

Oscillatory correlates of the primacy effect in episodic memory

Per B. Sederberg,^a Lynne V. Gauthier,^b Vitaly Terushkin,^b Jonathan F. Miller,^b
Julia A. Barnathan,^b and Michael J. Kahana^{b,*}

^aDepartment of Neuroscience, University of Pennsylvania, Philadelphia, PA 19104, USA

^bDepartment of Psychology, University of Pennsylvania, Philadelphia, PA 19104, USA

Received 13 February 2006; revised 6 April 2006; accepted 17 April 2006
Available online 30 June 2006

Both intracranial and scalp EEG studies have demonstrated that oscillatory activity, especially in the gamma band (28 to 100 Hz), can differentiate successful and unsuccessful episodic encoding [Sederberg, P.B., Kahana, M.J., Howard, M.W., Donner, E.J., Madsen, J.R., 2003. Theta and gamma oscillations during encoding predict subsequent recall. *Journal of Neuroscience*, 23(34), 10809–10814; Fell, J., Klaver, P., Lehnertz, K., Grunwald, T., Schaller, C., Elger, C.E., Fernandez, G., 2001. Human memory formation is accompanied by rhinal–hippocampal coupling and decoupling. *Nature Neuroscience*, 4 (12), 1259–1264; Gruber, T., Tsivilis, D., Montaldi, D., and Müller, M. (2004). Induced gamma band responses: An early marker of memory encoding and retrieval. *Neuroreport*, 15, 1837–1841; Summerfield, C., Mangels, J.A., in press. Dissociable neural mechanisms for encoding predictable and unpredictable events. *Journal of Cognitive Neuroscience*]. Although the probability of recalling an item varies as a function of where it appeared in the list, the relation between the oscillatory dynamics of successful encoding and serial position remains unexplored. We recorded scalp EEG as participants studied lists of common nouns in a delayed free-recall task. Because early list items were recalled better than items from later serial positions (the primacy effect), we analyzed encoding-related changes in 2 to 100 Hz oscillatory power as a function of serial position. Increases in gamma power in posterior regions predicted successful encoding at early serial positions; widespread low-frequency (4–14 Hz) power decreases predicted successful memory formation for later serial positions. These results suggest that items in early serial positions receive an encoding boost due to focused encoding without having to divide resources among numerous list items. Later in the list, as memory load increases, encoding is divided between multiple items.

© 2006 Elsevier Inc. All rights reserved.

Keywords: EEG; Gamma; Free-recall; Episodic memory; Encoding

Introduction

Much of the debate in the psychological literature regarding the behavioral mechanisms of episodic memory involves the enhanced probability of recalling items from early list positions, known as the primacy effect. One proposed source of the primacy effect is that subjects rehearse items from early serial positions throughout the list (Rundus, 1971; Brodie and Murdock, 1977). Thus, the boost in recall of early items is attributed to a combination of having recently rehearsed these items, as well as having spent additional time encoding them throughout the presentation of the list (Tan and Ward, 2000). A second account claims that early list items simply receive enhanced attentional resources and, consequently, are better encoded, regardless of how many additional rehearsals they received (Atkinson and Shiffrin, 1968; Neath and Crowder, 1990).

Brain activity recorded while participants encode items may help to differentiate these two explanations of the primacy effect. Subsequent memory paradigms, where measures of neural activity during item encoding are segregated by the subsequent ability to recall those items, provide a detailed account of the changes in brain activity associated with successful encoding, referred to as *subsequent memory effects* (SMEs) (Paller and Wagner, 2002). Thus, subsequent memory analyses, applied separately to items from primacy (early) and plateau (middle) serial positions, would allow us to isolate the components of brain activity that predict successful memory formation at different serial positions.

The free-recall paradigm is well suited for studying subsequent memory effects, having been successfully employed in scalp electroencephalogram (EEG), intracranial EEG (iEEG), and functional magnetic resonance imaging (fMRI) studies (Paller et al., 1987; Fernandez et al., 1999; Fell et al., 2001; Sederberg et al., 2003, in press; Weiss et al., 2000). Furthermore, the delayed free-recall task, in which subjects study a list of individually presented words and then attempt to recall as many words as possible in any order after a filled delay period, typically exhibits strong primacy effects (Postman and Phillips, 1965).

While traditional measures of brain activity have focused on event-related potentials (ERPs) and hemodynamic responses,

* Corresponding author. Fax: +1 215 746 6848.

E-mail address: kahana@psych.upenn.edu (M.J. Kahana).

Available online on ScienceDirect (www.sciencedirect.com).

researchers have recently begun to explore the role of oscillations, which are inherent in both scalp and intracranial EEG, in brain function. Both evoked and induced gamma oscillations (28 to 100 Hz) have been linked to communication between brain regions and top-down attentional processing in both humans and animals (Tallon-Baudry et al., 2005; Tiitinen et al., 1993; Debener et al., 2003; Rodriguez et al., 1999; Fries et al., 2001; Womelsdorf et al., 2006). Furthermore, intracranial and scalp EEG recordings have pointed to a role for gamma oscillations in successful memory formation (Fell et al., 2001; Sederberg et al., 2003, in press; Miltner et al., 1999; Gruber et al., 2004; Summerfield and Mangels, in press), but the relationship between gamma oscillations and the interaction between memory performance and serial position is unexplored.

Oscillations at lower frequencies may also play a role in successful memory formation (Sederberg et al., 2003). Klimesch et al. (1996) found significant increases in scalp-recorded theta (4 to 8 Hz) power during episodic encoding of words that were subsequently recalled. Similarly, increased oscillatory coherence between frontal and posterior scalp electrode sites, as well as significant increases in 1 to 4 Hz power, predicted subsequent recall for visually and auditorally presented nouns (Weiss and Rappelsberger, 2000). In a more recent study of the role of context in episodic encoding, Summerfield and Mangels (2005) observed increases in bilateral frontoposterior theta coherence that distinguished successful from unsuccessful encoding of combined item and context information.

Our goals in this study were to characterize better the role of oscillations in episodic memory formation and to determine whether distinct patterns of oscillations underlie successful encoding of items from early versus later serial positions. To accomplish this, we recorded scalp EEG while participants studied and later recalled items in a delayed free-recall task.

Materials and methods

Participants

Thirty-nine paid volunteers were recruited via fliers posted around the University of Pennsylvania campus. Participants were provided with a base monetary compensation plus an additional performance-based monetary incentive to ensure full effort. Our research protocol was approved by the Institutional Review Board at the University of Pennsylvania, and informed consent was obtained from all participants. Four participants were excluded from all analyses because they consistently employed a serial recall strategy instead of following the free recall instructions. The remaining 35 subjects (11 females) included in the analyses had a mean age of 21.4 years.

Experimental paradigm

Participants studied lists of words for a delayed free-recall task. Over the course of three sessions, participants received 48 study-test lists. Lists were composed of 15 common nouns, chosen at random and without replacement from a pool of nouns (mean frequency 49.0, <http://memory.psych.upenn.edu/wordpools.php>) (Friendly et al., 1982). A computer controlled stimulus presentation and recorded participants' responses. At the start of each trial, a plus sign appeared for 1600 ms at the center of the screen to alert

participants to upcoming word presentations at that location on the screen. The plus sign was followed by an 800 to 1200 ms blank interstimulus interval (ISI). The computer then displayed each list item in capital letters for 1.6 s, followed by an 800 to 1200 ms blank ISI. This temporal jitter served to decorrelate the physiological responses from successive word presentations. To minimize artifacts, we asked participants to avoid blinking and remain motionless during word presentations. To encourage elaborative encoding, participants were instructed to visualize each word as it was presented.

