Synchronous and asynchronous theta and gamma activity during episodic memory formation

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Abstract

Although it has been hypothesized that neural oscillations synchronize to mediate memory formation, direct evidence linking oscillatory phase-synchrony to successful memory encoding is limited. Using electrocorticography (ECoG) recorded from 68 neurosurgical patients participating in a free recall task, we compared phase-synchrony and spectral power during successful versus unsuccessful encoding using a region of interest approach and a graph theoretic metric. During successful memory encoding, theta synchrony increased in the left prefrontal cortex immediately after word presentation. Following this encoding related increase in theta synchrony we observed decreases in theta synchrony, and theta power, in both the prefrontal cortex as well as more widespread brain regions. Whereas gamma power increased during successful memory encoding, increases in gamma synchrony were limited to a small network in the right peri-sylvian region. In the left hemisphere, where gamma power displayed maximal increases during encoding, gamma activity was more asynchronous than expected by chance, contrary to theoretical predictions concerning the role of gamma power during memory formation. Our results demonstrate the dissociation between spectral power and phase-synchronous oscillations, and highlight the need to directly assess network interactions when interpreting the electrophysiologic correlates of cognitive functions.
Introduction

Studies examining the electrophysiological correlates of memory encoding have demonstrated power fluctuations in theta (3-8 Hz) and gamma (> 40 Hz) frequency bands that reliably co-vary with episodic memory formation (Kahana, 2006; Nyhus & Curran, 2010). One interpretation of these changes in spectral power is that they reflect oscillatory activity that mediates memory formation through phase-synchronization (Axmacher et al., 2006; Jensen et al., 2007; Jutras & Buffalo, 2010; Fell & Axmacher, 2011).

Despite experimental support in humans (Weiss & Rappelsberger, 2000; Fell et al., 2001; Summerfield & Mangels, 2005), the interpretation that episodic memory formation is mediated through phase-synchronization is complicated by two observations. First, although localized increases in theta activity have been demonstrated in the temporal cortex and hippocampus (Klimesch et al., 1996; Mölle et al., 2002; Sederberg et al., 2003; Hanslmayr et al., 2011; Lega et al., 2011), memory encoding is more often marked by an extensive decrease in theta power (Sederberg et al., 2007; Guderian et al., 2009). Second, the observed increases in gamma power during successful memory encoding occur across a wide range of frequencies extending from 30-100 Hz (Sederberg et al., 2007b). Such broadband activity is inconsistent with a mechanism that relies on precise narrow-band phase-synchronization (Ray & Maunsell, 2010). An alternative hypothesis that has gained traction outside of the memory literature is that the observed increases in gamma activity often reflect an arrhythmic and intrinsically asynchronous process (Miller et al., 2009; Manning et al., 2009; Ray & Maunsell, 2011).

To disentangle whether the observed changes in spectral power reflect oscillatory or asynchronous activity, it is necessary to directly assess metrics of phase-synchrony during successful versus unsuccessful memory encoding. In particular, if oscillations serve to bind a spatially distributed memory representation, then overall synchrony should increase. Conversely, if asynchronous activity dominates the changes in spectral power, synchrony will likely decrease. Previous studies examining theta and gamma functional connectivity during memory formation have limited the search for phase-synchrony to specific anatomical circuits hypothesized to participate in memory encoding (Fell et al., 2001). Power fluctuations during memory formation, however, appear across widespread cortical and sub-cortical
regions. Determining whether these spatially distributed power fluctuations represent synchronous oscillatory activity requires the implementation of analysis techniques specifically designed to aggregate large-scale network connections (Varela et al., 2001; Bullmore & Sporns, 2009; Siegel et al., 2012).

Here, we use recordings from intracranial electrodes implanted in 68 participants engaging in a free recall task to simultaneously investigate changes in spectral power and phase during successful and unsuccessful memory encoding. We use a region of interest approach and a graph theoretic based metric of phase-synchrony to localize both oscillatory and asynchronous activity in order to interpret the observed changes in spectral power. We found specific time intervals and anatomical locations that exhibit changes in both theta and gamma synchrony during memory formation. By separating phase-synchronous oscillations from asynchronous changes, our results help clarify the role of rhythmic neural activity in the memory system.
Material and Methods

Participants

76 participants with medication-resistant epilepsy underwent a surgical procedure in which platinum recording contacts were implanted subdurally on the cortical surface as well as deep within the brain parenchyma. In each case, the clinical team determined the placement of the contacts so as to best localize epileptogenic regions. Data were collected at 4 different hospitals: Children’s Boston (Boston, MA), Hospital of the University of Pennsylvania (Philadelphia, PA), Freiburg University Hospital (Freiburg, Germany), and Thomas Jefferson University Hospital (Philadelphia, PA). Our research protocol was approved by the institutional review board at each hospital and informed consent was obtained from the participants and their guardians. We restricted our analysis to include only those patients who were left-hemispheric language dominant, as assessed by either the patients' handedness, a clinically administered intracarotid injection of sodium amobarbital (Wada test), or functional MR imaging using a verb generation task (Thomas Jefferson Hospital). Our final participant pool consisted of 68 patients (27 female; Table 1).

Free Recall Task

Each patient participated in a delayed free-recall task (Figure 1A). In each trial of this task, participants are instructed to study a list of words and are then asked to freely recall as many words as possible. Lists were composed of either 15 (54/68 patients) or 20 common nouns, chosen at random and without replacement from a pool of high frequency nouns (https://memory.psych.upenn.edu/WordPools). Words were presented sequentially and appeared in capital letters at the center of the screen. Each word remained on the screen for 1600 ms, followed by a randomly jittered 800-1200 ms blank inter-stimulus interval (ISI). The random duration of the ISI served to decorrelate the physiological responses from successive word presentations.

Following the final word in each list, participants were given a distraction task designed to attenuate any advantage in recalling the most recently studied items (Kahana, 2012). The distraction task was a series of arithmetic problems of the form $A+B+C=??$, where $A$, $B$ and $C$ were randomly chosen integers.
ranging from 1-9. The distraction interval lasted at least 20 sec, but patients were allowed to complete any problem that they started resulting in a variable distraction interval (average duration, 22.7 sec).

Following the distraction period, participants were given 45 seconds to recall as many words as possible from the list in any order. Vocalizations were digitally recorded and subsequently manually scored for analysis. Words that were presented during the encoding period and successfully retrieved during the recall period are considered successfully encoded (e.g. the words DOG, TREE, and LIME in Figure 1A). Likewise, words that were not retrieved during the recall period are considered unsuccessfully encoded (e.g. the words CAT and BALL in Figure 1A).

