



Review

Functional role of gamma and theta oscillations in episodic memory

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ABSTRACT

The primary aim of this review is to examine evidence for a functional role of gamma and theta oscillations in human episodic memory. It is proposed here that gamma and theta oscillations allow for the transient interaction between cortical structures and the hippocampus for the encoding and retrieval of episodic memories as described by the hippocampal memory indexing theory (Teyler and DiScenna, 1986). Gamma rhythms can act in the cortex to bind perceptual features and in the hippocampus to bind the rich perceptual and contextual information from diverse brain regions into episodic representations. Theta oscillations act to temporally order these individual episodic memory representations. Through feedback projections from the hippocampus to the cortex these gamma and theta patterns could cause the reinstatement of the entire episodic memory representation in the cortex. In addition, theta oscillations could allow for top-down control from the frontal cortex to the hippocampus modulating the encoding and retrieval of episodic memories.

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1. Introduction

Research in cognitive neuroscience thus far has focused on the functional role of particular brain regions. However, to perform the myriad of cognitive tasks that make us human it is recognized that

particular brain regions do not work alone, but interact through complex and dynamic neural networks. A major question currently faced by cognitive neuroscientists is: How do the functionally specialized brain areas interact to perform rich cognitive abilities (Başar and Schürmann, 2001; Miller and Wilson, 2008; Varela et al., 2001)? Neural assemblies involve neurons with reciprocal connections that interact at different spatial scales. Neurons in local populations process information whereas larger neural assemblies, including neurons connected across separate brain

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areas, combine multiple processes that are important for higher-level cognitive tasks. Because cognitive demands change over time, we must not only look at slowly changing anatomical connections but also at quickly changing (transient) interactions between neural assemblies. Both local and global neural assemblies can transiently interact with each other to perform immediate cognitive tasks. Neural oscillations could allow for transient neural network interactions responsible for complex cognitive tasks.

Fluctuations in postsynaptic potentials produce local oscillations. In addition, oscillators in one brain region can phase synchronize with oscillators in another region through long-range connections. A mechanism for interaction for both local populations of neurons and large neural assemblies is through phase synchronization of oscillations. As neurons oscillate, they effectively open and close their window to both send and receive information (Buzsáki and Draguhn, 2004; Womelsdorf et al., 2007). For information to be transferred from one neuronal group to another, the sending neuron must be excitable at the same time that the receiving group is excitable. This requires the coupling of oscillations between sending and receiving neurons through phase synchronization (Fries, 2005). This pattern of neural interaction allows for efficient neural communication through the transient coupling of neurons firing synchronously forming functional neural networks. It has been shown that the temporal coincidence of postsynaptic potentials has a greater impact on postsynaptic firing than non-coincident firing (Salinas and Sejnowski, 2001). In addition, this pattern of interaction causes precise timing of input and output from sending and receiving neurons (Mainen and Sejnowski, 1995). Therefore, neurons must bundle their signal by firing together synchronously to effectively send their signal to a target neuron. Neural assemblies interact at different temporal scales. In local neural assemblies, with close connections between neurons, communication can happen during faster, higher frequencies. In large-scale brain assemblies, with long-range connections between neurons, communication happens during slower, lower frequencies (Fries, 2005). There is also evidence that different bands of activity can multiplex such that slower oscillations provide a framework for other faster oscillations to operate such that fast oscillations communicate content while slow oscillations mediate transient connectivity (Buzsáki and Draguhn, 2004; Fries, 2005; Varela et al., 2001; Ward et al., 2006).

Research has shown that synchronized neural firing can allow for the transient interaction between visual areas for visual perception. It is proposed here that neural oscillations not only allow for synchronized neural firing for the transient interaction between brain areas for perceptual tasks but also for complex cognitive tasks. The following provides a general model of how neural oscillations can allow for synchronized neural firing for the transient interactions important for complex cognitive tasks. During a cognitive task oscillations can allow for local neurons to fire synchronously at high frequencies to process information. Multiple processes can then be combined through large-scale brain networks whose oscillations become phase synchronized causing neurons within these large-scale brain networks to fire synchronously. Transient linking through synchronous firing provides a mechanism to amplify relevant processing (synchronously firing neurons) and filter out irrelevant neural firing (asynchronously firing noise). When processing is complete, phase desynchronization of oscillations can cause neurons to stop firing synchronously. New brain networks whose oscillations become phase synchronized can then cause the same neurons to synchronously fire with other neurons to form a different neural assembly to perform a different cognitive task. Therefore, oscillations provide a robust mechanism for neurons to effectively form transient neural networks depending on the demands of the present cognitive task.

Episodic memory is a complex cognitive function that involves many interacting brain regions and allows us to store the content of experience that can be retrieved later. Episodic memory is unique from semantic memory in that it stores contextual (spatial and temporal) information about individual events that can be later retrieved. In addition, episodic memories are robust to interference, allowing us to store and retrieve separate but similar experiences. Although episodic and semantic memories are distinct, semantic memories may be originally encoded through episodic processes and the encoding of episodic memories may rely on semantic elaboration. By this definition all of the studies reviewed employ episodic memory tasks.

Neural oscillations have been linked to various cognitive phenomena in humans. There is not an exact mapping of oscillatory rhythms to specific cognitive processes. Instead, neural oscillations in a specific frequency range in one brain region may function in one cognitive process and in another cognitive process in another brain region. In addition, different neural oscillations can each function in a specific cognitive phenomenon (Başar et al., 1999; Kahana, 2006; Klimesch et al., 2008). The primary aim of this review will be to examine evidence for a functional role of gamma and theta oscillations in human episodic memory systems.

The review will focus on gamma and theta rhythms because recent evidence has suggested a functional role of gamma (25–100 Hz) and theta (4–8 Hz) oscillations in episodic memory. Other rhythms such as delta (1–4 Hz), alpha (8–12 Hz), and beta rhythms (15 Hz) will not be discussed because they have not been consistently reported as being related to episodic memory and the cortical–hippocampal network. Delta and beta rhythms have been reported in only a few studies (Düzel et al., 2003, 2005; Hanslmayr et al., 2009; Klimesch et al., 2000a; Mormann et al., 2005; Sederberg et al., 2007a,b; Weiss and Rappelsberger, 2000), but do not always correlate with episodic memory (Doppelmayr et al., 1998; Hanslmayr et al., 2009; Klimesch et al., 2001b, 2008; Osipova et al., 2006).

Separating the neural rhythms involved in semantic and episodic memory is often difficult as episodic tasks often include semantically meaningful items. There is convincing evidence that different neural rhythms contribute to semantic and episodic memory. The alpha rhythm has been related to semantic memory because it consistently phase desynchronizes with the presentation of semantically related items (Klimesch, 1996, 1999; Klimesch et al., 1994, 1997, 2000b, 2004, 2008; Mölle et al., 2002). Importantly, neural rhythms have been shown to dissociate when comparing semantic and episodic memory tasks. For example, Klimesch (1999) reviews a series of studies comparing alpha and theta modulations while subjects performed a semantic or episodic task. In the semantic task subjects were given a concept prime (e.g. eagle) and then a target feature (e.g. claws) and they had to judge whether the target was semantically congruent with the prime. In the episodic task subjects were given a concept and feature and they had to judge whether the concept/feature pair was previously shown at study. Comparing these two designs several studies found a consistent post-target decrease in alpha power for the semantic task and a post-target increase in theta power for the episodic task. Klimesch (1999) posits that the alpha rhythm likely involves the thalamo–cortical network whereas the theta rhythm likely involves the hippocampal–cortical network. These results are consistent with other results indicating that alpha is related to semantic memory whereas theta is related to episodic memory.