Immediately following each list presentation, participants were given a series of simple arithmetic problems. This end-of-list distractor task served to reduce the large advantage accorded to end-of-list items during recall. Each problem took the form of $A + B + C$, where A , B , and C were randomly chosen one-digit positive integers. Participants were asked to respond by typing the answer into the keyboard. Immediate feedback was given in the form of a high-pitched tone for correct entries and a low-pitched tone for incorrect answers. After 20 s of arithmetic problems, subjects were shown a row of asterisks accompanied by a 300 ms tone signaling the start of the recall period. Participants were given 45 s to recall items from the current list in any order (standard free-recall instructions). Vocal responses, which were digitally recorded during the trial, were scored for analysis following each session.

Electrophysiological recordings and data processing

EEG measurements were recorded via commercially available equipment (Net Amps 200 Amplifier, Netstation 4.0 acquisition environment, from Electrical Geodesics, Inc.). Geodesic Sensor Nets provided 129 standardized electrode placements across participants. All channels were digitized at a sampling rate of 500 Hz, and the signal from the caps was amplified via the Net Amps 200 amplifier. Recordings were initially referenced to Cz and later converted to an average reference. Peripheral and facial electrodes, defined as the outermost electrodes of the Geodesic Sensor Net, were excluded from the average reference because they frequently exhibited muscle artifacts or high impedance that contaminated the signal. Channels that demonstrated high impedance or poor contact with the scalp were also excluded after manually analyzing raw EEG traces. Channels excluded at re-referencing were also excluded from subsequent analyses and are not included in any figure. Additionally, electrodes were excluded on a subject basis if they were manually rejected due to noise in two of three sessions.

To identify epochs contaminated with eyeblink and other movement artifacts, electrooculogram (EOG) activity was monitored bipolarly using right and left electrode pairs. An individual word presentation event was rejected from subsequent analyses if the weighted running average for either the right or the left EOG pair exceeded a 100 μ V threshold, based on Net Station's eyeblink and movement detection algorithm (Electrical Geodesics, 2003).

Oscillatory analysis

After down-sampling the data to 200 Hz and notch-filtering around 60 Hz to remove line noise, we used the Morlet wavelet transform (with a wave-number of 6) to compute spectral power as a function of time for all our EEG signals. We then log-transformed the power values and down-sampled each word presentation event to 50 Hz. To normalize power values both

within and across subjects, we Z-transformed the power of each encoding event for each electrode, based on the mean and standard deviation of each subject's encoding events, separately for each session. Frequencies were sampled logarithmically at 46 intervals between 2 and 100 Hz and split into six distinct bands – 2 to 4 Hz (delta), 4 to 8 Hz (theta), 10 to 14 Hz (alpha), 16 to 26 Hz (beta), 28 to 42 Hz (low gamma), and 44 to 100 Hz (high gamma) – by taking the mean of the Z-transformed power in each frequency band.

A Wilcoxon rank sum test was then used to compare between two sets of encoding events, such as recalled versus not recalled items, based on the mean of the Z-transformed wavelet power during the encoding period (a 2 s interval beginning with presentation onset). This comparison was made separately for each electrode and frequency band. A positive SME indicates greater oscillatory power during the encoding of subsequently recalled words with respect to the encoding of not recalled words; a negative SME indicates lower oscillatory power during the encoding of subsequently recalled words.

Aggregating across subjects and correcting for multiple comparisons

We used a permutation procedure to account for correlations between electrodes and to generate an unbiased empirical estimate of the Type I error rate (Efron, 1979; Gibbons and Shanken, 1987; Sederberg et al., 2003). First, we generated 1000 random samples of the experimental data by randomly swapping events from the two comparison conditions. Next, we performed a rank sum test on the 1000 random shuffles of data for all electrodes and frequency bins.

To determine significant electrodes across subjects, we applied the inverse normal transformation (*Z* score) to both the *P* value obtained by comparing two sets of events and the distribution of the *p* values from the permutation test. This produced a *Z* score and an empirically determined random distribution of *Z* scores of what would be expected by chance. We then summed the *Z* scores across subjects for each electrode, thus producing a summed *Z* score and an empirically determined random distribution of summed *Z* scores for each of the electrodes. We determined a significance threshold by combining all of the empirical distributions into a single distribution and selecting the summed *Z* value from each tail of the distribution that would give rise to one significant electrode by chance. We then applied these positive and negative thresholds to each summed *Z* value from the actual data at each electrode to determine if it was significant.

To test for an interaction between successful memory formation and serial position, we computed the significance of the difference between the SMEs at early versus middle serial positions. Using the permutation procedure described above, we first calculated a *Z* score and an empirical distribution of *Z* scores for the comparison between recalled and not recalled items, separately for items from early and middle serial positions. We then took the difference between both the two *Z* scores from the actual data and the two empirical distributions of *Z* scores, giving rise to a difference *Z* score and an empirical distribution of difference *Z* scores at each electrode and subject. To determine significance across subjects and account for multiple comparisons, we summed the difference *Z* scores across subjects and picked positive and negative significance thresholds as above.

Results

Task performance

Participants recalled an average of 51.1% of the items on each study list. Fig. 1 depicts the probability of recalling a word as a function of serial position. Early serial positions exhibited the standard primacy effect, while the end-of-list distractor reduced the recency effect. We divided the list into three nonoverlapping sets of serial positions: early (1 through 4, $61.6 \pm 2.4\%$), middle (6 through 10, $45.1 \pm 2.3\%$), and late (12 through 15, $50.0 \pm 2.4\%$). A one-way repeated measures ANOVA revealed a significant main effect of serial position on recall probability ($F(2,68) = 30.71$, $P < .00001$). Follow-up paired *t* tests indicated that all possible comparisons between the sets of serial positions were significantly different (early versus middle, $t(34) = 8.95$, $P < .00001$; middle versus late, $t(34) = -3.22$, $P < .003$; early versus late, $t(34) = 4.02$, $P < .001$).

Given that our end-of-list distractor task did not completely eliminate the recency effect, as indicated by the increase in recall probability for late compared to middle serial positions, we can assume that the enhanced probability of recalling items from late serial positions is due in part to working memory processes, and not simply better episodic memory encoding. Therefore, we focused our subsequent analyses on the difference between early (primacy) and middle (plateau) serial positions to avoid confounds between episodic and working memory processes.

Oscillatory serial position effects

Our first step in uncovering the interaction between serial position and the oscillatory correlates of successful memory formation was to characterize the change in oscillatory power as a function of serial position. Fig. 2 shows the topography of the electrodes exhibiting significant differences in mean power between early and middle serial positions for each frequency band. To visualize the significant power changes with each list item, we show the mean power for each frequency band as a function of serial position based on data averaged across all significant electrodes.

