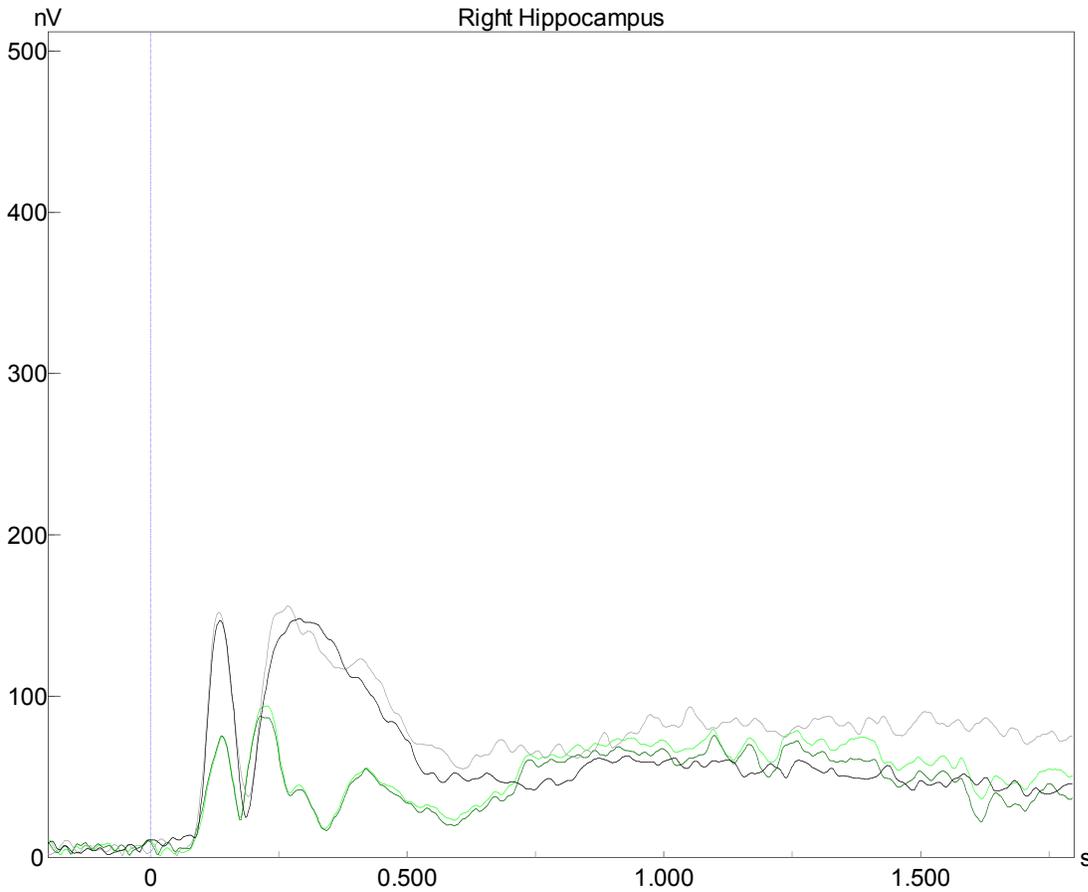


Figure 25. Beamformer file for each condition (old and new) for both picture and word experiment. New picture (light gray) and old picture (black) are not significantly different on the measure of peak amplitude. New word (light green) and old word (dark green) are not significantly different on the measure of peak amplitude. There are significant differences between the picture and word peak amplitudes.