First, the methods used to measure rhythmic neural activity will be discussed. Second, the basis of neural oscillations will be discussed. Third, a review of the animal literature will provide the anatomical and physiological basis for understanding the role of gamma and theta oscillations in cortical–hippocampal episodic

memory networks. Finally, a review of recent evidence from recording the electrical activity of the human brain will explore the functional role of gamma and theta oscillations in human episodic memory. To date, little work has been done to synthesize the findings from these studies. This review will aim to synthesize these findings by connecting them to what is known about gamma and theta oscillations at a neural and systems level in the animal brain. Integrating these levels of analysis will elucidate the functional role of gamma and theta oscillations in episodic memory.

2. Measurement methods

The following review will include studies from animals and humans showing rhythmic neural activity. The review of the animal literature includes studies using single or multi-unit recording and local field potentials (LFPs). The review of the human literature includes studies using intracranial electroencephalography (iEEG) in patients with epilepsy and scalp electroencephalography (EEG) and magnetoencephalography (MEG) in normal subjects. Single and multi-unit recording intracellularly represents the firing of action potentials whereas LFPs recorded extracellularly represents fluctuations in postsynaptic potentials. Like LFPs, iEEG recorded extracellularly represents fluctuations in postsynaptic potentials. EEG and MEG measured externally represent the summed postsynaptic potentials of synchronously active regions of cortex and hippocampus that has spread through the brain, skull, and scalp. Although they often coincide, it should be noted that firing of action potentials are not necessarily related to oscillations of postsynaptic potentials. In addition, oscillations of postsynaptic potentials do not always result in the firing of postsynaptic action potentials. To maintain the distinction between the firing of action potentials and fluctuations in postsynaptic potentials we will refer to rhythmic and synchronous neural firing when referring to patterns of action potentials and we will refer to oscillations and phase synchronization when referring to fluctuations in postsynaptic potentials.

3. Neural mechanism of rhythmic activity

To understand how gamma and theta oscillations contribute to episodic memory, it is essential to first consider their basic underlying neural mechanisms of rhythmic activity. Studies using single unit and multi-unit recording show that rhythmic firing can occur because of intrinsic firing patterns of excitatory principle cells or common input from a pacemaker like the thalamus. More commonly in the cortex and the hippocampus, rhythmic firing is an emergent property of interactions between excitatory principle cells and inhibitory interneurons (Whittington et al., 2000). Rhythmic firing can happen at different spatial scales depending on the length of inhibitory interneuron to excitatory principle cell connections (Fries, 2005; Soltesz and Deschênes, 1993; Whittington et al., 2000) and at different temporal scales depending on the duration of inhibition (Buzsáki and Chrobak, 1995). In addition, rhythmic firing at different frequencies can multiplex such that faster rhythms are modulated by and nested within slower rhythms (Bragin et al., 1995; Chrobak and Buzsáki, 1998; Csicsvari et al., 2003; Penttonen et al., 1998; Soltesz and Deschênes, 1993).

In the cortex and hippocampus the collective activity of excitatory principle cells and inhibitory interneurons leads to neurons firing together and being inhibited together – creating rhythmic firing patterns (Buzsáki, 2006). Activation of excitatory principle cells leads to excitation of inhibitory interneurons. Inhibitory interneurons then act to inhibit further excitation. As inhibition wears off excitatory principle cells are free to fire again. Excitatory principle cells and inhibitory interneurons are both

important for the stable rhythmic firing patterns (Whittington et al., 2000). Excitatory principle cells receive variable excitation from presynaptic neurons. This variability in excitatory drive results in variability in the firing rate of postsynaptic excitatory principle cells. Excitatory principle cells and inhibitory interneurons act together to stabilize a network with variable firing rates. Stable rhythmic firing occurs when the firing rate of excitatory principle cells is averaged by inhibitory neurons firing synchronously and effectively defining a window in which the excitatory principle cells can fire. The firing rate of excitatory principle cells must be fast enough that they fire every time inhibition wears off and inhibition must wear off fast so that excitatory principle cells are ready to fire again when mutual inhibition among inhibitory interneurons fades.

3.1. Neural mechanism of gamma and theta rhythms

The neural mechanism responsible for gamma and theta rhythmic firing in the cortex and the hippocampus is similar, but primarily differs in the speed of inhibitory neurons. Whereas gamma rhythmic firing occurs through the interaction of excitatory principle cells and fast basket cell inhibitory interneurons (Banks et al., 2000; Bartos et al., 2007; Buhl et al., 1994; Mann and Paulsen, 2005; Penttonen et al., 1998; Whittington et al., 2000) acting on fast Gamma-aminobutyric acid (GABA_A) receptors (Banks et al., 2000; Soltesz and Deschênes, 1993; Traub et al., 1996; Whittington et al., 2000), theta rhythmic firing occurs through the interaction of excitatory principle cells and slow stellate cell inhibitory interneurons (Dickson et al., 2000; Rotstein et al., 2005) acting on slow GABA_A receptors (Banks et al., 2000; reviewed in Buzsáki, 2002; Cobb et al., 1995; Soltesz and Deschênes, 1993). It has also been shown in the hippocampus that gamma rhythms are more prevalent in the short-range connections through the activity of local interneuron networks whereas theta rhythms are more prevalent in further reaching areas through the activity of long-range interneuron to principle cell connections (Gloveli et al., 2005).

Although there is little evidence of the mechanism responsible for nesting of gamma rhythms within theta rhythms, some researchers have speculated that theta rhythms modulate gamma rhythms through the action of inhibitory interneurons (Bragin et al., 1995). The rhythmic firing of inhibitory interneurons firing at theta frequency provide a depolarizing and hyperpolarizing current that activates and deactivates inhibitory interneurons firing at gamma frequency. Supporting this idea, it has been shown that inhibitory interneurons acting on slow GABA_A receptors can also inhibit the activity of inhibitory interneurons acting on fast GABA_A receptors (Banks et al., 2000). This results in the activity of slow inhibitory interneurons inhibiting fast inhibitory interneurons that cause gamma rhythms. Therefore, theta rhythms can modulate gamma rhythms providing a possible mechanism for the nesting of gamma rhythms within theta rhythms.

4. Unified model of gamma and theta oscillations in episodic memory

Neural oscillations in the gamma and theta frequencies have been found in cognitive tasks such as those used to investigate episodic memory (reviewed in Başar et al., 1999; Bastiaansen and Hagoort, 2003; Herrmann et al., 2004b; Jensen et al., 2007; Kahana, 2006; Kahana et al., 2001; Klimesch, 1996, 1999; Klimesch et al., 2010, 2008; Sauseng et al., 2010). The following section will provide a comprehensive review of studies measuring gamma and theta oscillations using iEEG in patients with epilepsy and scalp EEG and MEG in normal subjects that have shown gamma and theta power modulations, phase synchronization between brain regions, and gamma/theta coupling during the encoding and retrieval of episodic memories. Table 1 provides details of the

Table 1
Episodic memory-related oscillations in humans.