ECoG recordings

Data from our 68 patient database were collected over a 13-year period in collaboration with 4 different hospitals. Whereas each hospital used the same general implantation procedures and data-acquisition techniques, our analysis had to account for technical details that varied by institution. Electrocorticography (ECoG) data were recorded using a Bio-Logic, DeltaMed (Natus), Nicolet, Grass Telefactor, or Nihon-Khoden EEG system. Depending on the amplifier and the discretion of the clinical team, the signals were sampled at 256, 400, 500, 512, 1000, 1024, or 2000 Hz. Signals were referenced to a common contact placed either intracranially or on the scalp or mastoid process. All recorded traces were re-sampled at 256 Hz, and a fourth order 2 Hz stopband butterworth notch filter was applied at either 60 Hz or 50 Hz to eliminate electrical line noise. The experimental laptop sent ±5 V analog pulses, via an optical isolator, into a pair of open lines on the clinical recording system to synchronize the electrophysiological recordings with behavioral events.

We collected electrophysiological data from surgically implanted subdural and depth recording intracranial contacts. Subdural contacts were arranged in both grid and strip configurations with an inter-contact spacing of 10 mm. Depth contacts (6-8 linearly arranged contacts spaced 8 mm apart) were placed in 46/68 patients; all depth contacts were placed in the medial temporal lobe except for one patient whose depths were placed in the superior temporal gyrus near auditory cortex (TJUH 17; see Table 1). Contact localization was accomplished by co-registering the post-op CTs with the post-op MRIs using FSL Brain Extraction Tool (BET) and FLIRT software packages. Pre-op MRI’s were used
when post-op MR images were not available. The resulting contact locations were mapped to both MNI and Talairach space using an indirect stereotactic technique and OsiriX Imaging Software DICOM viewer package (Figure 1B). Details regarding each patient’s montage, behavioral performance, and amplifier filter settings can be found in Table 1.

Two concerns when analyzing bi-variate interactions between closely spaced intracranial contacts are volume conduction and confounding interactions with the reference line. We use bipolar referencing to eliminate such confounds when analyzing the neural signal (Nunez & Srinivasan, 2006). We defined the bipolar montage in our dataset based on the geometry of ECoG electrode arrangements. For every grid, strip and depth probe, we isolated all pairs of contacts that were positioned immediately adjacent to one another; bipolar signals were then found by differencing the signals between each pair of immediately adjacent contacts (Anderson et al., 2010). The resulting bipolar signals were treated as new virtual electrodes (henceforth referred to as electrodes throughout the text), originating from the mid-point between each contact pair (red circles in Figure 1C). All subsequent analyses were performed using these derived bipolar signals. We excluded pairs sharing a common contact when calculating synchrony in order to remove all confounding interactions due to shared information. In total, our dataset consisted of 6,946 electrodes (3,237 left-hemispheric; 3,709 right hemispheric).

Data Analysis and Spectral Power

To quantify memory related changes in spectral power and synchrony, we convolved the downsampled (256 Hz) bipolar ECoG signals with complex valued Morlet wavelets (wave number 10) to obtain magnitude and phase information (Addison, 2002). We used six wavelets with center frequencies spaced 1 Hz apart within the theta (3-8 Hz) frequency range, and eleven wavelets with center frequencies spaced 5 Hz apart within the gamma (45-95) frequency range. Each wavelet was convolved with 3750 ms of ECoG data surrounding each word presentation, from 1000 ms before word onset to 2750 ms after word onset (a 1000 ms buffer was included on both sides of the clipped data). We subsequently binned the continuous time transforms into 1000 ms epochs with 75% overlap, yielding 12 total temporal epochs surrounding each word presentation. 1000 ms epochs were chosen so that each window contained at least three cycles of the lowest frequency analyzed (3 Hz).
To assess memory related changes in spectral power within theta and gamma frequencies, we squared and log-transformed the magnitude of the continuous time wavelet transform to generate a continuous measure of instantaneous power. For each word presentation, we averaged the instantaneous power across each time epoch, and separately across theta and gamma frequencies. To account for changes in power across sessions, we z-transformed power values separately for each session with the mean and standard deviation for a set of baseline events, which were 1000 ms windows spaced every 60 ± 10 seconds during the testing session. For every electrode and for every temporal epoch, we assessed the difference in spectral power during memory formation by calculating a Welch’s parametric t-statistic on the distributions of average power values during successful and unsuccessful encoding for both theta and gamma frequencies.

**Synchrony and Functional Connectivity**

To obtain an estimate of the synchrony between two electrodes, $e_p$ and $e_q$, during a single time epoch for a given frequency, $f$, we calculated the phase locking value ($R_{pq}$) between their continuous time phase signals, $ϕ_p(t, f)$ and $ϕ_q(t, f)$ (Lachaux et al., 1999):

$$R_{pq}(f) = \frac{1}{N} \left| \sum_{t=1}^{N} e^{i(ϕ_p(t, f)−ϕ_q(t, f))} \right|$$

(1)

where $N$ is the total number of samples within the temporal epoch of interest. We averaged $R_{pq}(f)$ across all theta and gamma frequencies to generate a theta and gamma phase locking value, $R_{pq}(θ)$ and $R_{pq}(γ)$, for each temporal epoch during each word presentation for every electrode pair, $e_p, e_q \forall p \neq q$ and $p, q \in \{1, 2, \ldots P\}$, where $P$ is the total number of electrodes in the montage.

To assess the difference in phase locking value during memory formation for an individual participant, we used a parametric $t$-test to compare the distribution of phase locking values during successful and unsuccessful memory encoding for each temporal epoch, frequency band, and electrode pair. Electrode pairs exhibiting statistically significant ($p < 0.05$) increases or decreases in phase locking value in an individual participant were visualized by rendering red and blue lines, respectively, between each electrode (Figure 6A).

To more precisely localize memory related changes in synchrony, we identified electrodes that either
increased or decreased their total connections to all other electrodes during successful encoding using a metric derived from graph theory. We defined every electrode as a node, $e_p$, in a network, and every possible connection between that node and every other node, $e_q$, as an edge, $K_{p,q}$. Every edge can take on one of three values, depending on whether there was a statistically significant change in the phase-locking value, $\overline{R}$, between any two nodes, $e_p$ and $e_q$, during successful encoding:

$$K_{p,q} = \begin{cases} 
+1 & \text{statistically significant increase in } \overline{R} \\
0 & \text{no change in } \overline{R} \\
-1 & \text{statistically significant decrease in } \overline{R} 
\end{cases}$$

For a given node, $e_p$, we then define the change in degree, $\Delta d_p$, as the net change in the value of all edges connected to that node:

$$\Delta d_p = \sum_{q=1}^{P} K_{p,q} \quad \forall \ q \neq p$$

(2)

where $P$ represents the total number of electrodes in the montage. $\Delta d_p$ quantifies the extent to which one electrode or node changes its functional connections to all other electrodes during successful encoding. If an electrode, $e_p$, participates in many connections with statistically significant increases or decreases in $\overline{R}$, then the subsequent change in degree, $\Delta d_p$, would be very positive or negative, respectively.

