

Direct brain recordings fuel advances in cognitive electrophysiology

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Electrocorticographic brain recordings in patients with surgically implanted electrodes have recently emerged as a powerful tool for examining the neural basis of human cognition. These recordings measure the electrical activity of the brain directly, and thus provide data with higher temporal and spatial resolution than other human neuroimaging techniques. Here we review recent research in this area and in particular we explain how electrocorticographic recordings have provided insight into the neural basis of human working memory, episodic memory, language, and spatial cognition. In some cases this research has identified patterns of human brain activity that were unexpected on the basis of studies in animals.

Brain oscillations and cognition

Neuronal oscillations are a fundamental component of normal brain function. In both humans and animals, neuronal oscillations exhibit specific spatiotemporal patterns that show active brain regions, indicate the types of neuronal computations that occur, and reveal how information flows through the brain. For ethical reasons, researchers typically examine these phenomena only in animals. However, in the past decade researchers have increasingly examined electrocorticographic (ECoG) recordings of brain oscillations in patients with surgically implanted electrodes. These recordings measure human brain activity with higher spatial and temporal resolution than other recording techniques. During ECoG monitoring, patients are typically conscious and capable of performing complex cognitive tasks in free time between clinical procedures. Thus, researchers can use these recordings to study electrophysiological correlates of a wide range of cognitive processes [1,2].

Here we review recent research using ECoG recordings of brain oscillations to analyze the neural basis of cognition. First, we outline the patterns of oscillations that appear in human ECoG recordings and describe how these signals relate to neuronal spiking. Then we explain how this research expands our understanding of the neural basis of four complex cognitive domains: working memory, episodic memory, language, and spatial cognition.

Human electrocorticographic recordings

Because they measure brain activity with high spatial and temporal resolution, surgically implanted electrodes help physicians to diagnose and treat neurological conditions such as epilepsy, Parkinson's disease, and tumors. Here

our focus is on ECoG recordings in patients undergoing invasive monitoring for drug-resistant epilepsy. In this procedure, surgeons implant ~40–120 electrodes in widespread brain regions (Figure 1a) to identify epileptic foci for potential surgical resection. Electrodes remain implanted throughout each patient's ~1–3-week hospitalization. These electrodes include grid and strip electrodes (Figure 1b,c), which record ECoG signals from the cortical surface, and depth electrodes (Figure 1d), which penetrate the cortex to record field potentials from deep brain structures. In this review we use the term ECoG to refer to both surface and depth recordings. On occasion, surgeons implant microelectrodes, which record individual action potentials (Figure 1e). Here we discuss microelectrode recordings only briefly because this procedure is rare and has been reviewed recently [3].

ECoG recordings measure brain activity directly with a resolution of ~4 mm² [4]. This high spatial resolution is a unique feature of ECoG compared to noninvasive methods such as scalp electroencephalography (EEG) and magnetoencephalography (MEG). Noninvasive recordings, even with advanced localization algorithms, sometimes miss signals that are clearly visible with ECoG [5]. Furthermore, with noninvasive techniques it is difficult to isolate activity from deep brain structures and they are relatively susceptible to muscle artifacts [6]. Thus, ECoG is considered the clinical 'gold standard' for accurate identification of seizure foci [1,7]. For the same reasons that ECoG recordings are useful to doctors, these data are beneficial for researchers.

Each ECoG electrode measures the combined synaptic activity across the local population of neurons, rather than recording individual action potentials [1,8]. Owing to this

Glossary

Broadband power: the overall energy, or variance, of a time series. Whereas changes in broadband power appear at many or all frequencies, changes in narrowband power are often specific to a given frequency band.

Gamma oscillation: rhythmic neural activity in the ~30–200-Hz frequency range. Gamma oscillations have been implicated in a wide range of cognitive processes including perception, attention, and memory [11,23].

Phase synchrony: two or more neural assemblies oscillating together with a consistent phase relationship.

Phase reset: an oscillation exhibiting an altered phase as the result of an external event.

Phase–amplitude coupling: a pattern whereby the amplitude of one oscillation varies with the phase of a slower oscillation. Phase–amplitude coupling is prevalent in human neocortex, where gamma oscillations have greater amplitude at the trough of theta oscillations [31].