Authors and year	Memory paradigm	Sample size (N)	Recording and analysis methods	Results	Conclusions
Burgess and Ali (2002)	Word recognition Remember/Know responses	(10)	EEG, wavelet power and coherence	Greater frontal and parietal gamma power (300–500 ms) and coherence for “remember” than “know” responses. Theta modulated gamma coherence.	Gamma is related to feature binding or consciousness and modulation by theta may be related to binding.
Burgess and Gruzelier (1997)	Word recognition	(15)	EEG, ERD power	Greater frontal theta power 125 ms and (500–750 ms) for hits than correct rejections.	Theta phase synchronization is associated with word recognition.
Doppelmayr et al. (1998)	Word recognition	(26)	EEG, ERD power	Greater right lateralized parietal theta power (500–1000 ms) for good memory performers. Greater bilateral parietal theta power (500–1000 ms) for bad memory performers.	Right hemisphere is more involved in episodic memory.
Doppelmayr et al. (2000)	Word recognition	(26)	EEG, IBP, ERBP	Greater evoked theta power (<400 ms) for good than bad memory performers. Induced theta power (>400 ms) for good and bad memory performers.	For good memory, early coordination of sensory and episodic areas interact (evoked) and later represent memory (induced).
Düzel et al. (2003)	Word recognition	(14)	MEG, wavelet power and phase locking factor	Greater theta power (200–700 ms) for hits than correct rejections. Greater theta/gamma coupling for hits than correct rejections.	Medial temporal lobe theta modulates gamma.
Düzel et al. (2005)	Word recognition	(8)	MEG, wavelet power and phase locking factor	Greater frontal midline induced theta/gamma coupling for hits than correct rejections.	Induced theta represents large-scale integration of distributed information by the medial temporal lobe.
Fell et al. (2003)	SM word recall	Epilepsy patients (9)	iEEG, wavelet power and coherence	Greater rhinal-hippocampal theta coherence for subsequently recalled than not recalled words. Greater theta/gamma coupling for subsequently recalled than not recalled words.	Gamma holds memory representation and theta escorts memory to medial temporal lobe structures.
Fell et al. (2001)	SM word recall	Epilepsy patients (9)	iEEG, wavelet power and circular variance phase synchronization	Greater MTL-hippocampal gamma phase synchronization (100–600 ms) for subsequently recalled than not recalled words.	Gamma provides a mechanism to transiently couple neural populations such as hippocampus and cortex for memory tasks.
Gruber et al. (2001)	PAL and CR control task	(10)	EEG, wavelet power, PLV, and PLS	Greater frontal and centro-parietal induced gamma power (400–500 ms) for paired associate than control task. Anterior–posterior gamma phase synchrony (140–240 ms) for paired associate than control task.	Induced gamma over form widespread cell assemblies for the storage of associative information.
Gruber et al. (2008)	Recognition of pictures with Old/New + source judgment (encoding task)	(14)	EEG, wavelet power	Greater widespread parieto-occipital induced gamma power (210–330 ms) for hits than correct rejections. Greater fronto-central induced theta (600–1200 ms) for correct than incorrect source judgments.	Induced gamma is related to familiarity or the binding of cortical representations and induced theta is related to recollection.
Gruber et al. (2004)	SM paradigm for word recognition	(19)	EEG, wavelet power	Greater widespread induced gamma power (200–300 ms) for subsequently recognized than not recognized words and for hits than correct rejections.	Gamma at encoding and retrieval indicates establishment and retrieval of cortical object representations.
Guderian and Düzel (2005)	Face recognition Old/New + source judgment (background)	(9)	MEG, wavelet power and phase locking factor	Greater prefrontal, mediotemporal, visual cortex induced theta for correct than incorrect source judgments.	Theta oscillations are related to the binding of distributed cortical representations during recollection.
Hanslmayr et al. (2009)	SM word recognition	(25)	EEG, ERD power	Greater gamma power for the deep and shallow encoding task. Greater theta power for the shallow encoding task.	Gamma relates to both semantic and non-semantic episodic encoding whereas theta only relates to non-semantic episodic encoding.
Klimesch et al. (1997)	SM word recognition	(18)	EEG, ERD power	Greater left frontal (0–250 and 750–100 ms) theta power for subsequently recognized than not recognized words and for hits than correct rejections and misses.	Theta phase synchronization is important for successful episodic encoding and retrieval.

Klimesch et al. (2000a)	Word recognition	(25)	EEG, IBP	Greater induced theta power (375–750 ms) for hits than correct rejections.	Theta from hippocampus is feedback to cortex where it acts to suppress neural firing to favor the retrieval of relevant information and suppression of irrelevant information.
Klimesch et al. (2001a)	Picture recognition	(13)	EEG, ERD power	Greater theta power during retrieval than encoding. Numerically greater theta power for hits than correct rejections.	Theta relates to retrieval mode rather than memory trace or retrieval success.
Klimesch et al. (2001b)	Word recognition Remember/Know responses	(13)	EEG, ERBP	Greater widespread theta power (300–450 ms) for “know” than “remember” responses. Greater widespread theta power (450–625 ms) for “remember” than “know” responses.	Theta relates to conscious retrieval related to both remembering and knowing.
Klimesch et al. (1994)	Semantic congruency and word recognition	(12)	EEG, ERD power	Frontal and occipital theta power (~400 ms) for word recognition.	Theta related to word recognition.
Klimesch et al. (2000b)	Word recall	(60)	EEG, power	Less theta during rest for good than bad memory performers.	Less baseline theta and increased event-related theta is related to good memory performance.
Möller et al. (2002)	SM word and face pair cued recall	(17)	EEG, FFT power	Greater left frontal and temporal theta power for subsequently recalled than not recalled words. Greater right parietal theta power for subsequently recalled than not recalled faces.	Theta interactions in cortical–hippocampal circuit indicate intentional learning.
Mormann et al. (2005)	Word recognition	Epilepsy patients (12)	iEEG, wavelet power and phase (entropy)	Theta phase reset and greater theta power (>190 ms) for hits and correct rejections. Theta modulated gamma power in perirhinal cortex for correct rejections and hippocampus for hits.	Gamma represents memory encoding and retrieval in the perirhinal cortex and hippocampus, respectively. Theta serves a general facilitating function during memory tasks.
Osipova et al. (2006)	SM picture recognition	(13)	MEG, multitaper power	Greater occipital gamma power for subsequently recognized than not recognized pictures and for hits than correct rejections and misses. Greater right temporal–parietal theta power for subsequently recognized than not recognized pictures and for hits than rejections and misses.	Gamma is phase synchronized activity in perceptual areas that are then sent to memory system where theta can then act to encode those items.
Sederberg et al. (2003)	SM word recall	Epilepsy patients (10)	iEEG, wavelet power	Greater widespread gamma power (600–1300 ms) for subsequently recalled than not recalled words. Greater right temporal and frontal theta power (600–1300 ms) for subsequently recalled than not recalled words.	Gamma is related to attention to items to improve encoding. Theta is involved in successful memory encoding.
Sederberg et al. (2007b)	SM word recall	Epilepsy patients (35)	iEEG, wavelet power	Greater frontal gamma power and greater gamma power in left temporal and hippocampal later for subsequently recalled than not recalled words. Greater left frontal theta power early for subsequently recalled than not recalled words.	Suggest that early gamma in frontal areas is related to attention, then hippocampal gamma related to encoding, and temporal gamma related to semantic elaboration leading to more hippocampal gamma.
Sederberg et al. (2007a)	SM word recall	Epilepsy patients (52)	iEEG, wavelet power	Greater hippocampus, left temporal, inferior prefrontal, and occipital cortex gamma power for subsequently recalled than not recalled words. Greater hippocampal (500–400 ms before response), left temporal, and inferior prefrontal cortex (250 ms before response) gamma power for hits than false alarms.	Gamma activity at encoding is reinstated at retrieval when the hippocampus activates and reinstates cortical representations.
Summerfield and Mangels (2005a)	SM word recognition Old/New + source judgment (font color)	(19)	EEG, ICA, wavelet coherence	Greater left frontal theta power for subsequent hits with incorrect source judgments. Greater left frontal and posterior theta coherence for subsequent hits with incorrect source judgments. Greater right and bilateral frontal theta power (400 ms) for subsequent hits with correct source judgment than incorrect source judgments. Greater right frontal and posterior theta coherence (800 ms) for subsequent hits with correct source judgment than incorrect source judgments.	Theta coherence may be important for brain regions to exchange information during learning, with left hemisphere processing item information and right hemisphere processing context.