Anatomical localization

In order to identify whether a particular anatomic area exhibited task-related changes in power or phase-synchrony, we grouped spatially similar electrodes from different participants using both a region of interest and a voxel based approach.

In the region of interest (ROI) approach, we segregated electrodes into five anatomical lobes (frontal, temporal, parietal, occipital, and limbic) and one hippocampal region from each hemisphere to generate 12 mutually exclusive ROIs (Lancaster et al., 2000; Manning et al., 2011). For the hippocampal ROI, a clinician experienced in neuroanatomical localization manually reviewed post-OP CT and MRI images to accurately identify all depth contacts located within the hippocampus (Lega et al., 2011; Serruya et al., In Press.). A bipolar pair was categorized into the hippocampal ROI if at least one
contact within the pair was determined to lie within this structure, yielding 361 hippocampal electrodes from 44 patients.

In the voxel based approach, we divided Talairach space into 5,484 overlapping 12.5 mm radius spheres evenly placed every 6.25 mm in the \( x \)-, \( y \)-, and \( z \)- directions. Only spherical voxels and ROIs with electrodes from 5 or more patients were included in statistical analyses (Figure 1E). We averaged statistics within each individual so that a single region was not over-represented by a participant who happened to have many electrodes within that region.

**Statistical Analyses**

We assessed whether changes in spectral power were significant across participants for a given ROI or spherical voxel using a non-parametric permutation procedure. We calculated a \( t \)-statistic on the distribution of log-power values during successful and unsuccessful encoding for both theta and gamma frequencies during a single temporal epoch for every electrode and from each participant. We then permuted the labels for the conditions \( N \) times (\( N = 2,000 \) for spherical voxels and \( N = 20,000 \) for ROIs) to generate a distribution of \( N \) shuffled \( t \)-statistics. We averaged the true and permuted \( t \)-statistics across all electrodes within each ROI and within each spherical voxel for each participant. For each region, we then summed the true and permuted averaged values across all participants (Sederberg et al., 2003, 2007, 2007b). To generate a \( p \)-value for changes in spectral power for a given region, we determined the position of the summed true \( t \)-statistics in the distribution of summed permuted values. Given the relatively small number of regions in the ROI power analysis, multiple comparisons were Bonferroni corrected across time, frequency band, and ROI.

To assess changes in phase-synchrony between ROIs, we used a similar non-parametric permutation procedure. For every ROI pair containing electrode pairs from 5 or more patients, we calculated the average phase locking value, \( \bar{R} \), across all electrode pairs spanning the two ROIs (or across all electrode pairs within a single ROI) for a given participant. We calculated a \( t \)-statistic on the distribution of average \( \bar{R} \)'s during successful and unsuccessful encoding for both theta and gamma frequencies during every temporal epoch. We then permuted the labels for the conditions 20,000 times to generate a null distribution for each \( t \)-statistic. For each ROI pair, we summed the true and permuted \( t \)-statistics across
all participants and determined the position of the true $t$-statistics in the distribution of summed permuted values. To correct for multiple comparisons across time, frequency and ROI pairs, a false discovery rate (FDR) procedure was applied using both a conservative ($Q = 0.05$) and more liberal ($Q = 0.1$) threshold (Genovese et al., 2002). ROI pairs exhibiting a statistically significant increase or decrease in phase-synchrony were visualized by rendering red and blue lines, respectively (Figure 5).

To assess whether more precisely localized changes in phase-synchrony were significant across participants, we used a similar non-parametric permutation procedure to examine changes in degree ($\Delta d$), or functional connectivity, for each spherical voxel. For a given electrode, $e_p$ from a single participant, we calculated the change in degree, $\Delta d_p$, between successful and unsuccessful encoding for both theta and gamma frequencies during a single temporal epoch. We then permuted the labels for the conditions 2000 times to generate a distribution of 2000 shuffled $\Delta d_p$'s. We averaged the true and permuted changes in degree across all electrodes within each 12.5 mm spherical region for each participant. As for power, for each region, we then summed the true and permuted averaged changes in degree across all participants, and determined the position of the summed true values in the distribution of summed permuted values to generate a $p$-value.

**Topographic plots**

To plot spatial changes in spectral power and synchrony, we identified spherical voxels that exhibited a statistically significant ($p < 0.001$) increase or decrease in power or functional connectivity across participants. At each location of each spherical voxel, we calculated the percentage of spherical voxels with centers within a surrounding region of 12.5 mm that exhibited identical encoding related effects. We translated these percentages to color saturation and rendered these values onto cortical and sub-cortical topographical plots using a standard Montreal Neurological Institute brain with information from the WFU PickAtlas toolbox (Maldjian et al., 2003). Increases in power and functional connectivity were rendered with red colors while decreases were rendered with blue. Colored values were smoothed using a three dimensional Gaussian kernel ($\text{radius} = 12.5 \text{mm}; \sigma = 6.25 \text{mm}$). The maximal color saturation in either direction corresponded to 25% of local spherical voxels. All regions with fewer than 5 patients were colored black and were not analyzed. Grayscale rendering in other regions represented the
percentage of spherical voxels surrounding a given location with at least 5 patients, and thus represented regions that were analyzed but that did not exhibit significant effects.
Results

We set out to determine whether power fluctuations that accompany successful memory encoding represent phase-synchronous neural oscillations. We investigate this issue in two data-analytic stages. First, we characterize the anatomical distribution and timing of spectral power changes that correlate with successful encoding. Second, we characterize the degree to which ECoG activity recorded in a given brain region is synchronous with ECoG activity recorded elsewhere in the brain. Of particular interest is whether regions that show increased spectral power in our first analysis show increased or decreased synchrony in our second analysis.

We briefly note that we have operationalized successful encoding by contrasting the ECoG signals measured during encoding of items that are subsequently recalled (24.9% of studied items in our delayed free recall task) with those items that are not subsequently recalled. Whereas this method has been widely used to investigate the neurological basis of memory formation in a number of studies (Paller & Wagner, 2002), we recognize that this operationalization is limited insofar as retrieval factors will account for much of the variation in subsequent recall (Kahana, 2012).