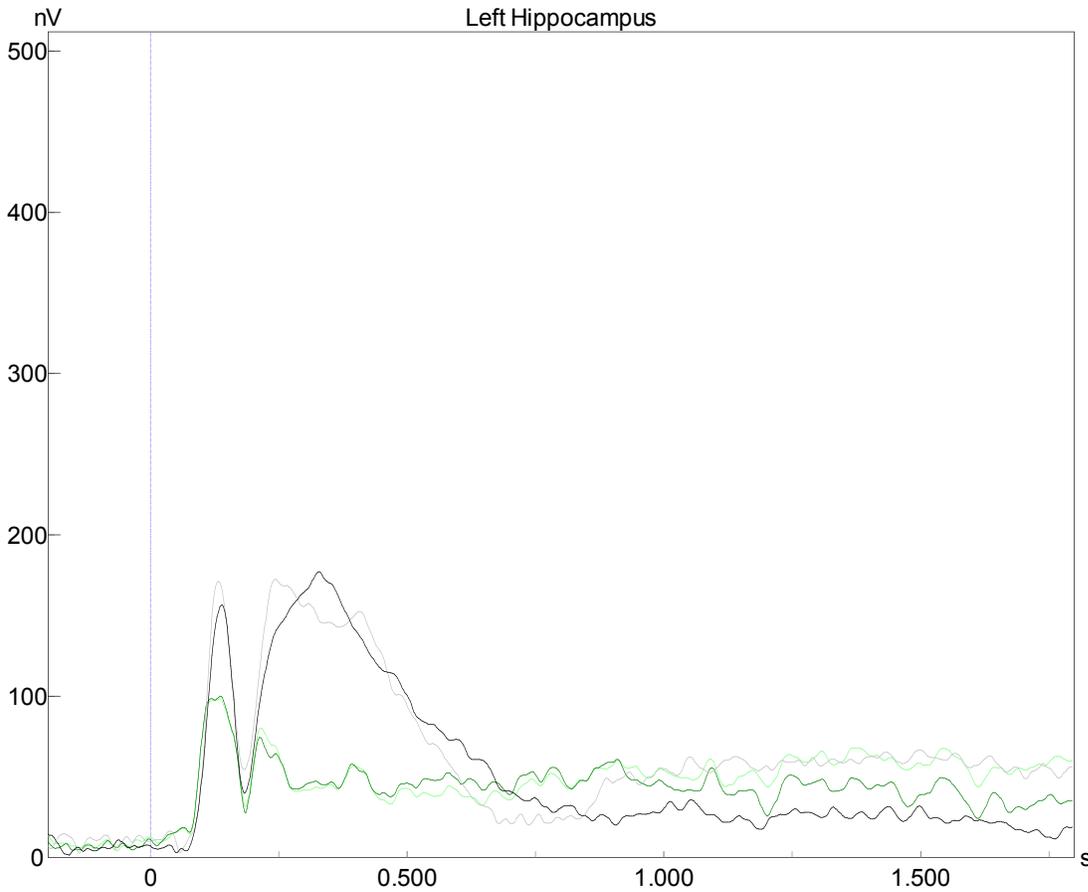


Figure 26. Beamformer analysis for the Left Hippocampus for both conditions (old and new) and both experiments (word and picture). As noted in the previous figure, there are no significant differences for the repetitions of the stimuli within each experiment, however there are significant differences in the peak amplitudes for picture versus word.

Peak detection analysis was applied to the beamformer files for each condition and subject. The early components of these files were analyzed to determine whether peak amplitude and latency were significantly different. In the picture experiment, two peaks were defined as “100” (.08ms-.18ms post-stimulus) and “300” (.20-.80ms post stimulus. No significant differences were found for repetition for these defined peaks. In the word experiment, similar defined peaks revealed no significant differences in amplitude and latency for the two conditions.

The beamformer file is created by using talairach coordinates. The location of the beamformer does not evaluate the electrical fields of the hippocampus in its entirety; rather, it is a very restricted region of the hippocampus, only including a relatively small amount of neurons when comparing it to the hippocampus as a whole. It is possible to create and apply many beamformers to the data set. This allows other areas of the hippocampus to be assessed. Since no significant differences of repetition were found in either the left or right hippocampus (using the coordinates that were previously mentioned), additional beamformers were created to assess a wide range of other areas within the hippocampus.

Figure 27 shows seven additional hippocampus zones that a beamformer was created for and used to assess the electrical activity in both of the conditions of the picture experiment. Figure 28 illustrates these seven hippocampus zones for the word experiment.