Table 1 (Continued)

Authors and year	Memory paradigm	Sample size (N)	Recording and analysis methods	Results	Conclusions
Summerfield and Mangels (2005b)	DRM word recognition	(19)	EEG, ICA, wavelet coherence	Greater frontal gamma power (>100 ms) for hits than correct rejections. Greater parieto-occipital gamma power (>100 ms) for hits than false alarms. Greater parieto-occipital and right frontal gamma coherence (600 ms) for hits than correct rejections and false alarms.	Gamma phase synchronization important for frontal areas to provide top-down control to recapitulate sensory representations in posterior regions.
Weiss and Rappelsberger (2000)	SM word recall	(23)	EEG, FFT power and coherence	Greater temporal and parietal theta coherence for subsequently recalled than not recalled words.	Theta phase synchronization between distant brain regions enables efficient encoding of verbal memory.
Weiss et al. (2000)	SM word (concrete and abstract) recall	(23)	EEG, FFT power and coherence	Greater left frontal, temporal, parietal, and occipital theta coherence for subsequently recalled than not recalled words.	Theta coherence represents the difference between successfully and unsuccessfully encoded words.

SM: subsequent memory; DRM: Deese–Roediger–McDermott; PAL: paired associate learning; iEEG: intracranial electroencephalography; EEG: electroencephalography; MEG: magnetoencephalography; FFT: fast Fourier transform; ICA: independent components analysis; ERD: event-related desynchronization; ERBP: event-related band power; IBP: induced band power; PLV: phase locking value; PLS: phase locking statistic; MTL: medial temporal lobe.

episodic memory paradigm, recording and analysis methods, results, and conclusions for each study reviewed below.

A unified model will be proposed here that describes a functional role for gamma and theta oscillations in human episodic memory by integrating what is known about gamma and theta oscillations at the neural and behavioral level in animals into the framework of the influential hippocampal memory indexing theory (Teyler and DiScenna, 1986; Teyler and Rudy, 2007). It is proposed here that gamma and theta oscillations allow for the interaction between cortical structures and the hippocampus for the encoding and retrieval of episodic memories. This model incorporates and extends previous models of gamma and theta oscillations in episodic memory. The proposed model incorporates previous theories of the functional role for gamma (Herrmann et al., 2004a; Jensen et al., 2007; Klimesch et al., 2008) and theta oscillations (Bastiaansen and Hagoort, 2003; Klimesch, 1996, 1999; Klimesch et al., 2010, 2008; Sauseng et al., 2010) and gamma/theta interactions (Jensen and Colgin, 2007; Jensen and Lisman, 2005; Lisman, 1999, 2005) in episodic memory. It extends these previous models by providing a unified model of gamma and theta oscillations that allow for the cortical–hippocampal interactions described by the hippocampal indexing memory theory.

4.1. Unified model for encoding

For encoding, the hippocampal memory indexing theory (Teyler and DiScenna, 1986) states that when presented a stimulus, spatio-temporal patterns of cortical activity project to the hippocampus. The hippocampus binds these representations from diverse cortical regions into a sparse, unified episodic memory representation. It does this by quickly modifying synaptic strength between input neurons and hippocampal neurons and between hippocampal neurons activated by the cortical inputs through long-term potentiation (LTP).

4.1.1. Gamma rhythmic firing modulates perceptual feature binding

Just as visual perception consists of several visual features that must be integrated into a perceptual whole, episodic memory consists of several different individual memory representations that include several features that must be integrated into an individual memory representation. The animal and human literature is consistent with the proposal that gamma and theta oscillations in the cortex and the hippocampus lead to the encoding of episodic memories.

Research on the animal visual system has provided a plausible functional role for gamma oscillations in the cortex. In order to perceive objects in a visual image, the distributed parallel processing of features in a single object must be combined. To solve the “binding problem” the “binding by synchrony” (BBS) theory (von der Malsburg and Schneider, 1986) proposes that the neurons representing features of an object are transiently coupled through synchronous firing. The BBS theory is supported by multi-unit recording studies showing that gamma rhythmic firing is synchronized with contiguous visual input in primary visual cortex (V1), secondary visual cortex (V2), and posteromedial lateral suprasylvian area (Engel et al., 1991a,b; Frien et al., 1994; Gray et al., 1989). Although these results indicate that the binding of visual features for coherent visual representations is supported by synchronous firing between neurons in areas of visual cortex, the BBS theory remains controversial (Shadlen and Movshon, 1999). The BBS theory has not been supported by studies showing that synchronous firing was not related to contour grouping in V1 (Roelfsema et al., 2004), was not greater for non-coherent than coherent motion (Thiele and Stoner, 2003) or for bound objects in