Changes in spectral power during encoding

We examined changes in theta (3-8 Hz) and gamma (45-95 Hz) power following word presentation during successful and unsuccessful memory encoding. We used 5,484 identical three-dimensional spherical regions uniformly placed across Talairach space to group spectral activity from nearby electrodes for each participant (Figure 1D). For each frequency band, we calculated an average t-statistic for all electrodes in each region by comparing theta and gamma power between successfully and unsuccessfully remembered items during each temporal epoch following word presentation. To assess whether spectral changes are statistically reliable across participants, we used a permutation procedure to map encoding related changes in theta and gamma power to each region (see Materials and Methods). We visualized spherical voxels that exhibited a statistically significant \( p < 0.001 \) change in theta and gamma power during successful memory encoding on a standardized three-dimensional brain (Figures 2A and 2B) during two representative temporal epochs, 0-1000 ms (early word presentation) and 500-1500 ms (late word
presentation).

We found a reliable decrease in theta power following the presentation of words that were successfully remembered compared to words that were not remembered across several brain regions (Figure 2A). The decreases in theta power were more prominent in posterior temporal regions during early word presentation, but expanded to include frontal and anterior temporal regions during late word presentation. Whereas decreased theta power with successful encoding was by far the most prevalent pattern observed across cortical and medial temporal regions, smaller increases in theta power were observed in the right anterior temporal lobe and in the left anterior frontal lobes immediately after word presentation.

When we examined changes in gamma power (Figure 2B), we found that memory encoding had a very different effect on gamma power as compared to theta power. Specifically, a large number of regions exhibited a reliable increase in gamma power following the presentation of words that were successfully remembered compared to words that were not remembered. As with theta power, the changes we observed in the gamma band were more prominent in posterior cortices early after item presentation and expanded anteriorly during later intervals. In addition, the increases we observe in the gamma range lateralized to the left hemisphere; gamma activations in the right hemisphere were more spatially discrete and co-occurred alongside pockets of decreased gamma power. The left hemispheric bias of gamma activations likely reflects the language comprehension component of our task.

To investigate the temporal evolution of these effects, we separately counted the number of spherical voxels that exhibited a statistically significant change in power in each time bin (Figures 3A and 3B). Given our significance threshold \( p < 0.001 \) and that our analysis was conducted over 5,484 spherical regions and two frequency bands, we expected to find 11 total regions showing a significant change in power during any given time epoch by chance (5.5 regions in each tail of the distribution; dashed line, Figures 3A and 3B). Figure 3 demonstrates that decreases in theta power and increases in gamma power during memory formation far exceeded this expectation and are also tightly-linked to item presentation. The precise timing of these effects suggests that the observed changes in power are driven specifically by item presentation as opposed to more non-specific cognitive processes, such as global shifts in attention.
For each electrode in our database, we also visually examined the raw log-transformed power values during successfully encoded, unsuccessfully encoded and baseline events. Four representative examples of electrodes that individually show the effects described in Figures 2 and 3 are shown in Figure 4, and highlight two important features in our data. First, the simultaneous increase in gamma power and decrease in theta power that accompany memory formation can be detected even at the level of individual electrodes. Second, compared to baseline, theta power tends to decrease and gamma power tends to increase during the presentation of all items, but these changes are amplified during the presentation of successfully encoded items.

Changes in phase-synchrony during encoding

In order to assess whether the observed memory-related power fluctuations represent phase-synchronous oscillations, we spatially localized changes in phase-synchrony during memory formation to specific anatomic areas using both a region of interest (ROI) approach and a voxel based graph theoretic metric. Both approaches reduce the complex feature space of pair-wise electrode interactions in order to extract memory specific information, and complement each other to build a more complete picture of phase-synchronous activity during memory encoding.

To assess temporospatial changes in phase-synchrony associated with successful memory encoding, we defined ROIs based on anatomical lobes of the brain and calculated phase-synchrony between each ROI pair (see Materials and methods). We compared these memory-related changes in phase-synchrony to memory-related changes in spectral power in each ROI (Figure 5). During successful memory encoding, we found that theta phase-synchrony demonstrated significant initial increases in the occipital and temporal lobes that subsequently rapidly spread to a distributed set of ROI pairs and eventually concentrated in the left frontal lobe. This initial increase in theta synchrony was immediately followed by a decrease in both theta synchrony and power that spatially progressed in a similar posterior to anterior manner. Significant changes in gamma synchrony during encoding were limited to small areas of decreased gamma phase-synchrony, which was surprising given the widespread increase in gamma power that occurred simultaneously during memory formation.

Using such ROIs to spatially aggregate phase-synchronous interactions across patients clearly
demonstrates that memory encoding modulates oscillatory phase-synchrony, particularly in the theta frequency band. However, a drawback of this approach is that it fails to leverage the principal advantage of ECoG over other modalities such as scalp EEG or MEG: very high spatial resolution. This is particularly important when investigating gamma phase-synchrony, which is correlated on a much finer spatial scale than theta activity (Logothetis et al., 2007).

In order to circumvent this problem, we aggregated pair-wise network connections using precisely defined spherical voxels and a graph theoretic metric. As illustrated for a single participant (TJUH-11; Figure 6), we first compared the distribution of phase locking values observed during successful versus unsuccessful memory encoding between each electrode pair. We used significant increases and decreases in phase-synchrony to create a spatial synchrony map of task related changes in phase-synchrony for every temporal epoch for every participant. To examine the temporal evolution of these changes, we collapsed the spatial information contained in each synchrony map into a single value by subtracting the number of electrode pairs exhibiting a statistically significant \((p < 0.05)\) decrease in phase synchrony during successful encoding from the number of pairs exhibiting a significant increase (Figure 6B). For this participant, there was a brief increase in theta synchrony immediately after word presentation followed by a much larger decrease in theta phase synchrony at the end of word presentation, mirroring the effects seen among ROIs across participants.

To more precisely spatially localize changes in phase synchrony during memory encoding, we used a graph theoretic approach. Briefly, we designated every electrode, \(e_p\), as a node in a larger network, and calculated the total number of other nodes in the network, \(e_q\), that share a statistically significant increase in synchrony with that node minus the total number of other nodes that share a statistically significant decrease in synchrony during successful memory encoding (Figure 6C; see Materials and methods). The resulting change in degree, \(\Delta d_p\), represents the extent to which each node in the network increases or decreases its phase-synchrony with the rest of the network during memory encoding. Defining each electrode’s functional connectivity in this manner allows us to localize anatomic areas where memory-related changes in synchrony were most concentrated. Spatially localizing the changes in theta synchrony observed in Figure 6A demonstrated that the temporal lobe was marked by increases in
theta synchrony during early word presentation, followed by prominent decreases in theta synchrony during late word presentation localized to the left lateral and inferior temporal cortex (Figure 6D).