Theta oscillation: rhythmic neural activity at ~3–10 Hz. Theta oscillations have been implicated in memory, both at the behavioral [19,49] and cellular level [50,51].

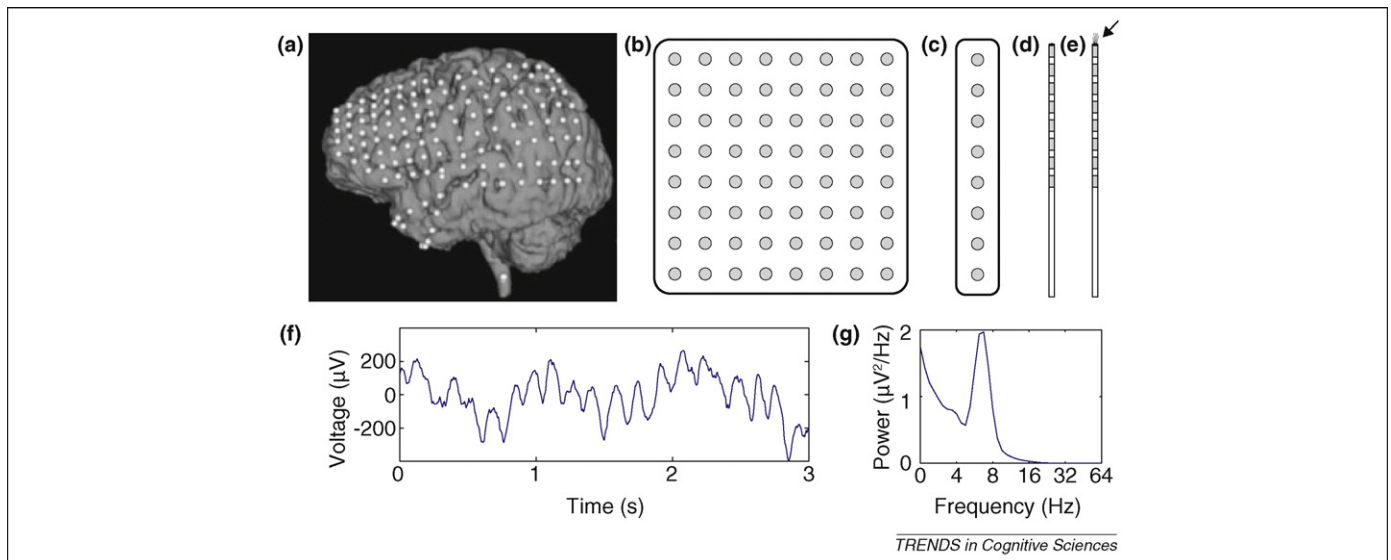


Figure 1. Performing electrocorticographic recordings in humans. (a) MRI image of one patient's brain with the locations of implanted ECoG electrodes indicated by white dots. Modified, with permission, from Ref. [56]. (b) Illustration of an 8×8 electrode grid; gray shading indicates the conductive surfaces of the electrodes (illustrations not to scale). (c) Illustration of an 8-electrode strip. (d) Depth electrode with eight contacts. (e) Depth electrode with microwires extending from the tip to record action potentials (marked by the arrow). (f) Recording of ECoG activity from the right temporal gyrus and (g) corresponding power spectrum, which shows that this trace exhibits a robust theta oscillation.

aggregation, ECoG recordings measure the electrical activity synchronized across these neurons, which often includes oscillations. Neuronal oscillations appear as sinusoidal changes over time in the voltage observed from an electrode (Figure 1f,g). They appear at frequencies from <0.1 to 500 Hz and are visible at multiple spatial scales, from scalp EEG to intracellular recordings. Researchers believe that oscillations play a critical role in large-scale neuronal computations. When an individual neuron oscillates, it undergoes rhythmic variations in its level of excitability [9]. Animal recordings and computational models indicate that oscillations facilitate communication in large neuronal networks because they cause groups of neurons to become excited synchronously to form new functional networks [10,11]. In general, slower oscillations synchronize large neuron groups across broad brain regions and faster oscillations coordinate smaller, localized neuronal assemblies [12]. However, sometimes relatively fast oscillations synchronize widely separated brain regions [13,14]. Although oscillations at different frequencies and regions are often caused by distinct physiological mechanisms [12], interneurons typically play a critical role [15,16]. Thus, the appearance of an oscillation in an ECoG recording generally indicates that nearby interneurons are especially active [8] and firing synchronously [17].