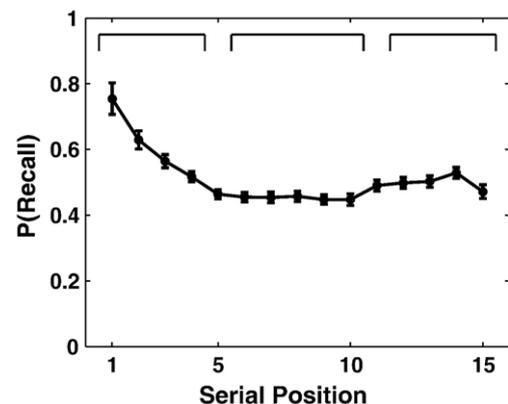


Fig. 1. Recall probability as a function of serial position. Brackets above the curve denote the three ranges of serial positions we examined: early (1 to 4), middle (6 to 10), and late (12 to 15). Error bars represent Loftus and Masson (1994) corrected ± 1 standard error of the mean.

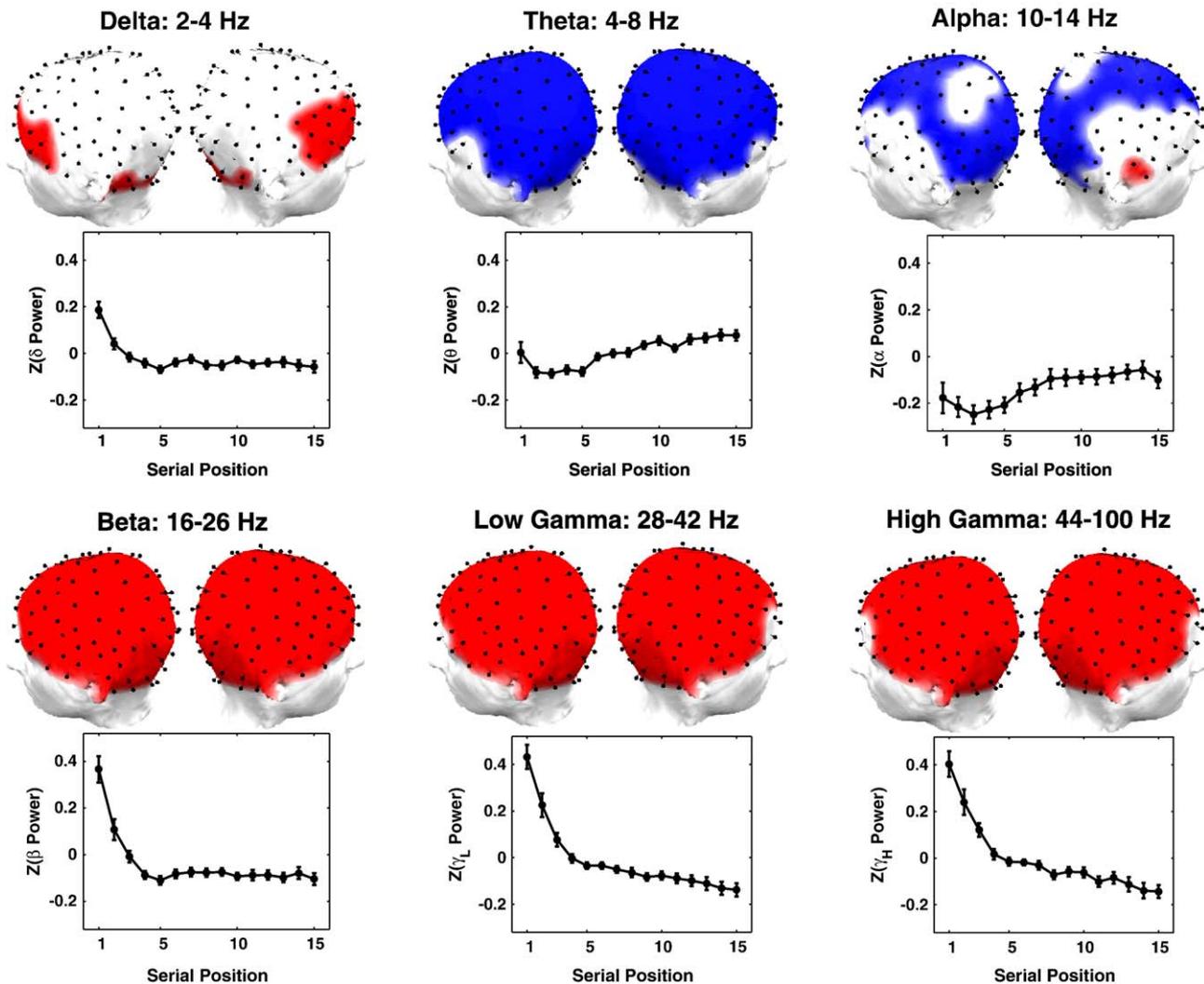


Fig. 2. Significant differences in oscillatory power between early and middle serial positions. The scalp topographies depict the electrodes that exhibited significant differences in mean power during the 0 to 2 s encoding interval between early (1 to 4) and middle (6 to 10) serial positions, independent of subsequent memory, for six frequency bands. Red areas denote more power for primacy items, whereas blue areas denote more power for middle serial positions. The line graph plots the mean Z-transformed power across subjects for the significant electrodes in each frequency bin. Error bars represent ± 1 standard error of the mean.

Delta, beta, and gamma power all started high and decreased as a function of serial position, while theta and alpha oscillations began low and increased with serial position. Although the increase in delta power for early serial positions was primarily confined to frontal electrode locations, the increased beta and gamma power for early and the increased theta and alpha power for middle serial positions occurred at widespread electrodes.

Oscillatory subsequent memory effects

Our next step was to determine the oscillatory correlates of subsequent memory performance, independent of serial position. Fig. 3 illustrates the topography and the direction of effect for those electrodes exhibiting significant differences in oscillatory power between successful and unsuccessful encoding combined across both early and middle serial positions. Gamma power increased at posterior electrode sites during successful relative to unsuccessful encoding. Conversely, decreases in theta and alpha power at widespread electrodes predicted successful encoding.

Interaction between serial position and subsequent memory

Having observed main effects of both serial position and subsequent memory performance on power, we set out to determine if these changes in power exhibited a significant interaction (see Materials and methods). We compared the difference in mean power between successfully and unsuccessfully encoded early list items (Early SME) to the difference in mean power between successfully and unsuccessfully encoded middle list items (Middle SME). Fig. 4 illustrates the topography of those electrodes exhibiting a significant interaction between serial position and subsequent memory. Numerous posterior and parietal electrodes exhibited greater power differences for the early as compared to the middle SME at widespread frequencies, but no electrodes exhibited a negative interaction at any frequency band. To discern between the relative increases or decreases in power that gave rise to the significant interaction, we calculated the SMEs for items from early and middle serial positions independently. The left and right columns of Fig. 5