Using this approach, we calculated the change in degree for each electrode for each participant and determined if the changes observed in a particular region were statistically significant across all participants. As for our power analysis, we used 5,484 identical spherical voxels uniformly placed across Talairach space to group nearby electrodes for each participant (Figure 1D). We used a permutation procedure to assess whether the changes in degree for each region are statistically significant across participants during early (0-1000 ms) and late (500-1500 ms) word presentation (see Materials and methods).

We found that successful memory encoding was marked by a reliable initial increase in theta synchrony localized to the left temporal, pre-frontal, and orbito-frontal cortex (Figure 7A). The increases in theta synchrony were not associated with a prominent increase in theta power (see Figure 2A), which suggested that power analyses alone were insufficient to isolate these phase-synchronous theta oscillations. After this initial increase, we found that theta synchrony during encoding exhibited reliable decreases localized diffusely throughout the brain, but which were most concentrated in the left medial temporal lobe. The decrease in theta synchrony overlapped in time and space with regions in which theta power also decreased. These results extend the ROI approach to demonstrate that the left pre-frontal cortex, more than any other region, is the major hub of the theta synchronous verbal episodic memory encoding network.

When we examined changes in gamma synchrony, on the other hand, we found distinct regions of gamma synchrony during memory encoding (Figure 7B). This result highlights the utility investigating spatially precise synchronous interactions. In particular, we found that successful memory encoding involved either no change or an overall decrease in gamma synchrony in the left hemisphere. This result was surprising given the highly reliable increases in gamma power that occurred simultaneously in the same region (see Figure 2B). In addition, we found increased gamma synchrony that localized to the right hemisphere in the frontal-temporal (peri-sylvian) areas of the brain.

Analogously to the power analysis in Figure 3, we examine the temporal evolution of changes in
phase-synchrony in Figure 8. For each time epoch, we separately counted the number of spherical voxels that exhibited statistically significant decreases or increases in synchrony, as measured by the change in degree, during successful memory encoding. The observed increases in theta synchrony peaked during early word presentation, whereas the decreases peaked during late word presentation. In both cases, the regions exhibiting these changes were more prominent in the left hemisphere (Figure 8A). Additionally, we found a consistent hemispheric lateralization of gamma phase-synchrony such that increases in phase-synchrony were prominent in the right hemisphere and decreases in phase-synchrony were prominent in the left hemisphere (Figure 8B). Although gamma synchrony was reliably modulated by memory formation, the temporal envelope defining these changes was not as well defined.

To further investigate the observed changes in phase synchrony revealed by our graph theoretic approach, we examined phase synchrony between every electrode pair across all 68 patients in our database as a function of inter-electrode distance. In our graph theoretic approach, phase synchrony between electrode pairs equally contribute to our measure of functional connectivity irrespective of the distance between them. When we examined the relation with distance, however, we found that both theta and gamma phase synchrony were modulated by distance in a highly reliable manner, and that this relation was independent of successful and unsuccessful encoding (Figure 9). Despite this relation with distance, however, our graph theoretic analysis only considers relative changes in the phase locking value between conditions. Hence, even when separated by variable distances, electrode pairs were evaluated on equal footing, which is a necessary control given this relation between neural synchrony and cortical distance (Logothetis et al., 2007). Nevertheless, the relation between phase synchrony and inter-electrode distance observed here is notable and may be useful in defining the baseline spread of theta and gamma oscillations in the human brain.
Discussion

By investigating spectral power and aggregate pair-wise phase-synchrony during successful memory encoding across the entire brain, our data address whether the observed changes in theta and gamma spectral power reflect oscillatory or asynchronous activity. In the setting of a diffuse decrease in theta power during successful memory encoding, we found an increase in theta phase-synchrony early after item presentation concentrated in the left prefrontal cortex that was subsequently followed by a decrease in theta phase-synchrony in the left frontal lobe and medial and lateral temporal lobes. Conversely, in the setting of a diffuse increase in gamma power, we found decreases in gamma synchrony throughout the left hemisphere and only small areas of increased synchronous gamma oscillations in the right hemisphere. The dissociation between power and phase has two major implications for the interpretation of spectral activity during memory formation. First, our data suggest that gamma activations are often asynchronous, indicating that the majority of gamma power increases during encoding do not represent temporally binding synchronous oscillations. Second, the finding that encoding involves both theta synchrony increases and decreases occurring very near to each other in time and space helps reconcile conflicting results regarding theta power during memory formation. More generally, by building a more complete picture of the electrophysiological profile accompanying human verbal episodic memory encoding, our results help clarify the role of rhythmic neural activity in the memory system.

Theta Phase Synchrony

During successful memory encoding, we found increases in theta synchrony during early word presentation, supporting the hypothesis that cortical synchronized theta oscillatory activity mediates memory formation (Düzel et al., 2010; Fell & Axmacher, 2011). Region-of-interest analyses and graph-theoretic based metrics localized these increases to posterior cortices followed rapidly by increases in the left prefrontal cortex (Figure 10). The spatially unique locus of increased theta synchrony in left prefrontal cortex suggests that this structure is highly synchronous to other regions during encoding, and likely acts as the network hub of theta oscillatory activity during memory formation. This finding is consistent with previous studies demonstrating enhanced theta synchrony between prefrontal cortex and
distant cortical areas during working memory tasks (Sarnthein et al., 1998; Sauseng et al., 2004; Payne & Kounios, 2009; Liebe et al., 2012) and during episodic memory encoding and retrieval (Weiss & Rappelsberger, 2000; Summerfield & Mangels, 2005; Fell et al., 2003; Anderson et al., 2010). Although prefrontal activity may reflect contextual information (Hyman et al., 2012), top-down interactions between cortical structures (Miller & Cohen, 2001), or communication between the neocortex and hippocampus (Jones & Wilson, 2005; Benchenane et al., 2010; Fujisawa & Buzsáki, 2011), the precise functional role of the observed synchronous theta oscillations in human episodic memory encoding remains to be determined.