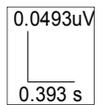
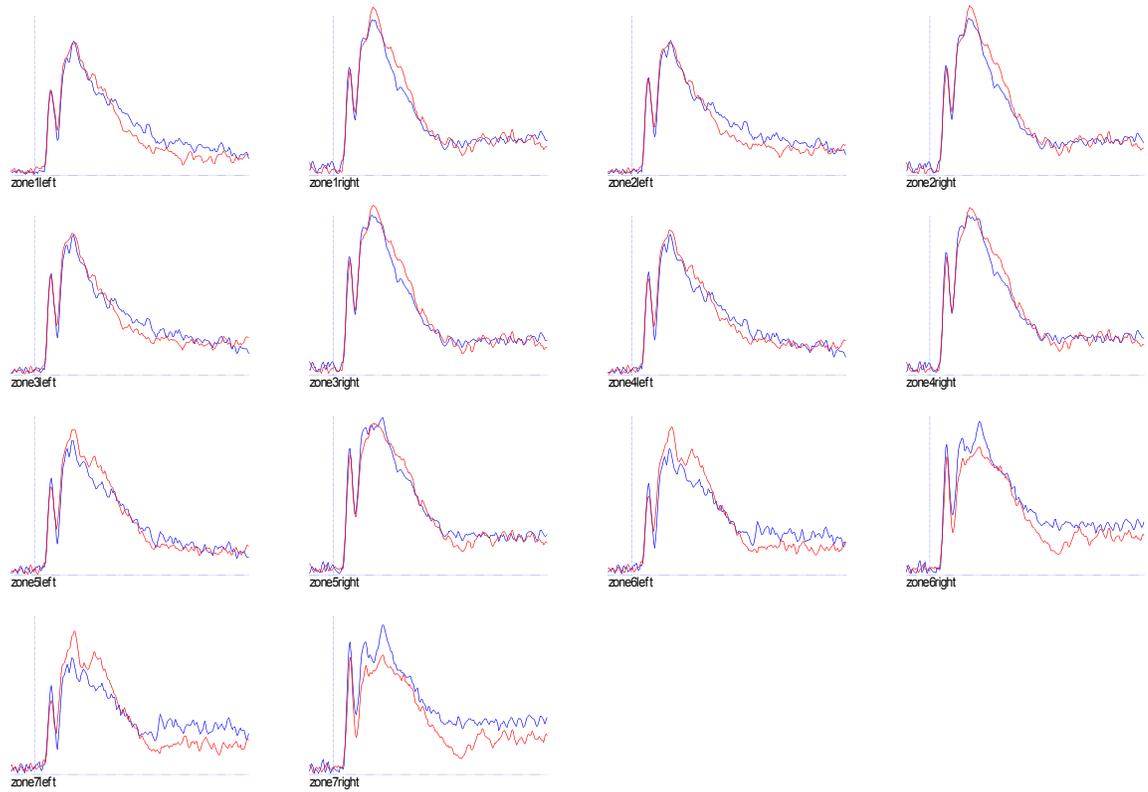


Figure 27. Beamformer analysis of seven additional areas of the hippocampus (left and right) for the picture experiment. Red line represents the pictures presented 3 times prior to test (“old”) and blue line represents novel pictures (“new”).