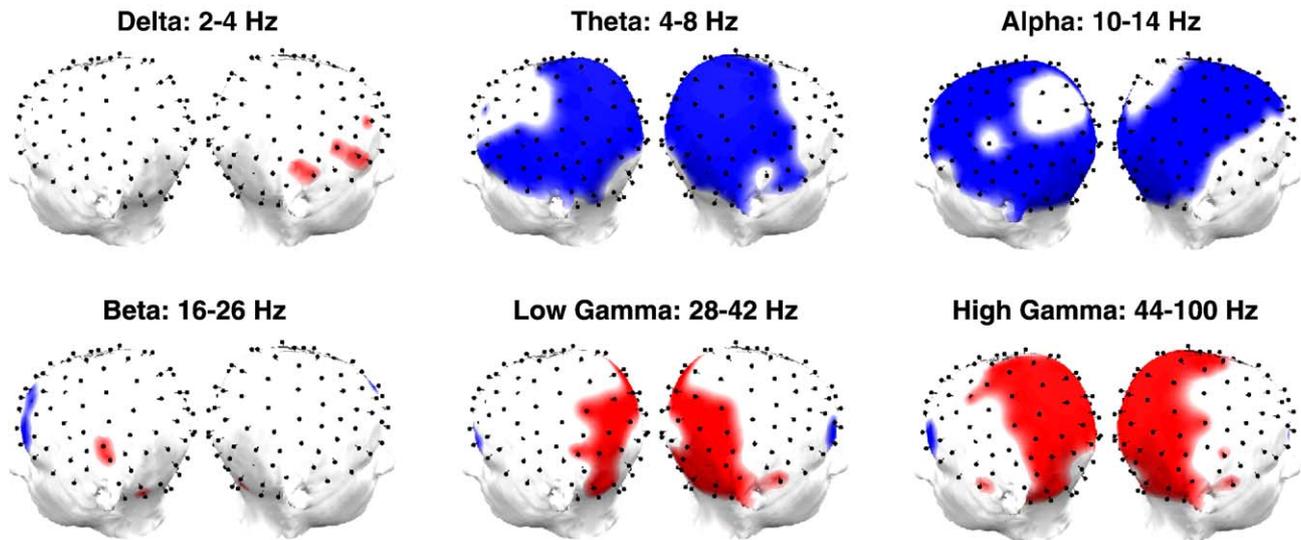


Fig. 3. Topography of significant subsequent memory effects for items from both early and middle serial positions. Each pair of scalp topographies illustrates the electrodes exhibiting significant increases (red) or decreases (blue) in power during encoding that predicted successful retrieval for six distinct frequency bands.

illustrate the topography of the early and middle SMEs, respectively. For early serial positions, gamma power increased in the posterior regions during successful versus unsuccessful encoding. In addition to this early positive gamma SME, increased beta oscillations in left temporal and right-central posterior parietal electrodes also predicted successful encoding. For middle serial positions, however, negative low-frequency SMEs (4 to 14 Hz) were observed at most frontal, temporal, and parietal electrode sites.

Timing of the oscillatory SME

To assess the timing of the oscillatory SMEs, we calculated time-frequency spectrograms of the difference in mean Z-transformed power between successful and unsuccessful encod-

ing. For this analysis, we aggregated across the significant electrodes for a particular frequency and serial position bin. Figs. 6A and B show the time-frequency power difference spectrograms for the positive high-gamma SME from early serial positions (A) and the negative alpha SME from middle serial positions (B).

Gamma oscillations increased during the entire encoding interval for successfully recalled words. The alpha decreases during successful encoding of middle list items began approximately 500 ms following the onset of each item presentation and slightly tapered off near the end of the epoch. Given that the dominant effect for the middle serial positions is a broadband negative SME at most electrodes, the time-frequency spectrograms for the theta and alpha frequency bands exhibited the same pattern of power differences.

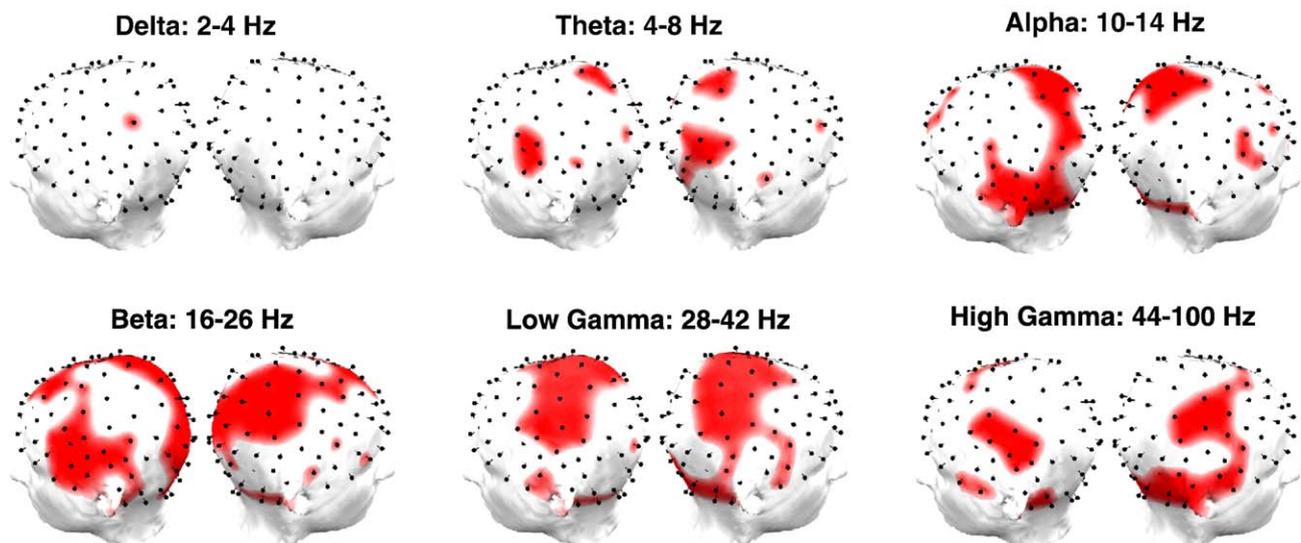


Fig. 4. Topography of significant interaction effects between subsequent memory and serial position. Each pair of scalp topographies illustrates the electrodes exhibiting a significant interaction between subsequent memory and serial position (*Early SME*–*Middle SME*) for one of six distinct frequency bands. Positive interactions, where the difference in power was greater for the *Early SME* than for the *Middle SME*, are in red, while negative interactions are in blue.