Following these observed increases, we found subsequent decreases in theta phase-synchrony during later temporal epochs of successful memory encoding, localized to the left hemisphere and accompanied by broad anteriorly-spreading decreases in theta power (Figure 10). The degree to which memory formation involves this decrease in theta power represents perhaps the most striking finding in our data, and is consistent with previous EEG and MEG findings (Sederberg et al., 2007; Guderian et al., 2009, see Figure 2). Such task-related decreases in low frequency power have been traditionally classified as event related desynchronizations (Crone et al., 1998; Pfurtscheller & Lopes Da Silva, 1999) under the assumption that they reflect a decrease in synchronized local neural activity (Singer, 1993). Here, we show that the decrease in theta power during memory formation is also accompanied by late decreases in long-range theta synchrony. This asynchronous activity may simply reflect a passive deactivation following theta synchronization, but another possibility is that the asynchronous activity itself may play a role in memory formation. Indeed, decreases in low-frequency power and synchrony correlate with the BOLD signal (Kilner et al., 2005; Niessing et al., 2005) and have been shown to co-vary with transitions to active cortical states (Harris & Thiele, 2011; Poulet et al., 2012). Whether memory formation represents a similar transition to a more active cortical state is unclear, but the asynchronous activity we detect here suggests this intriguing possibility.

It is notable that the decreases in theta power observed during successful memory encoding in our data and in other studies (Sederberg et al., 2007; Fell et al., 2008; Guderian et al., 2009) seem to stand in conflict with other reports of increased theta power during encoding (Klimesch et al., 1996; Mölle et al.,
2002; Sederberg et al., 2003; Hanslmayr et al., 2011; Lega et al., 2011). The tendency for theta phase synchrony to both increase and decrease during successful encoding (Figures 5-8) helps to explain this ambiguity by suggesting that theta power reflects two dissociable processes: power decreases vs. synchronous oscillations. Each of these two competing effects may be detected to a lesser or greater degree depending on the particular experimental conditions or post-processing steps implemented. By precisely categorizing the subtle yet reliable nuances of theta activity during memory formation, it is possible to interpret apparently diverging results within a common electrophysiological framework (Figure 10).

**Gamma phase synchrony**

In our analysis of gamma frequencies, consistent with predictions regarding the role of gamma synchrony in memory formation (Jensen et al., 2007; Jutras & Buffalo, 2010; Fell & Axmacher, 2011), we observed increases in gamma synchrony in the peri-sylvian areas of the right hemisphere. These data suggest that the increases in gamma power co-localized to these areas reflect true narrow-band gamma oscillations. That such synchronous gamma oscillations were limited in scope may reflect the smaller spatial extent of synchronous gamma activity. But given the hypothesized role of synchronous gamma oscillations in the visual attentional system (Tallon-Baudry & Bertrand, 1999; Fries et al., 2001; Gregoriou et al., 2009), the presence of gamma synchrony throughout the word presentation interval during successful memory encoding demonstrated here may reflect right hemispheric visual-spatial top-down attentional mechanisms (Corbetta et al., 1993; Thiebaut de Schotten et al., 2005).

Conversely, the most reliable increases in gamma power during memory formation were localized to the left hemisphere and were accompanied by less synchrony than expected by chance during memory formation (Figure 10). It is unlikely that our failure to observe increases in gamma synchrony in the left hemisphere reflects a methodological shortcoming. Although our temporal windows of 1000 ms are large relative to the length of a gamma cycle, we calculated phase-synchrony using wavelets with a finer temporal resolution \(2\sigma\) temporal envelope of the 95 Hz and 45 Hz wavelets: 33.5 ms and 70.7 ms), which was sufficient to detect transient increases in gamma synchrony in other brain regions. Instead, the decreases in high frequency synchrony we observe here likely reflect asynchronous noise fluctuations.
related to multi-unit neural activity (Ray & Maunsell, 2011; Manning et al., 2009; Miller et al., 2009) or transient "bottom-up" responses (Ossandón et al., 2012), and suggest that increases in gamma power in these regions do not represent temporally binding synchronous oscillations (Jutras & Buffalo, 2010; Fell & Axmacher, 2011). Although the origins of high-frequency activations are still unclear (Crone et al., 2011; Buzsáki & Wang, 2012; Lachaux et al., 2012), our results suggest that the degree of synchrony within the gamma band can dissociate between gamma oscillations on the one hand and broadband activations on the other (Jia et al., 2011).

**Conclusion and future directions**

Although our analyses focus on changes in spectral power and synchrony, it is important to account for the role that evoked potentials may play in modulating phase-synchrony. Trial-by-trial variability in the evoked response has been shown to interact with spectral responses and coherence measures (Wang et al., 2008; Wang & Ding, 2011). Whereas it is possible to factor out such evoked responses, doing so requires special models and analytical techniques (Truccolo et al., 2002; Xu et al., 2009). Future studies would benefit from incorporating such models to further dissociate induced synchronous activity from asynchronous evoked sources.

The presence of both synchronous and asynchronous high frequency activity in our data is consistent with recent electrophysiological studies in both humans (Crone et al., 2011) and non-human primates (Ray & Maunsell, 2011) that demonstrate the segregation of gamma activity into oscillations and asynchronous processes. Similarly, the presence of both synchronous and asynchronous low-frequency activity both supports the hypothesis that low-frequency oscillations may mediate memory formation (Axmacher et al., 2006; Nyhus & Curran, 2010; Düzel et al., 2010; Fell & Axmacher, 2011) and highlights the possible role of decorrelated low-frequency activity in human memory. Overall, our data demonstrate that phase-synchrony can be used to disentangle oscillatory from asynchronous activity in the context of the observed changes in spectral power. Importantly, we found that both synchronous and asynchronous processes shape the frequency spectrum during memory formation, suggesting that theories regarding the role of spectral activity in the memory system should incorporate both asynchronous spectral patterns as well as synchronous oscillatory activity.
References


Table 1. Electrocorticographic free recall patient database. For each participant, the identification number (ID), gender, age, percentage of correctly encoded words (% Rec), number of bipolar electrode pairs (#BPD), pass-band of the amplifier’s filter settings, and a brief anatomical description of the electrode coverage are listed. CHB: Children’s Hospital Boston; FRUH: Freiburg University Hospital; TJUH: Thomas Jefferson University Hospital; HUP: Hospital of the University of Pennsylvania; DC: amplifiers allowed DC signal to be recorded. † The electrode montage was changed during the hospital stay. The second montages from patients TJUH 3, TJUH 9, TJUH 23, and TJUH 25 contained 81, 50, 133, and 140 bipolar derivations. The third montage from patient TJUH 9 contained 139 bipolar derivations.