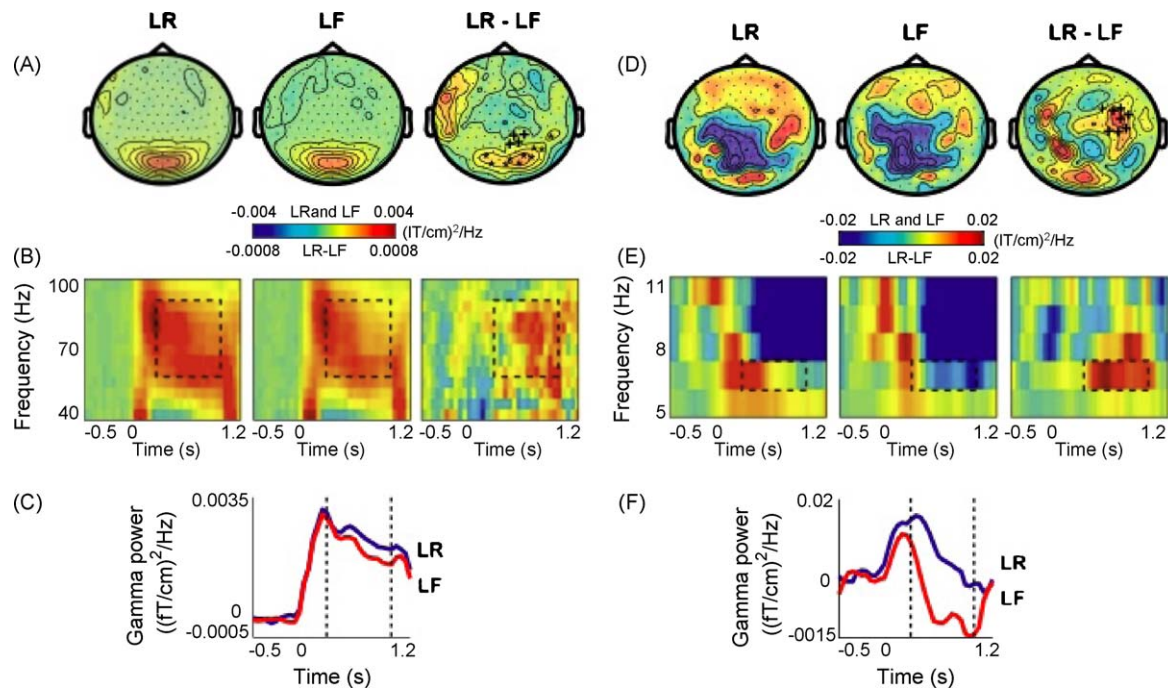


Fig. 1. Gamma and theta power during encoding. (A) Grand average of the topography of gamma power for later remembered (LR), later forgotten (LF), and their difference (LR – LF). Plus signs represent right temporal sensors that showed a significant power increase for LR compared to LF. (B) Grand average time–frequency plots of power from one significant right temporal sensor showing the time course of gamma oscillations for LR, LF, and LR – LF. (C) Grand average gamma power averaged between 60 and 90 Hz for LR and LF for the same sensor as B. (D) Grand average of the topography of theta power for LR, LF, and LR – LF. (E) Grand average time–frequency plots of power from one significant sensor showing the time course of theta oscillations for LR, LF, and LR – LF. (F) Grand average theta power averaged between 4.5 and 8.5 Hz for LR and LF for the same sensor as E (reprinted with permission from Osipova et al., 2006). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

MT (Palanca and DeAngelis, 2005). One carefully controlled study (Dong et al., 2008) showed that synchronous firing was not greater for one versus two objects in V1 and V2, but was greater for border selective neurons, which could indicate that synchronous firing is a marker of higher-level visual binding. These results suggest that cortical gamma rhythmic firing could provide a mechanism to bind relevant stimulus features for perceptual representations and provide a coherent pattern of activity as input to the hippocampus.

In humans there should be gamma power increases in modality specific perceptual areas during the encoding of new memories. Many studies have shown greater gamma power in posterior cortex for subsequently remembered than forgotten items (Gruber et al., 2004; Hanslmayr et al., 2009; Osipova et al., 2006; Sederberg et al., 2003, 2007a,b) (see Fig. 1(A)–(C)).

4.1.2. Gamma oscillations lead to spike-timing-dependent plasticity

The animal literature has also shown that gamma oscillations provide the precise timing necessary for spike-timing-dependent plasticity. LTP results when calcium enters the postsynaptic neuron initiating a cascade of molecular processes for synaptic modification and memory formation. Spike-timing-dependent plasticity is a form of LTP that depends on the timing of presynaptic neuron firing relative to postsynaptic neuron firing (Skaggs et al., 1996). Spike-timing-dependent plasticity occurs when two circumstances are met. First, the presynaptic neuron must release glutamate that binds to N-methyl-D-aspartic acid (NMDA) receptors. Second, the postsynaptic neuron must be depolarized in order to remove a magnesium plug that blocks the NMDA receptor. The binding of glutamate occurs slowly (~ 20 ms) but removal of the magnesium plug occurs very rapidly (< 1 ms). Based on these constraints, spike-timing-dependent plasticity occurs when the presynaptic neuron fires and releases glutamate prior to postsynaptic depolarization. It has recently been proposed that LFP gamma oscillations are important for spike-timing-dependent

plasticity to occur (Axmacher et al., 2006). Neural oscillations modulate when excitatory principle cells can fire. Excitatory principle cells are more likely to fire on the positive peak of neural oscillations. Because gamma oscillations occur at 25–100 Hz, the pattern of inputs has the exact timing parameters necessary for spike-timing-dependent plasticity. Slower oscillations would not provide the tight timing parameters necessary for coincident activation of presynaptic and postsynaptic neurons. And faster oscillations would have multiple cycles within the time-period of spike-timing-dependent plasticity. This would cause ambiguity as the window for LTP would include presynaptic neuron spikes before and after postsynaptic spikes. Although gamma oscillations have been implicated in spike-timing-dependent plasticity, it has not yet been shown that gamma oscillations are linked to memory in animals. Therefore, gamma phase synchronization between cortical and hippocampal neurons and between hippocampal neurons could provide the mechanism by which individual memory representations get encoded.

In humans this would result in gamma phase synchronization between these structures during the encoding of new episodic memories. This idea is supported by an iEEG study showing gamma phase synchronization between medial temporal (rhinal) cortex electrodes and hippocampal electrodes during successful encoding of words (see Fig. 2, Fell et al., 2001).

4.1.3. Theta oscillations modulate LTP

The animal literature has also shown that theta oscillations influence the encoding of new episodic memories. The positive peak of the LFP theta oscillation causes depolarization which leads to the opening of NMDA channels causing calcium influx initiating the cascade of molecular processes for synaptic modification and memory formation (Huerta and Lisman, 1995). A number of studies have shown that stimulating at theta frequency is optimal for the induction of LTP in dentate gyrus (Greenstein et al., 1988)

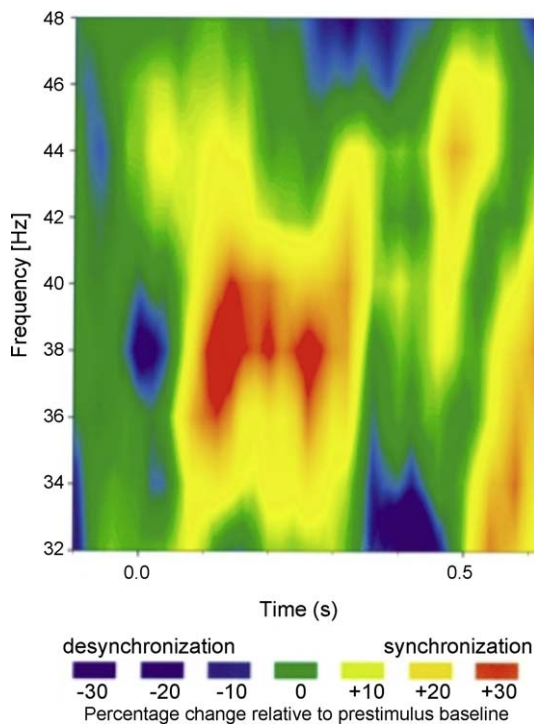


Fig. 2. Gamma phase synchronization for encoding. Difference of phase synchronization between rhinal cortex and hippocampus (%) relative to prestimulus baseline for subsequently recalled minus not recalled words. Blue indicates more phase desynchronization, red indicates more phase synchronization, ranging from -30% to $+30\%$ change from prestimulus baseline. Phase synchronization differences for successfully recalled versus not recalled were greatest for 36–40 Hz from 100 to 300 ms and 500–600 ms (reprinted with permission from Fell et al., 2001). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

and CA1 neurons (Larson and Lynch, 1986; Larson et al., 1986; Rose and Dunwiddie, 1986) in the hippocampus. In addition, studies have found LTP in dentate gyrus (Pavlidis et al., 1988) and CA1 neurons (Hölscher et al., 1997; Huerta and Lisman, 1995; Hyman et al., 2003) in the hippocampus when stimulating at the positive peak of the theta oscillation and no effect or depotentiation of previously potentiated synapses when stimulating at the trough of the theta oscillation. These results indicate that the firing of neurons at the peak of the theta oscillation is optimal for synaptic plasticity.