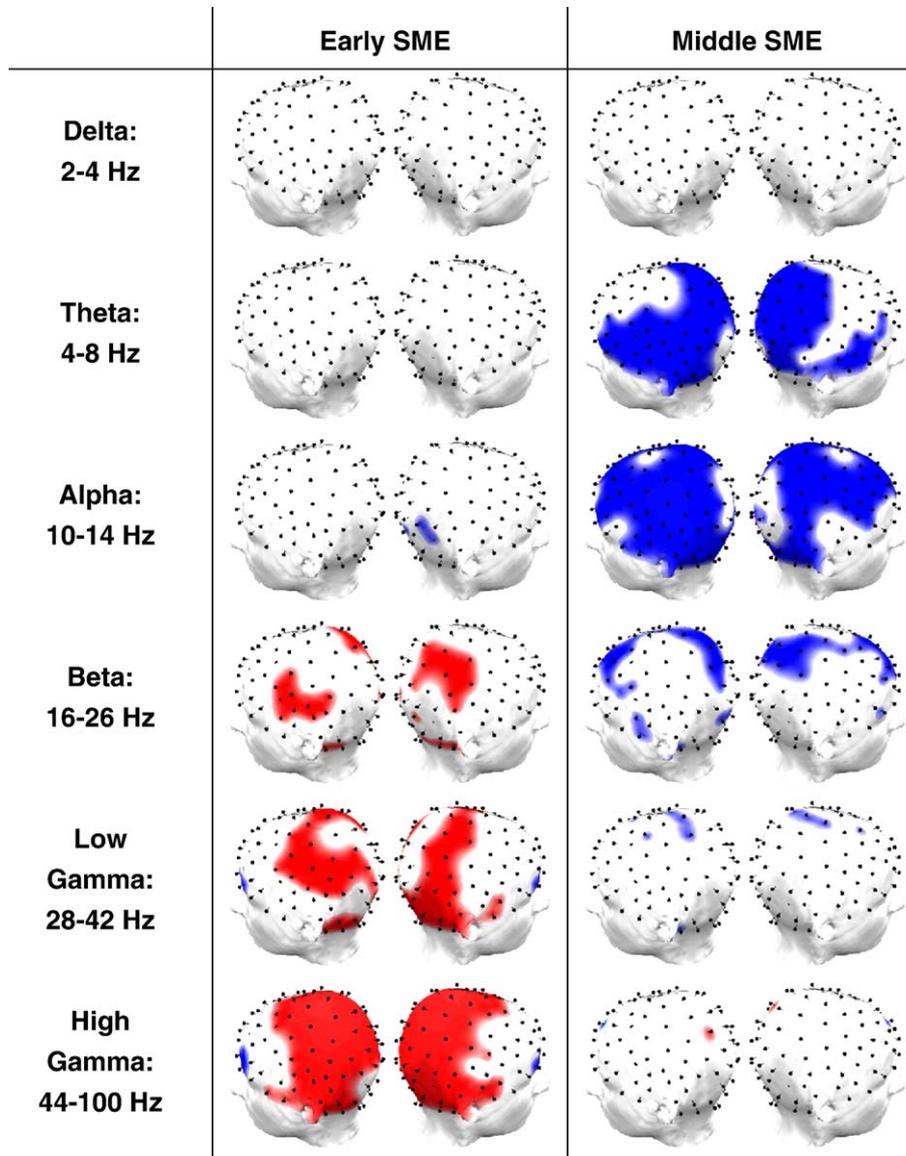


Fig. 5. Topography of significant early and middle subsequent memory effects. Each column illustrates the electrodes exhibiting significant increases (red) or decreases (blue) in power during encoding that predicted successful retrieval, analyzed separately for early (left) and middle (right) serial positions. The rows correspond to each of the six frequency bands.

Positive delta and theta SME

Previous studies (Weiss and Rappelsberger, 2000; Summerfield and Mangels, 2005, in press) have demonstrated positive low-frequency SMEs, but the above analyses revealed only positive high-frequency SMEs, and only for early serial positions. Given that the delta and theta SMEs reported in the existing literature occurred within the first second after the item presentation, it is possible that our 2 s analysis window prevented a weak positive low-frequency SME from crossing the significance threshold. To test this, we repeated the analyses outlined above on a smaller window between 300 and 500 ms following stimulus onset. While the pattern of high-frequency SME topographies remained the same, a right fronto-temporal positive delta SME (Fig. 7A) and a small right frontal positive theta SME (Fig. 7B) emerged across early and middle serial positions. As is evident from the time-frequency spectrogram across the electrodes exhibiting significant

delta and theta SMEs (Figs. 7A and B, bottom), the magnitude of the increases was lower than those of the high-frequency SMEs, explaining why this effect did not remain significant for the 0 to 2 s analysis interval.

Discussion

This study explored whether distinct patterns of oscillations underlie the successful encoding of items studied at early versus later serial positions. The large primacy effect seen in our data (Fig. 1) is typical of intentional learning tasks, and likely reflects subjects' use of elaborative rehearsal strategies to help associate items and encode them into memory (Craig and Tulving, 1975). Such elaborative rehearsal strategies (e.g., making a story out of the list items) will result in increased rehearsal of early list items during later item presentations (Modigliani and Hedges, 1987; Tan

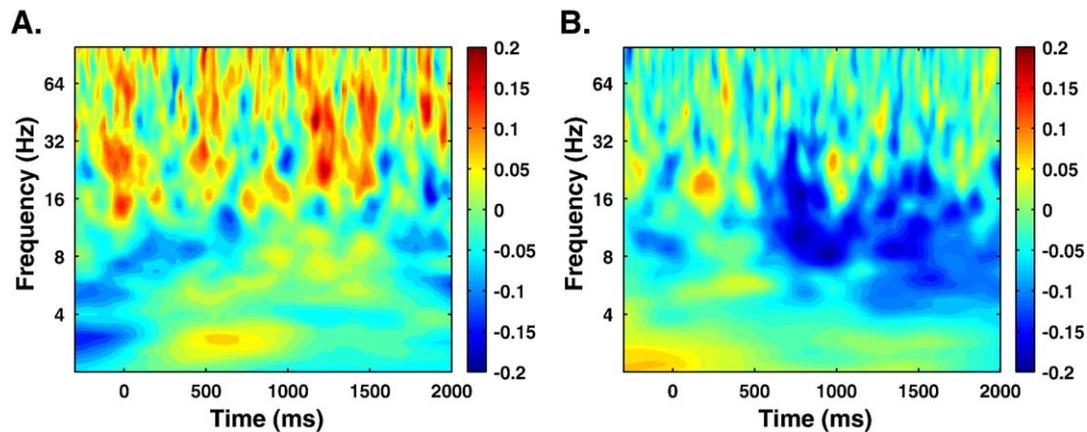


Fig. 6. Timing of significant oscillatory subsequent memory effects. Each time-frequency spectrogram illustrates the difference in Z-transformed power between successful and unsuccessful encoding events. Power differences were aggregated across all subjects and significant electrodes for two frequency and serial position bins: (A) electrodes exhibiting significant increases in high gamma power during successful encoding of early serial positions and (B) electrodes exhibiting significant decreases in alpha power during successful encoding of middle serial positions (see Fig. 5).

and Ward, 2000), and consequently more divided encoding of these later list items. Whereas it has been demonstrated that subjects' tendency to rehearse early list items in later list positions contributes to the primacy effect (Rundus, 1971; Tan and Ward, 2000), our electrophysiological results point to a second supporting mechanism. Gamma power was higher both during early as compared with later item presentations, and during the study of successfully encoded items from early serial positions. Coupled with the absence of any negative oscillatory SME for early list items, these results suggest that gamma oscillations are associated with focused encoding at early serial positions. Conversely,

broadband low-frequency negative SMEs covered most of the scalp later in the list, indicating a shift from focused to divided encoding.