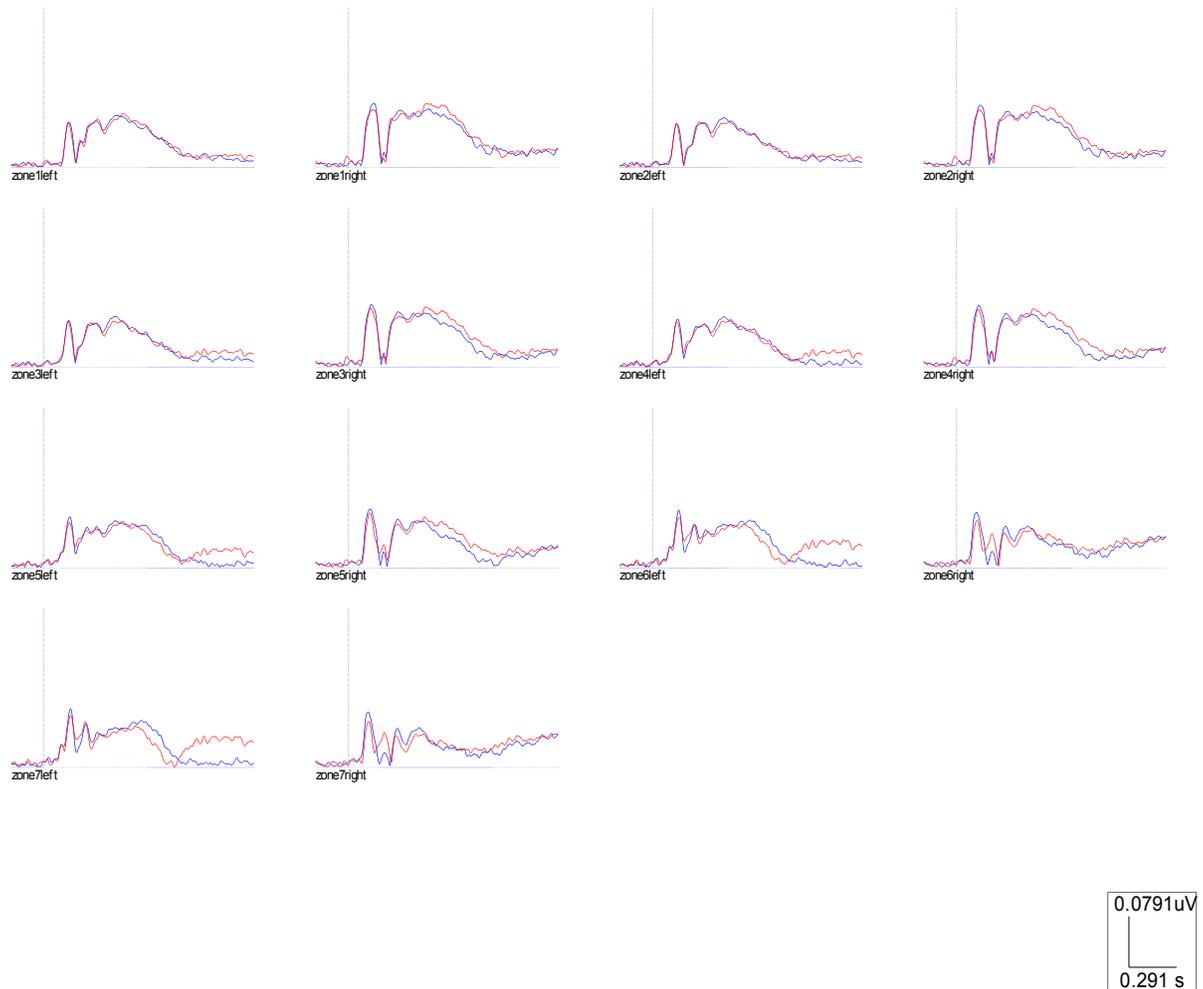


Figure 28. Beamformer analysis of seven additional areas of the hippocampus (left and right) for the word experiment. Red line represents the words presented three times prior to test (“old”) and blue line represents novel pictures (“new”).

DISCUSSION

There are important findings from the new data presented here that agree with previous research on recognition memory. Electrical signatures associated with recognition memory were clearly apparent in the present experiments, and the typical repetition pattern was also observed. Previous research has offered topographical explanations of electrical field potentials that are associated with various recognition memory paradigms but have been unable to explain structural mechanisms that are involved with this process. In this study, an attempt was made to verify the electrical potentials from a suspecting generator: the hippocampus. Before discussing this analysis, further examination of the paradigm itself must be addressed.