The following studies used *in vivo* hippocampal preparations and behavioral measures to examine whether theta oscillations affect learning and performance on commonly used memory tasks. The level of theta activity prior to training and during training positively correlated with the rate of acquisition on classical conditioning paradigms (reviewed in Berry and Seager, 2001). In addition, lesioning the septum as well as pharmacologically blocking acetylcholine has been shown to decrease theta oscillations in the hippocampus and decrease the rate of acquisition on classical conditioning paradigms (reviewed in Berry and Seager, 2001). Blocking theta oscillations by lesioning the septum has also been shown to decrease the rate of learning on a spatial maze task (Winson, 1978) whereas enhancing theta oscillations by pharmacologically blocking serotonin increased performance on a radial maze task (Stäubli and Xu, 1995). In addition, hippocampal theta activity positively correlated with rats performance on a Morris maze task (Olvera-Cortés et al., 2002) and theta oscillations were greater for correct non-matched compared to incorrect matched odors in a delay non-match to sample task (Wiebe and Stäubli, 2001). Combined, these studies show the presence of theta oscillations in the cortical–hippocampal network and indicate

that theta oscillations are important for synaptic plasticity, learning, and performance on memory tasks.

In humans there should be theta power increases in posterior regions during the encoding of new memories. Some studies have used the subsequent memory paradigm and found greater theta power for subsequently remembered than forgotten items (Hanslmayr et al., 2009; Osipova et al., 2006; Sederberg et al., 2003) (see Fig. 1(D)–(F)).

4.1.4. The theta/gamma code model and episodic memory

Although the hippocampal memory indexing theory (Teyler and DiScenna, 1986) does not specify how multiple memories make up coherent episodes, individual memory representations must be combined and temporally ordered in episodic memory. In rats, pyramidal neurons in the hippocampus fire for a particular location in the environment. These “place cells” fire strong bursts of spikes when the rat runs through a location in the environment, the “place field”, and less strongly on the periphery of the place field. Pyramidal neurons in the hippocampus fire at the peak of theta oscillations as the rat enters the place field and then fire progressively earlier on later theta cycles as the rat runs from location to location (reviewed in Buzsáki, 2002; O’Keefe and Recce, 1993; Skaggs et al., 1996; reviewed in Yamaguchi et al., 2007). For example, if a rat is moving along a path from position A to position C the neurons coding position A will originally fire late in the theta cycle and then will fire progressively earlier in the theta cycle as the rat approaches position C (Lisman, 1999). This modulation of pyramidal cell firing in relation to the phase of theta oscillations is called phase precession. Phase precession has been shown in the CA1 region of the hippocampus (O’Keefe and Recce, 1993) and more broadly across the entire hippocampus (Skaggs et al., 1996).

The following explains how LTP leads to phase precession (Axmacher et al., 2006) (see Fig. 3). When the animal enters a place field, theta oscillations reset so that the cells firing to the place field will be activated at the peak of the theta cycle. As described above, inputs arriving at the peak of theta oscillations induce LTP (reviewed in Buzsáki, 2002; Hölscher et al., 1997; Huerta and Lisman, 1995; Pavlidis et al., 1988). The activated place cells are then strengthened by LTP so that the same environmental cues will evoke firing at earlier phases of theta oscillations on subsequent cycles. After learning, when the animal enters a familiar place field, the same input arrives at potentiated synapses, leading to activation of the postsynaptic neuron even when it is not in its depolarized state at the peak of theta oscillations. Therefore, experience can cause LTP that allows neurons to fire at progressively earlier phases of the theta cycle leading to phase precession.

It has been proposed that the interaction between gamma and theta oscillations encodes and temporally orders working memory representations (Lisman and Idiart, 1995). Extending this theory, it has been suggested that the theta/gamma code model can work as a working memory buffer for encoding episodic memories (Jensen and Lisman, 2005) and for ordering place and episodic memories

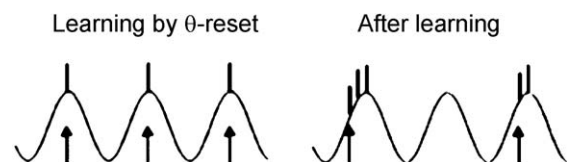


Fig. 3. Phase precession. When the animal enters a place field, the theta rhythm resets so that the cells firing to the place field will be activated at the peak of the theta cycle. Inputs arriving at the peak of the theta rhythm induce LTP. The activated place cells are then strengthened by LTP so that the same environmental cues will evoke firing at earlier phases of the theta rhythm on subsequent cycles (reprinted with permission from Axmacher et al., 2006).

(Lisman, 1999). The theta/gamma code may also be a more domain general coding scheme for representing order in the cortex (Jensen and Colgin, 2007; Lisman, 2005). For episodic memory temporal ordering, the theta/gamma code model posits that in each gamma cycle a set of neurons fires for a given episodic memory representation. Different assemblies of neurons representing different episodic memory representations fire in different gamma cycles. Gamma cycles are superimposed onto different phases of the theta cycle. The coupling between gamma and theta oscillations is not static but changes over time with learning. Through phase precession, as episodes are presented, each gamma cycle representing a specific episodic memory representation fires at an earlier phase of the theta cycle. The theta/gamma code suggests that populations of neurons do not fire continuously within the theta cycle, but within gamma cycles superimposed on the theta rhythm. Consistent with this suggestion, research has shown that populations of neurons fire 5–7 times within the theta cycle (Bragin et al., 1995; Csicsvari et al., 2003; Soltesz and Deschênes, 1993). For example, episodic memories include a series of specific memory representations such as “Jerry dropped candy”, “Monkey in cage grabbed it”, “Jerry sad” (Lisman, 1999). Analogous to the rat moving along a path from position A–C the neurons coding “Jerry dropped candy”, “Monkey in cage grabbed it”, and “Jerry sad” will originally fire late in the theta cycle and then will fire progressively earlier in the theta cycle. Therefore, neurons coding for each memory representation will be active in a different phase of the theta cycle and will maintain the temporal order of the sequence of events making up the episodic memory. Therefore, the interaction between gamma and theta oscillations provides a mechanism for the binding and temporal ordering of individual episodic memory representations from dispersed cortical regions for encoding episodic memories.

In humans this should be represented by gamma/theta coupling during encoding of episodic memories. Although there is no direct evidence of temporal ordering of gamma oscillations superimposed on theta oscillations during episodic encoding, consistent with this idea, one iEEG study has shown coherence between rhinal and hippocampal areas and gamma/theta coupling for successfully encoded words (Fell et al., 2003). Therefore, there is growing evidence in animals and humans that gamma power increases in posterior cortical regions and theta modulation of gamma oscillations in medial temporal lobe regions support the encoding of new episodic memories.

4.2. Unified model for retrieval

For retrieval, the hippocampal memory indexing theory (Teyler and DiScenna, 1986) states that, when part of the memory representation is re-presented, cortical activity spreads to the hippocampus, which in turn activates the entire unified memory representation in the hippocampus. The hippocampus then reactivates the spatio-temporal pattern of activity in the cortex for the entire unified episodic memory representation.