Oscillatory serial position effects

As stated above, changes in oscillatory power as a function of serial position may indicate a shift from focused to more divided encoding. We found that delta, beta, and gamma power was high for early serial positions, but decreased as more items were presented. Early in the list, one can focus on encoding the first

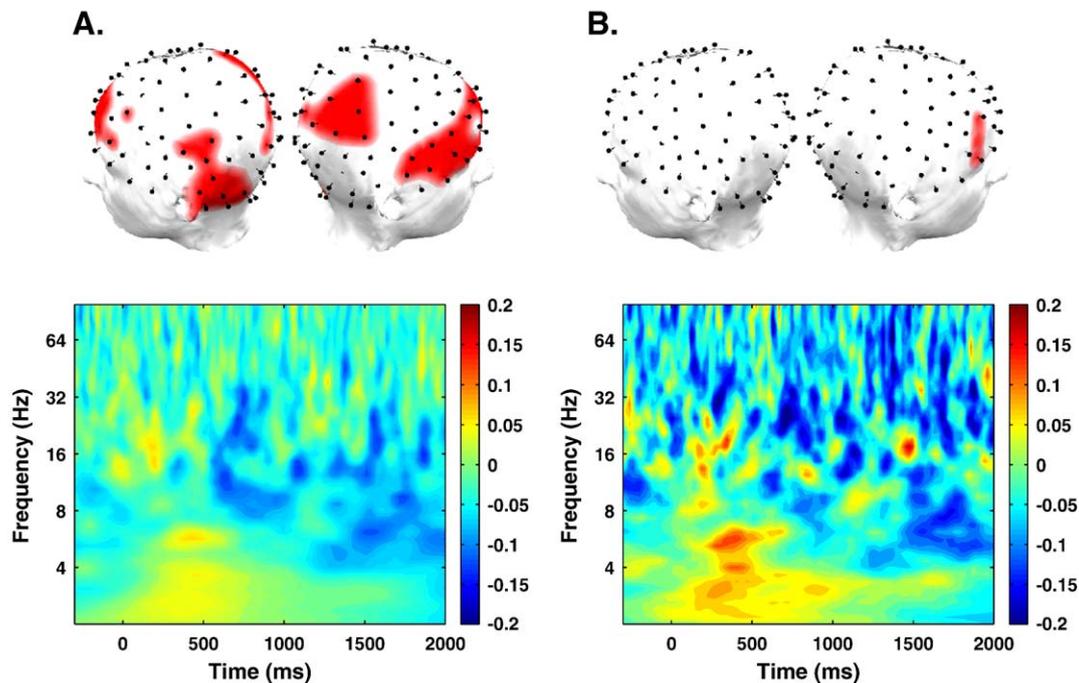


Fig. 7. Delta and theta power predicts successful encoding across early and middle serial positions. (A) Illustrates the topography and timing of the electrodes exhibiting significant increases (red) or decreases (blue) in delta (2 to 4 Hz) power between 300 and 500 ms after stimulus onset for successful versus unsuccessful encoding. (B) The topography and timing of significant theta (4 to 8 Hz) subsequent memory effects. The time-frequency spectrograms below the topography maps illustrate the difference in Z-transformed power between successful and unsuccessful encoding events, averaged across all subjects and significant electrodes from the topography above.

few items without interference from other list items. Such focused encoding may be linked to increases in high-frequency power associated with increases in top-down attention or allocation of resources (Engel et al., 2001). For example, evoked gamma power has been found to increase when subjects selectively attend to target stimuli (Tiitinen et al., 1993) and process rare, as opposed to common, targets (Debener et al., 2003), while induced gamma power increases when subjects retain images in short-term memory (Tallon-Baudry et al., 1998), successfully recognize ambiguous objects (Rodriguez et al., 1999), and better encode predictable as opposed to unpredictable items (Summerfield and Mangels, *in press*). As more items are presented, encoding becomes divided between more items and the overall level of high-frequency oscillations decreases, while low-frequency power increases. As reported by Jensen et al. (2002), the increase in alpha power at later serial positions may correlate with the increase in working memory load due to there being more items to encode.

Positive gamma SME for early serial positions

Forming part of the interaction between successful encoding and serial position, distinct patterns of gamma power changes predicted successful encoding at early versus middle serial positions. Early in the list, gamma power was higher during successful as opposed to unsuccessful encoding, specifically in the posterior parietal, temporal, and occipital regions. While the increased gamma power during encoding of items from early serial positions was greater for successfully recalled items, as overall gamma power decreased with additional item presentations, there was no significant difference in gamma power between successful and unsuccessful encoding. Therefore, the gamma SME for early serial positions (Fig. 5) accounts for the main effect of subsequent memory seen in the gamma band (Fig. 3).

In addition to the similarity of our gamma results with previous work relating gamma and attention, the topography of the positive gamma SME for early serial positions overlaps with significant changes in event related potentials (ERPs) associated with successful encoding reported in previous scalp EEG studies. Studying the effects of focused versus divided attention on episodic encoding, Mangels et al. (2001) found that subsequently remembered items exhibited a larger posterior negative potential than missed items, and that focused attention gave rise to larger negative potentials than divided attention. Thus, along with the decrease in gamma power with serial position, the change in the gamma SME with serial position likely marks the transition from focused to divided encoding.

The timing of the gamma SME for early serial positions further supports the theory that the increased gamma response correlates with an enhanced encoding state. As seen in Fig. 6A, gamma power increases for successfully encoded items from early serial positions were sustained throughout the encoding epoch. This differs from the more transient induced gamma SMEs reported from two recent studies (Gruber et al., 2004; Summerfield and Mangels, *in press*), and may instead be related to sustained activity that corresponds to a general increase in attentional resources. Thus, the increased resources available during the first few item presentations would give rise to an enhanced encoding state, which manifests as increased gamma power that is not time-locked to stimulus onset.

Negative SMEs for middle serial positions

The second component of the interaction between successful encoding and serial position was the decrease in theta and alpha power associated with successful encoding of items from middle serial positions. As more items were presented, theta and alpha power increased independently of memory performance and the early positive high-frequency SMEs were replaced by low-frequency negative SMEs covering most of the scalp (Fig. 5). As stated earlier, memory load increases with the presentation of additional items and encoding shifts from focused to divided item processing. With fewer attentional resources to boost encoding of specific words, to increase the chance of encoding a nonprimacy item from the middle of the list, a participant would be required to inhibit the rehearsal of earlier list items and to encode the current item, which becomes more difficult with increasing numbers of items. Thus, one interpretation of increased alpha oscillations is that it indicates the breakdown of encoding processes due to increased memory load (Jensen et al., 2002).

A similar interpretation is that increases in theta and alpha power correlate with inattention and, thus, predict unsuccessful encoding of middle list items. One may interpret an increase in gamma power as an increase in synchronous firing, either because of functional connectivity between other regions and the recorded region, or because of activity within the region, itself (Logothetis et al., 2001; Herrmann et al., 2004; Kaiser and Lutzenberger, 2005; Fries, 2005). Thus, increased gamma power indicates the active participation of a brain region in the task. In contrast, broadband increases in power may indicate noise due to desynchronized input or activity within a region. Such broadband increases would be expected to accompany the shift from focused to divided encoding with more list items. Furthermore, increases in alpha power have been correlated with decreases in simultaneously recorded fMRI BOLD signals in widespread brain regions (Goldman et al., 2002; Laufs et al., 2003; Mukamel et al., 2005) and with decreased memory performance (Klimesch et al., 1997; Klimesch, 1999). Therefore, increases in alpha oscillations, which we found to increase 500 ms following stimulus onset and often became broadband late during the unsuccessful encoding epoch of an item, may indicate periods of inattention (Fig. 6B).