It can be affirmed that recognition memory was engaged in this experiment. Subjects' choice accuracies for both "old" pictures and words was well above chance performance and their sensitivities (d') to "old" versus "new" pictures and words were also high. A previous study from this lab using only pictures as stimuli detected similar accuracy data to that observed in the present study. In order to prevent the electrophysiological data from contamination by data from low performing subjects, data from two subjects that had low d' scores were not included in the ERP analysis. Additionally, the current analysis does not include data from 15 subjects that for whom electrophysiological data were collected at a different sampling rate. The analysis of the additional data from these individuals will enable us to confirm, or disconfirm, the results of the peak detection analysis and beamformer spatial filtering analysis observed in the present study.

The results from these experiments reported in this thesis lend strong support to previous reports of repetition effects for pictures and words. The repetition effect, as reviewed by Rugg (1995), is manifest as a more positive going wave that is elicited by novel stimuli in

comparison to familiar stimuli. Discrepancies exist in the literature in regards to whether this remains true across different classes of stimuli. For instance, the repetition effect that Rugg mentions is for verbal stimuli while other researchers have found that the repetition of visual stimuli results in a suppression of the wave form (Rugg et al., 1995; Van Petten & Senkfor, 1996; Penney et al. 2001).

Consistent with previous research in our laboratory, the repetition of pictures did produce a significant attenuation of the P300 component at the frontal electrode Af7 and a significant amplitude deflection for the posterior electrode P10. This is an interesting finding in that it represents the dipolar nature of electrical fields within the brain. This frontal negativity is associated with the positive posterior wave. Previous studies using fewer electrode locations did not observe the posterior effects detected in the present study.

While the repetition effect in these experiments was not pervasive, it was statistically significant at selective electrodes. Consistent with previous studies that have used EEG and ERP analysis to quantify the difference in electrical potentials in recognition memory, these experiments call for further elaboration.

The repetition effect was not widespread in the peak detection analysis. The ERP components chosen to be analyzed in the picture experiment were the P100, P300, and N400. Since the aim of this thesis project was to characterize the early ERP components of recognition memory, an analysis of late components was not included. However, it may prove to be beneficial to analyze the later components since previous studies (Ally & Budson, 2007) have shown late recognition memory effects, though the validity of late ERP effects (post 1000 ms) are disputed by some researchers (Luck 2005).

It is possible to consider the ERP repetition effect that was observed in these experiments to be confirmatory rather than exploratory analysis. Confirmatory in the sense that it has been shown twice from our laboratory that repeated stimuli produces signal amplitude differences that have been observed in other studies as well. However, it is also possible to consider this research as exploratory as well. The electrodes that showed the repetition effect in our laboratory are different from previous studies. It is possible that we are finding repetition effects at different electrode sites because of the array of electrodes that are being used differ from other studies. Two experiments from our lab show that pictures produce this ERP repetition effect at electrode Af7 and P10. Words were not previously used as stimuli in our laboratory and we did not observe the P300 repetition effect for any of the selected electrodes. However, a peak amplitude difference was observed for N170.

An interesting finding in the word experiment was the repetition effect that was seen at the N170 component. The most significant peak amplitude difference for the N170 component was at electrode F8 ($t=-3.09$ $p=.01$) and P10 ($t=2.21$, $p=.04$). Research supporting the N170 component suggests that the component is associated with the early processing stage of recognizing a visual pattern. Previous research shows N170 amplitude related to top-down processes of recognition, that is if the subject learns to recognize novel fictional objects, the N170 is still evoked (Jemel, Pissani, Calabria, Crommelinck, & Bruyer, 2003). Simon et al. (2007) showed that the massive repetition of words produced larger N170 amplitude.

The clearest evidence of a stimulus repetition effect was observed in P300 component of the ERP. As discussed earlier, this component is perhaps the most widely studied ERP component. Donchin (1981) proposed that the P300 wave may be associated with context updating. Hundreds of studies using various experimental paradigms have shown that the P300

is more positive going when novel stimuli are presented relative to when subjects see familiar stimuli. In the current analysis for the picture experiment, this can be seen at the frontal electrode Af7 and the posterior, parietal electrode P10. Also, there was a significant latency shift for the P300 component at electrode P10 for the word experiment with the P300 emerging earlier for familiar stimuli.