Figure 1. Behavioral task and data collection. A: Participants were shown a list of words during the encoding period and, after a distraction interval, were asked to verbally recall as many words as possible in any order. Words remained on the screen for 1600 ms after which the screen was left blank for 800 ms (plus a 0-400 ms uniformly distributed random temporal jitter) before presentation of the next word. B: Example radiographic image of a participant’s electrode arrangement. C: Electrodes from each participant were co-registered to a standardized brain in Talairach space. Bipolar signals (red circles) were found by differencing the voltage traces from immediately adjacent electrodes (black circles). D: Colored dots represent electrodes from 15 different participants clustered within a spherical region of 12.5 mm radius centered at $x = -32.00$, $y = -52.38$, $z = -16.25$ in Talairach space (Fusiform gyrus). E: Heat map showing spatial distribution of electrode locations. The number of patients with at least one electrode within 12.5 mm of each location on the standardized brain is shown (locations with fewer than 5 nearby patients are not colored).

Figure 2. Change in theta and gamma power across anatomical location. For two representative time epochs, 0-1000 ms (early word presentation) and 500-1500 ms (late word presentation), all spherical regions that exhibited a significant ($p < 0.001$) change in theta (A) and gamma (B) power with successful
memory encoding are displayed on a standardized three-dimensional brain. Increases ($R > N$) and decreases ($N < R$) in power are shown in red and blue, respectively. The color scale reflects the percentage of nearby ROI’s exhibiting identical encoding related effects. The horizontal dashed line on the sagittal views corresponds to the level of the axial cut in the third panel (the $z = -13.0$ plane in Talairach space). Grayscale rendering represents the percentage of spherical voxels surrounding a given location with at least 5 patients.

Figure 3. Temporal evolution of changes in theta and gamma power. A: The total number of regions exhibiting a significant decrease (left panel) or increase (right panel) in both theta (A) and gamma (B) power are displayed across time. Yellow circles represent the early and late word presentation intervals shown in Figure 2. Chance level ($p = 0.001$) is represented by the horizontal dashed line. The percentage of the regions in each hemisphere is proportional to the area of the light- and dark-colors, as indicated.

Figure 4. Examples of theta and gamma power fluctuations during successful memory formation. For four different electrodes, raw log-transformed power in the theta (3-8 Hz) and gamma (45-95 Hz) bands is shown for all subsequently recalled (R; red), subsequently not-recalled (NR; blue), and baseline (B; gray) events. Error bars represent the 95% CI. A: Patient: TJUH-11, Electrode location: Left lateral temporal lobe, Brodmann area 20, time epoch: 500-1500 ms; B: Patient: TJUH-19, Electrode location: Right posterior parahippocampal gyrus (depth electrode), time epoch: 250-1250 ms. C: Patient: TJUH-23, Electrode location: Right lateral temporal lobe, Brodmann area 20, time epoch: 500-1500 ms. D: Patient: TJUH-24, Electrode location: Right lateral temporal lobe, Brodmann area 21, time epoch: 500-1500 ms.

Figure 5. Change in theta and gamma lobe-wise synchrony during memory encoding. A: Inter- and intra-lobe synchrony was calculated across all patients for Frontal (F), Temporal (T), Occipital (O), Limbic non-hippocampal (L), hippocampal (H), and Parietal (P) lobes. Lobe-pairs with fewer than 5 subjects (gray lines) were not analyzed. The resulting lobe-wise synchrony is displayed separately for theta (B) and gamma (C) frequency bands. Increases and decreases in synchrony are shown in red and
blue, respectively. Thick and thin lines correspond to a conservative ($Q = 0.05$) and liberal ($Q = 0.10$) false-discovery rate correction for multiple comparisons. Analogous changes in power for each lobe are displayed by filling each circle using an identical color scheme. ROIs exhibiting a significant change in intra-lobe synchrony are displayed by coloring the outline of each circle. Power changes could occur either in the presence (+Sync) or absence (-Sync) of such intra-lobe synchrony.

Figure 6. Aggregating pair-wise network connections. A: All pairs of electrodes with significant ($p < 0.05$) increases (red lines) or decreases (blue lines) in theta synchrony during successful encoding are shown for two different time epochs for patient TJUH 11. B: For all time epochs, the difference between the total number of pairs exhibiting a significant increase and decrease in synchrony is shown. Yellow circles mark the epochs depicted in A. C: The change in degree, $\Delta d_p$, is found by tabulating significant increases or decreases in synchrony for each connection of each electrode. D: The change in degree, $\Delta d_p$, for each electrode is shown summarizing the changes in synchrony observed in A. Electrodes that exhibited an overall increase or decrease in synchrony with all other electrodes during memory formation are colored in red or blue, respectively. The size of each electrode is proportional to the number of connections demonstrating significant changes in synchrony.

Figure 7. Change in theta and gamma degree across anatomic locations. All spherical regions that exhibited a significant ($p < 0.001$) change in theta (A) and gamma (B) degree ($\Delta d_p$) during successful memory encoding are displayed on a standardized three-dimensional brain. Increases and decreases in phase-synchrony are shown in red and blue, respectively. The colorscale and grayscale reflect the percentage of surrounding regions with identical encoding related effects and with more than 5 patients, as in Figure 2.

Figure 8. Temporal evolution of changes in theta and gamma degree. The total number of regions exhibiting a significant decrease (left panel) or increase (right panel) in both theta (A) and gamma (B) connectivity ($\Delta d_p$) are displayed across time. Yellow circles represent the early and late word
presentation intervals shown in Figure 7. Chance level \((p = 0.001)\) is represented by the horizontal dashed line. Hemispheric bias is represented as in Figure 3.

Figure 9. Normalized phase-synchrony as a function of inter-electrode distance. Phase locking values (PLVs) from all electrode pairs were separately \(z\)-scored for each frequency bin for each patient. \(z\)-scored PLVs from recalled (red lines) and non-recalled (blue-lines) items were then categorized according to inter-electrode distance using seven bins ranging from 0 to 150 mm. The mid-point of each bin is represented on the x-axis. PLVs within each bin were then averaged across all patients. Errorbars represent 95% CI across patients. A Wilcoxon test was used to compare the recalled and non-recalled averaged PLVs within each bin across patients; no bins exhibited a significant \((p < 0.1)\) change in averaged PLV.