Positive delta and theta SMEs across early and middle serial positions

Given the proposed importance of theta oscillations in many forms of cognitive processing (Kahana, 2006), we were surprised not to find a positive theta SME at any time during encoding. However, we performed the SME analyses on a smaller time bin from 300 to 500 ms following stimulus onset, when most low-frequency results have been reported (Klimesch et al., 1996; Weiss and Rappelsberger, 2000; Summerfield and Mangels, 2005, *in press*). While the same basic pattern of high-frequency results remained, a strong positive frontal delta SME and a small positive frontal theta SME emerged (Fig. 7). The delta SME is similar to the increased delta power seen for successful encoding of both visually and auditorally presented nouns (Weiss and Rappelsberger, 2000). Furthermore, increased delta power may be related to the increased frontal positivity associated with elaborative encoding (Paller et al., 1987; Rushby et al., 2002) and communication between frontal and posterior sites during item processing (Sarthein et al., 1998). The fact that the theta results are the most prominent low-frequency

effect in the literature may be because much of the prior work only reports results based on a subset of the frequency bands, with no mention of delta results (Klimesch et al., 1996; Summerfield and Mangels, 2005, *in press*). When both delta and theta results are reported, the delta results are often the stronger of the two (Weiss and Rappelsberger, 2000). Furthermore, there is evidence that theta oscillations are part of an oscillatory hierarchy where delta phase is correlated with theta power increases (Lakatos et al., 2005). Thus, we found that the magnitude of the theta SME was smaller than the positive SMEs at higher frequencies and only emerged when we focused on the early encoding epoch because the small power increases were unable to overcome the strong negative low-frequency SME that emerged late in the encoding epoch. However, the theta SME may be linked to the strong delta SME seen in frontal and posterior regions.

Link between scalp and intracranial oscillations

One open question concerns the relationship between EEG activity recorded at the scalp and the more local signals recorded with intracranial EEG. Although the ideal way to study correlations between scalp and intracranial EEG would be with simultaneous recordings, useful information can be gained by comparing results obtained by means of identical tasks and analytical methods.

Our lab has recorded intracranial EEG from 35 patients while they performed the identical delayed free-recall task as the one performed by participants in this scalp study. As we report in Sederberg et al. (*in press*), increased gamma oscillations in the hippocampus, left inferior prefrontal cortex, left temporal lobes, and bilateral occipital lobes predicted successful encoding (also see Sederberg et al. (2003) for results on a subset of the patients). The strongest correspondence is between the posterior gamma SMEs, which both occur throughout the 2 s encoding interval. Widespread negative alpha and broadband SMEs also occur in both our intracranial and scalp data, and follow the same time course, increasing 500 ms into the encoding period. Thus, many of the same effects recorded at the scalp mirror results recorded intracranially, thereby forging part of a crucial link between scalp EEG and the local recordings typically achievable only from animals.

Conclusions

This study explored the role of scalp-recorded oscillations in episodic memory formation and whether distinct electrophysiological responses underlie successful encoding of primacy versus nonprimacy items. Although we can assume that items from early serial positions are rehearsed late into lists (Rundus, 1971; Tan and Ward, 2000), the gamma SME reported here supports the theory that early serial positions receive an encoding boost due to focused encoding without having to divide resources among numerous list items. Later in the list, when overall gamma power has decreased, increased alpha oscillations correlate with divided encoding due to increased memory load or the inability to maintain focused encoding throughout the task.

These theories can be further tested with modifications to the current paradigm. Increasing the presentation rate would diminish primacy effects by reducing divided encoding due to rehearsal of early list items late in the list (Howard and Kahana, 1999). Consequently, if rehearsing prior items controls the transition to divided encoding, faster presentation rates should slow the rate of

the gamma power decline and the alpha power increase with serial position and enhance the posterior positive gamma SME for middle serial positions. However, if the increase in alpha is due to increased memory load, which decreases the overall level of attentional resources, then there will be little effect on the middle list items, even when the primacy effect is reduced.

Acknowledgments

We would like to thank Josh Jacobs, Polly Johnsen, Sean Polyn, and Marieke van Vugt for helpful discussions and feedback on this manuscript. The authors acknowledge support from the Swartz Foundation, National Institutes of Health research grants MH61975, MH062196, and MH072138, and National Science Foundation grant SBE0354378.

References

- Atkinson, R.C., Shiffrin, R.M., 1968. Human memory: a proposed system and its control processes. In: Spence, K.W., Spence, J.T. (Eds.), *The Psychology of Learning and Motivation*, vol. 2. Academic Press, New York, pp. 89–105.
- Brodie, D.A., Murdock, B.B., 1977. Effects of presentation time on nominal and functional serial position curves in free recall. *J. Verbal Learn. Verbal Behav.* 16, 185–200.
- Craik, F.I.M., Tulving, E., 1975. Depth of processing and the retention of words in episodic memory. *J. Exp. Psychol.* 104 (3), 268–294.
- Debener, S., Herrmann, C.S., Kranczioch, C., Gembris, D., Engel, A.K., 2003. Topdown attentional processing enhances auditory evoked gamma band activity. *NeuroReport* 14 (5), 683–686.
- Efron, B., 1979. Bootstrap methods: another look at the jackknife. *Ann. Stat.* 7 (1), 1–26.
- Electrical Geodesics, I., 2003. Net station waveform tools technical manual. s-man-200-wtfr-001 (Tech. Rep.). EGI.
- Engel, A., Fries, P., Singer, W., 2001. Dynamic predictions: oscillations and synchrony in top-down processing. *Nat. Rev., Neurosci.* 2 (10), 704–716.
- Fell, J., Klaver, P., Lehnertz, K., Grunwald, T., Schaller, C., Elger, C.E., Fernandez, G., 2001. Human memory formation is accompanied by rhinal–hippocampal coupling and decoupling. *Nat. Neurosci.* 4 (12), 1259–1264.
- Fernandez, G., Effern, A., Grunwald, T., Pezer, N., Lehnertz, K., Dumpelmann, M., Van Roost, D., Elger, C.E., 1999. Real-time tracking of memory formation in the human rhinal cortex and hippocampus. *Science* 285, 1582–1585.
- Friendly, M., Franklin, P.E., Hoffman, D., Rubin, D.C., 1982. The Toronto Word Pool: Norms for imagery, concreteness, orthographic variables, and grammatical usage for 1,080 words. *Behav. Res. Meth. Instrum.* 14, 375–399.
- Fries, P., 2005. A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. *Trends Cogn. Sci.* 9 (10), 474–480.
- Fries, P., Reynolds, J.H., Rorie, A.E., Desimone, R., 2001. Modulation of oscillatory neuronal synchronization by selective visual attention. *Science* 291 (5508), 1560–1563.
- Gibbons, M.R., Shanken, J., 1987. Subperiod aggregation and the power of multivariate tests of portfolio efficiency. *J. Financ. Econ.* 19, 389–394.
- Goldman, R.I., Stern, J.M., Engel Jr., J., Cohen, M.S., 2002. Simultaneous EEG and fMRI of the alpha rhythm. *NeuroReport* 13 (18), 2487–2492.
- Gruber, T., Tsivilis, D., Montaldi, D., Müller, M., 2004. Induced gamma band responses: an early marker of memory encoding and retrieval. *NeuroReport* 15, 1837–1841.
- Herrmann, C.S., Munk, M.H.J., Engel, A.K., 2004. Cognitive functions of gamma-band activity: memory match and utilization. *Trends Cogn. Sci.* 8 (8), 347–355.