In view of previous research which has reported little, if any, evidence of a repetition effect on the P100 component of the ERP, it is not surprising to find that I only found evidence of marginally significant peak amplitude differences for repetition at P100. It was hypothesized that the P100 component would be elicited by the visual stimulus since it is associated with at least 30 visual areas (Luck, 2005). The present findings were also consistent with previous studies by our laboratory on the repetition effect.

The N400 is a language-related component that is largest when a word that does not fit the context is presented (Luck 2005). Holcomb and McPherson (1994) showed that the N400 is also associated with non-word stimuli however researchers have proposed that it is evoked by pictures when subjects name the stimulus sub-vocally. In that the current study used both pictures and words as stimuli, the clear N400 peaks observed under both picture and word stimulus conditions is consistent with such an explanation, though other accounts may also be possible.

When stimuli are presented repeatedly, recognition speed increases (Sanguinetti 2007). Therefore we hypothesized that ERP components that are sensitive to stimulus repetition would have earlier onsets when repeated stimuli were presented than when new stimuli were presented. However, few shifts in peak latencies of the ERP components differences were found. There were peak latency differences that were marginally significant. The marginally significant

electrode sites for the picture experiment were Af7 (P100 component) and P10 (P100 and N400). In the word experiment, the only marginally significant electrode site was F8 (P100) and there was a significant P300 component peak latency difference for electrode P10. The failure to find a robust effect on ERP latencies suggests that the electrode sites on which the largest ERP amplitudes are observed are not the optimal locations for detecting repetition-dependent changes in the latency of the electrophysiological processes that support recognition memory.

The beamformer spatial analysis did not reveal any significant differences in peak latencies or peak amplitude for the repetition of pictures or words. The initial beamformer file that was created did not reveal any significant effects of repetition of words or pictures. Seven additional beamformer files were created to explore the full extent the hippocampus in order to rule out the possibility that we were simply analyzing the wrong region of the hippocampus. Although a repetition effect was not detected in any of these areas of the hippocampus, a robust hippocampal signal was observed in response to both pictures and words. In essence, the hippocampus was clearly highly engaged in the experiment as seen from the amplitude change compared to motor cortex, the region used as a control.

The strength of the “old/new” paradigm may not be enough to evoke the differences between novel and familiar stimuli that are observed in the beamforming analysis in the hippocampus. It is shown that the hippocampus produces robust activity during this task. This is made evident by countless brain-lesioned individuals who suffer from severe episodic memory loss (Scoville 1954; Scoville and Milner, 1957; Zola-Morgan, Squire and Amaral, 1986; Manns, Hopkins, Reed, Kitchner, and Squire, 2003). Damage to the hippocampus results in loss of episodic memory as seen in both human and animal models of research (Meunier, Bachevalier, Mishkin, & Murray, 1993; Suzuki, Zola-Morgan, Squire, & Amaral, 1993; Mumby & Pinel,

1994). Also, the “old/new” paradigm is one of several paradigms used to assess recognition memory. Behavioral data supports the fact that individuals do recognize familiar stimuli. In this study, this is supported by the average d' score for the picture and word experiment, which was extremely high when picture stimuli were used and high when words were used. It is also seen that with repetition of stimuli, at certain electrodes, a repetition effect is present. The brain is engaged in a process of recognition of a previously seen stimulus and this is supported by both the behavioral and electrophysiological data. However, at the level of the hippocampus, the story does not seem as clearly defined.

There are multiple possibilities of where the repetition effect is originating. While the hippocampus structure failed to show this repetition effect to stimuli, it should not be ruled out completely. It is possible that the hippocampus is engaged in another process that is not being accounted for by this paradigm, such as encoding each stimulus presentation within its unique episodic context.