Figure 10. Summary of the ECoG verbal, episodic subsequent memory effect. In the left hemisphere immediately after word presentation, successful encoding is marked by an initial increase in theta synchrony in posterior ROIs, which becomes concentrated in the L. PFC. Asynchronous activity, in both low-(LF) and high-frequencies (HF), follows this increase in synchrony along a posterior to anterior pathway. In the right hemisphere (not shown), the changes are more complicated and involve synchronous gamma oscillations in the R. peri-sylvian region.
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</tr>
<tr>
<td>TJUH 11</td>
<td>F</td>
<td>34</td>
<td>26.7</td>
<td>95</td>
<td>0.03-600</td>
<td>L Depths + Temp Grid + Strips</td>
</tr>
<tr>
<td>TJUH 12</td>
<td>F</td>
<td>52</td>
<td>36.7</td>
<td>95</td>
<td>0.03-600</td>
<td>R Depths + Temp-Front Grid</td>
</tr>
<tr>
<td>TJUH 13</td>
<td>M</td>
<td>44</td>
<td>45.0</td>
<td>92</td>
<td>0.03-600</td>
<td>R Depths; b/l Temp-Front Strips</td>
</tr>
<tr>
<td>TJUH 14</td>
<td>M</td>
<td>33</td>
<td>32.0</td>
<td>105</td>
<td>0.03-600</td>
<td>b/l Temp-Front-Par Strips</td>
</tr>
<tr>
<td>TJUH 15</td>
<td>F</td>
<td>23</td>
<td>29.2</td>
<td>94</td>
<td>0.03-600</td>
<td>R Depths + Grid; b/l Temp Strips</td>
</tr>
<tr>
<td>TJUH 16</td>
<td>F</td>
<td>48</td>
<td>35.0</td>
<td>84</td>
<td>0.03-600</td>
<td>b/l Temp-Front-Occip Strips</td>
</tr>
<tr>
<td>TJUH 17</td>
<td>M</td>
<td>33</td>
<td>37.6</td>
<td>46</td>
<td>0.03-1200</td>
<td>L Temp Strips + STG Depths</td>
</tr>
<tr>
<td>TJUH 18</td>
<td>M</td>
<td>45</td>
<td>22.6</td>
<td>86</td>
<td>0.03-600</td>
<td>b/l Depths; b/l Temp-Front Strips</td>
</tr>
<tr>
<td>TJUH 19</td>
<td>M</td>
<td>23</td>
<td>37.2</td>
<td>78</td>
<td>0.03-600</td>
<td>R Depths; R Temp-Front-Par Strips</td>
</tr>
<tr>
<td>TJUH 20</td>
<td>M</td>
<td>53</td>
<td>18.1</td>
<td>83</td>
<td>0.03-600</td>
<td>b/l Depths; b/l Temp Strips</td>
</tr>
<tr>
<td>TJUH 21</td>
<td>M</td>
<td>29</td>
<td>48.3</td>
<td>63</td>
<td>0.03-600</td>
<td>b/l Temp + L Front-Occip Strips</td>
</tr>
<tr>
<td>TJUH 22</td>
<td>M</td>
<td>35</td>
<td>22.8</td>
<td>90</td>
<td>0.03-600</td>
<td>b/l Front-Temp Strips; b/l depths</td>
</tr>
<tr>
<td>TJUH 23</td>
<td>F</td>
<td>48</td>
<td>18.0</td>
<td>130†</td>
<td>0.03-600</td>
<td>b/l strips (all lobes); b/l depths</td>
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<tr>
<td>TJUH 24</td>
<td>F</td>
<td>20</td>
<td>43.1</td>
<td>126</td>
<td>0.03-600</td>
<td>b/l strips (all lobes); R depths</td>
</tr>
<tr>
<td>TJUH 25</td>
<td>M</td>
<td>20</td>
<td>30.8</td>
<td>63†</td>
<td>0.03-600</td>
<td>R Temp-Occip Strips; R depths</td>
</tr>
</tbody>
</table>

HUP 1 | M     | 38  | 22.5  | 69    | 0.16-134       | R Depths; R Temp-Occip-Front Strips |
| HUP 2 | M     | 30  | 18.0  | 72    | 0.16-134       | b/l Depths; b/l Front-Temp Strips   |
| HUP 3 | M     | 43  | 11.5  | 97    | 0.16-134       | R Front Grid; R Temp Strips         |
| HUP 4 | M     | 36  | 11.7  | 75    | 0.16-134       | b/l Depths; b/l Temp-Front Strips   |
| HUP 5 | M     | 25  | 22.5  | 53    | 0.16-134       | R Depths; R Strips                 |
| HUP 6 | F     | 18  | 23.1  | 64    | 0.16-134       | b/l Depths; b/l Front-Temp Strips   |
| HUP 7 | F     | 27  | 21.7  | 40    | 0.16-134       | b/l Depths; b/l Front-Temp Strips   |
| HUP 8 | M     | 40  | 31.7  | 47    | 1.6-134        | b/l Temp-Front-Par Strips          |
| HUP 9 | M     | 27  | 28.1  | 68    | 1.6-134        | b/l Depths; b/l Front-Temp Strips   |
| HUP 10 | M    | 37  | 25.1  | 123   | 1.6-134        | R Temp-Front-Par Grid + Strips      |
A.

- Time
- TREE
- LIME
- CAT
- BALL
- DOG

Encoding Period
- 627+3
- 5+7+3
- 3+7+3
- 1+7+3
- 9+7+3

Distractor
- Recall P

Recall Period
- A
- 0 ms 1600 ms 2400 ms + JITTER

LIME
- Cat
- B
- D

25 subjects

B.

C.

12.5 mm

D.

25 subjects

5 subjects
A  Theta SME (3-8 Hz)

Early Word Presentation (0-1000 ms)

Late Word Presentation (500-1500 ms)

R<NR  Significant Regions  R>NR

B  Gamma SME (45-95 Hz)

Early Word Presentation (0-1000 ms)

Late Word Presentation (500-1500 ms)
**A** Theta SME (3-8 Hz)

- Negative Regions
- Time (ms)
- Left Hem
- Right Hem

**B** Gamma SME (45-95 Hz)

- Negative Regions
- Time (ms)
- Left Hem
- Right Hem
A  Theta Functional Connectivity (3-8 Hz)

Early Word Presentation (0-1000 ms)

Late Word Presentation (500-1500 ms)

Significant Regions

R<NR

R>NR

Available Regions

B  Gamma Functional Connectivity (45-95 Hz)

Early Word Presentation (0-1000 ms)

Late Word Presentation (500-1500 ms)
A  Theta Functional Connectivity (3-8 Hz)

B  Gamma Functional Connectivity (45-95 Hz)
Synchronous Activity

Asynchronous Activity

Memory Encoding (Time)