- Howard, M.W., Kahana, M.J., 1999. Contextual variability and serial position effects in free recall. *J. Exper. Psychol., Learn., Mem., Cogn.* 25, 923–941.
- Jensen, O., Gelfand, J., Kounios, J., Lisman, J.E., 2002. Oscillations in the alpha band (9–12 Hz) increase with memory load during retention in a short-term memory task. *Cereb. Cortex* 12, 877–882.
- Kahana, M.J., 2006. The cognitive correlates of human brain oscillations. *J. Neurosci.* 26 (6), 1669–1672.
- Kaiser, J., Lutzenberger, W., 2005. Human gamma-band activity: a window to cognitive processing. *NeuroReport* 16 (3), 207–211.
- Klimesch, W., 1999. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Res. Brain Res. Rev.* 29 (2–3), 169–195.
- Klimesch, W., Doppelmayr, M., Russegger, H., Pachinger, T., 1996. Theta band power in the human scalp EEG and the encoding of new information. *NeuroReport* 7 (7), 1235–1240.
- Klimesch, W., Doppelmayr, M., Schimke, H., Ripper, B., 1997. Theta synchronization and alpha desynchronization in a memory task. *Psychophysiology* 34 (2), 169–176.
- Lakatos, P., Shah, A., Knuth, K., Ulbert, I., Karmos, G., Schroeder, C., 2005. An oscillatory hierarchy controlling neuronal excitability and stimulus processing in the auditory cortex. *J. Neurophysiol.* 3, 1904–1911.
- Laufs, H., Krakow, K., Sterzer, P., Eger, E., Beyerle, A., Salek-Haddadi, A., Kleinschmidt, A., 2003. Electroencephalographic signatures of attentional and cognitive default modes in spontaneous brain activity fluctuations at rest. *Proc. Natl. Acad. Sci. U. S. A.* 100 (19), 11053–11058.
- Loftus, G.R., Masson, M.E.J., 1994. Using confidence intervals in within-subject designs. *Psychon. Bull. Rev.* 1, 476–490.
- Logothetis, N., Pauls, J., Augath, M., Trinath, T., Oeltermann, A., 2001. Neurophysiological investigation of the basis of the fMRI signal. *Nature* 412, 150–157.
- Mangels, J., Picton, T., Craik, F.I.M., 2001. Attention and successful episodic encoding: an event-related potential study. *Cogn. Brain Res.* 11, 77–95.
- Miltner, W.H., Braun, C., Arnold, M., Witte, H., Taub, E., 1999. Coherence of gamma-band EEG activity as a basis for associative learning. *Nature* 397 (6718), 434–436.
- Modigliani, V., Hedges, D.G., 1987. Distributed rehearsals and the primacy effect in single-trial free recall. *J. Exper. Psychol., Learn., Mem., Cogn.* 13, 426–436.
- Mukamel, R., Gelbard, H., Arieli, A., Hasson, U., Fried, I., Malach, R., 2005. Coupling between neuronal firing, field potentials, and fMRI in human auditory cortex. *Science* 309 (5736), 951–954.
- Neath, I., Crowder, R.G., 1990. Schedules of presentation and temporal distinctiveness in human memory. *J. Exper. Psychol., Learn., Mem., Cogn.* 16, 316–327.
- Paller, K.A., Wagner, A.D., 2002. Observing the transformation of experience into memory. *Trends Cogn. Sci.* 6 (2), 93–102.
- Paller, K.A., Kutas, M., Mayes, A.R., 1987. Neural correlates of encoding in an incidental learning paradigm. *Electroencephalogr. Clin. Neurophysiol.* 67, 360–371.
- Postman, L., Phillips, L.W., 1965. Short-term temporal changes in free recall. *Q. J. Exp. Psychol.* 17, 132–138.
- Rodriguez, E., George, N., Lachaux, J.P., Martinerie, J., Renault, B., Varela, F.J., 1999. Perception's shadow: long-distance synchronization of human brain activity. *Nature* 397 (6718), 430–433.
- Rundus, D., 1971. An analysis of rehearsal processes in free recall. *J. Exp. Psychol.* 89, 63–77.
- Rushby, J.A., Barry, R.J., Johnstone, S.J., 2002. Event-related potential correlates of serial-position effects during an elaborative memory test. *Int. J. Psychophysiol.* 46, 13–27.
- Samthein, J., Petsche, H., Rappelsberger, P., Shaw, G.L., von Stein, A., 1998. Synchronization between prefrontal and posterior association cortex during human working memory. *Proc. Natl. Acad. Sci. U. S. A.* 95 (12), 7092–7096.
- Sederberg, P.B., Kahana, M.J., Howard, M.W., Donner, E.J., Madsen, J.R., 2003. Theta and gamma oscillations during encoding predict subsequent recall. *J. Neurosci.* 23 (34), 10809–10814.
- Sederberg, P.B., Schulze-Bonhage, A., Madsen, J.R., Bromfield, E.B., McCarthy, D.C., Brandt, A., Tully, M.S., Kahan, M.J., in press. Hippocampal and neocortical gamma oscillations predict memory formation in humans. *Cereb. Cortex*.
- Summerfield, C., Mangels, J.A., 2005. Coherent theta-band eeg activity predicts item-context binding during encoding. *NeuroImage* 24, 692–703.
- Summerfield, C., and Mangels, J.A., in press. Dissociable neural mechanisms for encoding predictable and unpredictable events. *J. Cogn. Neurosci.*
- Tallon-Baudry, C., Bertrand, O., Peronnet, F., Pernier, J., 1998. Induced gamma-band activity during the delay of a visual short-term memory task in humans. *J. Neurosci.* 18 (11), 4244–4254.
- Tallon-Baudry, C., Bertrand, O., Henaff, M.-A., Isnard, J., Fischer, C., 2005. Attention modulates gamma-band oscillations differently in the human lateral occipital cortex and fusiform gyrus. *Cereb. Cortex* 15 (5), 654–662.
- Tan, L., Ward, G., 2000. A recency-based account of the primacy effect in free recall. *J. Exper. Psychol., Learn., Mem., Cogn.* 26, 1589–1626.
- Tiitinen, H., Sinkkonen, J., Reinikainen, K., Alho, K., Lavikainen, J., Naatanen, R., 1993. Selective attention enhances the auditory 40-Hz transient response in humans. *Nature* 364 (6432), 59–60.
- Weiss, S., Rappelsberger, P., 2000. Long-range EEG synchronization during word encoding correlates with successful memory performance. *Cogn. Brain Res.* 9, 299–312.
- Weiss, S., Muller, H.M., Rappelsberger, P., 2000. Theta synchronization predicts efficient memory encoding of concrete and abstract nouns. *NeuroReport* 11, 2357–2361.
- Womelsdorf, T., Fries, P., Mitra, P.P., Desimone, R., 2006. Gamma-band synchronization in visual cortex predicts speed of change detection. *Nature* 439 (7077), 733–736.