The model proposed here suggests that at retrieval cortical gamma oscillations provide input to the hippocampus causing activation of the hippocampal gamma modulated representations of each individual memory representation temporally ordered by theta oscillations. Through feedback projections from the hippocampus to the cortex these gamma and theta patterns should cause the reinstatement of the entire memory representation in the cortex. Although the animal literature provides strong evidence for gamma and theta oscillations modulating encoding through LTP (Axmacher et al., 2006; reviewed in Berry and Seager, 2001; reviewed in Buzsáki, 2002; Greenstein et al., 1988; Hölscher et al., 1997; Huerta and Lisman, 1995; Larson and Lynch, 1986; Pavlides et al., 1988; Rose and Dunwiddie, 1986; Stäubli and Xu, 1995;

Winson, 1978), there is little evidence supporting the role of gamma and theta oscillations at retrieval. A few studies show that hippocampal theta rhythms during testing positively correlate with performance on spatial (Olvera-Cortés et al., 2002) and recognition memory tasks (Wiebe and Stäubli, 2001).

Although there is little support from the animal literature, the human literature is consistent with the proposal that at retrieval, gamma and theta oscillations cause the hippocampal reinstatement of memory representations in posterior cortex. In humans there is greater gamma (Gruber et al., 2001, 2004, 2008; Osipova et al., 2006; Summerfield and Mangels, 2005b) (see Fig. 4(A)–(C)) and theta power (Düzel et al., 2003; Klimesch et al., 2000a, 2001a; Mormann et al., 2005; Osipova et al., 2006) (see Fig. 4(D)–(F)) in hippocampal and posterior cortical regions for correctly remembered items than new items. Again, although there is no direct evidence of temporal ordering of gamma oscillations superimposed on theta oscillations during episodic retrieval, theta oscillations have been shown to modulate gamma oscillations in anterior temporal scalp locations (Düzel et al., 2003) and the hippocampus (Mormann et al., 2005) during successful retrieval. When given a partial cue, the cortical–hippocampal network is needed to retrieve the rich details of episodic memory. Retrieving details of the study episode, such as associated source information or the feeling of “remembering”, requires the reactivation of the entire cortical–hippocampal network. It has been shown that theta power increases in frontal, mediotemporal, and visual cortex with the retrieval of source information (background details) (Guderian and Düzel, 2005). Some research has shown greater gamma power over parietal scalp locations (Burgess and Ali, 2002) and theta power in widespread scalp locations (Klimesch et al., 2001b) for words given a “remember” than a “know” response. Therefore, there is some evidence in animals and humans consistent with the idea that the retrieval of episodic memory involves the reinstatement of encoded memory representations in posterior cortical regions through the activity of gamma and theta oscillations.

4.3. Frontal–hippocampal oscillations

Another important aspect of episodic memory to consider is how top-down control can guide encoding and retrieval. It has been proposed that theta oscillations allow for top-down control in episodic memory (Kahana et al., 2001; Klimesch, 1996, 1999; Klimesch et al., 2010, 2008; Sauseng et al., 2010). In rats it has been shown that neural firing in the medial prefrontal cortex, an analogue to the human dorsolateral prefrontal cortex, phase locked to the hippocampal theta rhythm (Hyman et al., 2005) and that medial prefrontal phase locking to the hippocampal theta rhythm positively correlated with behavior on spatial maze tasks (Jones and Wilson, 2005; Siapas et al., 2005).

4.3.1. Human frontal–hippocampal oscillations during encoding

In humans, many studies have implicated the ventrolateral prefrontal cortex in selecting goal-relevant information and inhibiting distracting information whereas the dorsolateral prefrontal cortex aids in ordering information for episodic encoding and retrieval (reviewed in Blumenfeld and Ranganath, 2007). The human studies presented are consistent with the idea that theta phase synchronization between frontal and posterior regions provides top-down control to modulate the encoding of episodic memories. Some studies have shown theta power increases in frontal areas (Klimesch et al., 1997; Sederberg et al., 2007b; Summerfield and Mangels, 2005a) and frontal and posterior scalp locations (Mölle et al., 2002; Sederberg et al., 2003) during encoding of successfully remembered items. Importantly, theta phase synchronization between frontal and posterior regions (including parietal and temporal cortex) has been

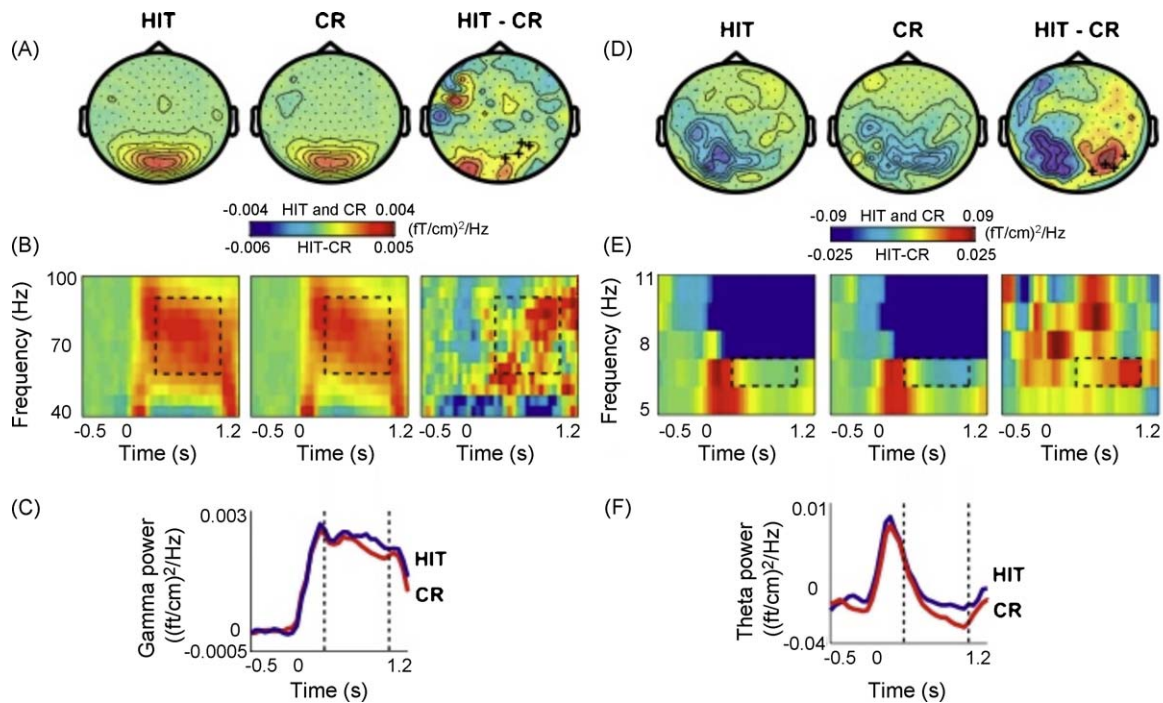


Fig. 4. Gamma and theta power during retrieval. (A) Grand average of the topography of gamma power for hits (HIT), correct rejections (CR), and their difference (HIT-CR). Plus signs represent right occipital sensors that showed a significant power increase for HIT compared to CR. (B) Grand average time–frequency plots of power from one significant right occipital sensor showing the time course of gamma oscillations for HIT, CR, and HIT-CR. (C) Grand average gamma power averaged between 60 and 90 Hz for HIT and CR for the same sensor as (B). (D) Grand average of the topography of theta power for HIT, CR, and HIT-CR. (E) Grand average time–frequency plots of power from one significant sensor showing the time course of theta oscillations for HIT, CR, and HIT-CR. (F) Grand average theta power averaged between 60 and 90 Hz for HIT and CR for the same sensor as (E) (reprinted with permission from Osipova et al., 2006). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

shown for successful memory encoding (Weiss et al., 2000; Weiss and Rappelsberger, 2000) including source information (Summerfield and Mangels, 2005a).