The hypothesis that the hippocampal activation observed in the present study was associated with memory encoding is consistent with a recent study by Wood, Dudchenko, Robitsek, Eichenbaum (2000) which showed that the firing pattern of neurons in the hippocampus during a response alternation task was associated with the encoding of information needed for representing certain memory episodes. Similar activation of hippocampal neurons during encoding has also been observed when delay match to sample procedures have been used (Hampson and Deadwyler 1996). Thus, it seems possible that the beamforming spatial analysis of the hippocampus may actually reflect the fact that the hippocampus is engaged during the encoding process during each stimulus presentation.

It is possible that in future studies, a larger number of subjects may contribute to significant findings in the beamforming spatial filtering analysis. Since this source estimation technique is very new with few published studies using it for EEG analysis, further exploration with other cortical areas will be beneficial in evaluating its utility as a neuroimaging method. The structure and location of the hippocampus also may be a factor for not finding peak amplitude differences. Since the hippocampus is relatively deep within the brain, it is extremely complicated to localize electrophysiological sources from this structure using scalp electrodes. Perhaps a simpler study to evaluate the validity of the beamforming spatial filtering technique would be one that targets a cortical region such as Broca's area in the frontal lobe during a word generating task.

It should be mentioned that normally the use of multiple t-test analysis raises questions of alpha inflation. Since both experiments are considered to be exploratory, peak amplitude difference and peak latency shifts are compared separately for each selected electrode site.

The focus over the past decade in cognitive science has been placed in functional magnetic resonance imaging and other imaging techniques such as positron emission tomography. However, there are many limitations of both of these imaging techniques. Both are comparably much more expensive than electroencephalogram. Also, EEG allows more precise detail of millisecond changes in electrical fields whereas fMRI and PET have very poor temporal resolution. While in the past EEG has not allowed for spatial interpretation, the beamforming analysis allows more understanding of the spatial relationship of evoked electrical fields in the brain.

In conclusion, this thesis has shed additional light into the area of electrical potentials that are related to recognition memory. It is shown that with the repetition of both pictures and

words, there is a significant difference in peak amplitude at certain electrode locations for the P300 component (i.e. Af7 and P10, for picture experiment) and N400 component (i.e. Af7 and P10, for picture experiment), and the N170 component (i.e. F8 and P10, for word experiment). This stands in line with previous studies that have shown a repetition effect at the scalp during an old/new experiment. The source estimation technique used in this analysis did not reveal a significant difference in amplitude or latency for the repetition of pictures or words. However, the beamforming spatial analysis showed a robust effect in the hippocampus during the recognition memory experiments when compared to the motor cortex. It is possible that other structures in the medial temporal lobe are responsible for the repetition effect that is observed at the scalp (i.e. perirhinal cortex, entorhinal cortex, or parahippocampal area).

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Appendix A. List of words used in Word Recognition experiment

Age	Feet	Rabbit
Air	Film	Race
Airplane	Fire	Rain
Album	Floor	Remote
Animal	Flower	Rent
Apple	Food	Ring
Baby	Game	Sand
Ball	Garden	School
Banana	Gene	Shell
Band	Glue	Speaker
Bank	Grass	Sponge
Bat	Hat	Spoon
Bear	Horse	Star
Bed	Joker	Store
Bike	King	Straw
Bird	Knife	Sun
Blanket	Knight	Table
Block	Lamp	Taxi
Boat	Laser	Teacher
Box	Lawyer	Teeth
Bridge	Letter	Toy
Bug	Light	Track
Bush	Mail	Train
Button	Milk	Tree
Cactus	Mirror	Truck
Cake	Money	Unit
Camera	Monkey	Water
Camp	Moon	Wave
Candle	Mountain	Window
Carrot	Mouse	Witch
Cartoon	Movie	Wolf
Chair	Music	
Coffee	Ocean	
Cookie	Office	
Couch	Orange	
Cow	Paper	
Cream	Party	
Crew	Photo	
Cup	Pillow	
Desk	Plate	
Dog	Pool	
Door	Potato	
Egg	Purse	
Empire	Queen	