4.3.2. Human frontal–hippocampal oscillations during retrieval

It has been proposed that the dorsolateral prefrontal cortex maintains temporal context and, when a partial cue is presented at retrieval, can provide top-down control to the hippocampus and posterior cortex to retrieve associated memory representations (Polyn and Kahana, 2008). The frontal cortex has also been implicated in post-retrieval processing or the monitoring and evaluation of the content of retrieved information in relation to the goals of the retrieval attempt (reviewed in Blumenfeld and Ranganath, 2007). The human studies presented here are consistent with the idea that theta phase synchronization between frontal and posterior regions provides top-down control to modulate the retrieval of episodic memories. Some studies have reported theta power increases in frontal scalp locations (Burgess and Gruzelier, 1997; Düzel et al., 2005; Klimesch et al., 1997) during successful retrieval and frontal and posterior scalp locations for retrieval of specific details of the study episode (Gruber et al., 2008; Guderian and Düzel, 2005). Some of these studies report theta power increases over frontal scalp locations early (before 200 ms) (Burgess and Gruzelier, 1997; Klimesch et al., 1997), supporting the role for theta oscillations in frontal top-down control to the hippocampus and posterior cortex to retrieve associated memory representations. Some studies report theta power increases over frontal scalp locations (Burgess and Gruzelier, 1997; Klimesch et al., 1997) and fronto-central scalp locations late (after 500 ms) (Gruber et al., 2008), supporting the role for theta oscillations in frontal top-down control to the hippocampus and posterior cortex for post-retrieval processing. Therefore, in addition to the direct influences on encoding and

retrieval of episodic memory representations, theta rhythms can allow for top-down control from frontal cortex for the encoding and retrieval of episodic memories.

Combined the studies described above suggest that modulation of gamma and theta oscillations and phase synchronization between brain regions play a role in episodic memory processes. Future research should be careful to distinguish between movement and cognitive correlates of oscillations. Some studies have shown a strong relationship between micro-saccades and the onset of induced gamma band responses (iGBR) (Jerbi et al., 2009; Trujillo et al., 2005; Yuval-Greenberg and Deouell, 2009; Yuval-Greenberg et al., 2008). Although micro-saccades are particularly problematic for scalp recorded EEG (Trujillo et al., 2005; Yuval-Greenberg and Deouell, 2009; Yuval-Greenberg et al., 2008), even iEEG can become contaminated by micro-saccades when recording electrodes are close to extraocular muscles (Jerbi et al., 2009). It is difficult to discriminate eye movement-related from cognitive-related iGBR because both vary depending on perceptual and cognitive processes. Future research is necessary to determine whether eye movements and/or cognitive processes lead to greater iGBRs for subsequently remembered than forgotten items and old than new items.

Performing an episodic memory task does not involve a unitary process but involves multiple processes distributed throughout the brain. For example, perceptual processes, attentional processes, working memory processes, memory retrieval processes such as familiarity and recollection, and decisional factors all contribute to performance on memory tasks. In order to clarify the role that gamma and theta oscillations play in encoding and retrieval of episodic memories, it is important to differentiate neural oscillatory patterns related to the different cognitive operations involved in episodic memory tasks, but few studies address the exact role that gamma and theta oscillations play in episodic

memory tasks. One promising approach in this direction is using multivariate analysis which can indicate whether neural oscillations in different brain regions correlate with different task variables (Kahana, 2006). Using a multivariate linear model on a working memory task Jacobs et al. (2006) were able to find that EEG theta oscillations in different brain regions correlate with different task variables on a the Sternberg task. Theta power increases in left parietal scalp locations correlated with memory: theta power was greater for recognized than correctly rejected words. Theta power increases in central scalp locations correlated with decision-making: theta power was greater for slower reaction times than faster reaction times. And theta power at widespread scalp locations correlated with memory load: theta power was greater for short than long study lists. Although these results are promising in showing that theta oscillations, possibly originating from different cortical regions, play a distinct role in contributing to working memory, further investigation is required to gain a clearer understanding of the relationship between neural oscillations in different frequency bands across different brain regions and the cognitive components of episodic memory. It is also important to specify how gamma and theta oscillations contribute to the interaction of these different processes. Further research is also needed to clarify how synchronization between brain regions leads to the complex network dynamics underlying episodic memory.

4.4. Predictions

The model proposed here not only helps guide understanding of gamma and theta oscillations in studies of episodic memory, but can direct future research. The model proposed here suggests that cortical gamma oscillations represent perceptual features that provide coherent input to the hippocampus for LTP during encoding. The gamma/theta patterns at encoding are reinstated at retrieval. These ideas could be tested with experiments requiring the encoding and retrieval of specific information such as the judgment of modality specific sources (e.g. visual, auditory). It would be expected that different modality specific sources would elicit different gamma oscillation patterns. In addition, the model proposed here suggests that gamma oscillations represent individual memory representations and theta oscillations act to temporally order memory representations. It would be expected that tasks requiring the encoding and retrieval of the temporal order of items would elicit greater phase locking of gamma and theta oscillations. Finally, it has been suggested that theta oscillations arising from frontal–hippocampal interactions provide top-down control for encoding and retrieval of episodic memories. It would be expected that unconstrained memory tasks requiring the use of strategic encoding and retrieval would elicit theta power increases in frontal cortex and theta phase synchronization between frontal and hippocampal areas.

5. Conclusions

Many current models of brain function involve the interaction of different brain systems, but little research has addressed how the functionally specialized areas of the brain interact to perform cognitive tasks. The brain is made up of neural assemblies with reciprocal connections that connect local populations to combine multiple processes that are important for higher-level cognitive tasks. Since cognitive demands change over time there must be transient interactions between neurons to perform immediate cognitive tasks. Neural oscillations could allow for transient network interactions in the brain responsible for complex cognitive tasks.

It was proposed here that gamma and theta oscillations allow for the interaction between cortical structures and the hippocampus for the encoding and retrieval of episodic memories. The animal literature and the human literature provided evidence for general principles of gamma and theta oscillations in episodic memory. These principles were integrated into a model of the cortical–hippocampal network leading to the encoding and retrieval of episodic memories. According to this model, cortical gamma oscillations bind relevant stimulus features for perceptual representations and provide a coherent pattern of activity as input to the hippocampus. Gamma phase synchronization between cortical and hippocampal neurons and between hippocampal neurons provide the mechanism by which individual episodic memory representations from diverse cortical regions get encoded into hippocampal representations. Therefore, gamma oscillations can act in the cortex to bind modality specific perceptual representations and in the hippocampus to bind the rich perceptual and contextual information from diverse brain regions into episodic representations. Theta oscillations act to temporally order these individual episodic memory representations. Through feedback projections from the hippocampus to the cortex, these gamma and theta patterns could cause the reinstatement of the entire memory representation in the cortex. In addition, theta oscillations could provide top-down control from frontal cortex to the hippocampus for selective encoding and retrieval of episodic memories. Therefore, this unified model demonstrates how neural oscillations allow for transient interactions between brain regions to perform complex cognitive tasks. Understanding the role of oscillations in the network dynamics involved in the encoding and retrieval of information is not only important for understanding episodic memory, but can also serve as a model for understanding large-scale brain network dynamics and their relation to other cognitive phenomena.

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