Studies in animals have shown that neuronal oscillations have a number of interesting functional properties. In general, the presence of an oscillation indicates that neurons in a region have an increased level of spiking relative to the baseline [9]. When groups of neurons oscillate together synchronously, they are more effectively able to communicate with each other [10,11]. Furthermore, oscillations underlie phase coding, a phenomenon in which neurons encode information, such as spatial location [18], by varying the phase of an oscillation when they spike [9].

To characterize the oscillatory brain patterns that support human cognitive processes, researchers measured the

amplitude of oscillations in ECoG recordings throughout cognitive tasks. This research revealed that oscillations at various frequencies change in amplitude according to task demands. For example, during memory tasks the amplitude of theta oscillations increases in widespread cortical regions [19,20]. This is consistent with research in animals that implicates theta in synaptic plasticity [21]. Behavior-related amplitude changes are also common in the gamma band. During motor and sensory processing, there is a focal increase in the amplitude of gamma activity in the neocortical region that corresponds to the body part that performs a movement or feels a percept [1]. Attention also plays a critical role in modulating the amplitude of brain oscillations. ECoG recordings from non-human primates and subsequent work in humans revealed that if a presented stimulus is attended, the resulting gamma oscillations have different properties – most notably, a larger amplitude – compared with the oscillations that appear after presentation of stimuli that are ignored [9,11,22–26]. As described below, attention also modulates the amplitude of oscillations related to other cognitive processes beyond perception.

In addition to amplitude, researchers also examined the relation between the phase of ECoG oscillations and the timing of behavioral events. A common oscillatory phenomenon is a phase reset, in which an oscillation changes its timing to exhibit a particular phase (e.g., a peak) after an external event [27]. Besides direct measurement of phase, a different technique for analyzing the temporal relation between ECoG activity and behavior is to compute an event-related potential (ERP). This involves computing the mean ECoG voltage at each time point after a stimulus. Although the ERP technique is designed to measure evoked ECoG waveforms rather than true oscillations, ERPs also measure oscillatory phase resets and thus sometimes it is difficult to distinguish between these phenomena [28,29]. In this review we emphasize research findings

Box 1. Oscillatory activity and neuronal spiking

Some epilepsy patients undergoing intracranial monitoring are implanted with special depth electrodes that have microwires extending from their tips (Figure 1e). These microwires record single-neuron action potentials, which allows researchers to examine the relation between neuronal spiking and simultaneous brain oscillations.

Research in animals has shown that brain oscillations provide a neuronal timing signal that allows neurons to encode information by spiking at a particular phase of an oscillation – a phenomenon called phase coding [9,18]. To examine the prevalence and properties of phase coding in humans, one recent study examined how neurons in widespread regions varied their instantaneous firing rate according to the phase of ongoing oscillations [30]. This work revealed that many neurons were *phase locked* to oscillations, a phenomenon in which they increased their firing rate at a particular phase of these oscillations. Figure 1a shows the activity of a neuron that exhibits this phenomenon by spiking just before the peak of the theta oscillation. The properties of neuronal phase locking varied between high- and low-frequency oscillations. Neurons phase locked to oscillations at frequencies slower than 10 Hz had various preferred phases, whereas neurons phase locked to oscillations faster than

10 Hz had preferred phases near the oscillation trough. This indicates that oscillations faster than ~ 10 Hz reveal specific times (the trough of the oscillation) when many neurons are active, whereas slower oscillations cannot predict population spike times with this level of precision.

A different set of studies examined the relation between the rate of neuronal spiking and the amplitude of oscillatory activity. In some cases, the neuronal firing rate is well predicted by the amplitude of simultaneous oscillations (Figure 1b). However, the details of this relation vary dramatically according to the oscillation and brain region being examined. Oscillations at high frequencies (>10 Hz) in sensory cortex correlate positively with neuronal spiking [17] and a similar, but weaker, pattern appears in hippocampus [45]. By contrast, low-frequency oscillations exhibit varied correlations with single-neuron spiking. In neocortex, theta- and alpha-band oscillatory power is negatively correlated with neuronal spiking [17], but in hippocampus these oscillations do not correlate with spiking rate [45]. Overall, this work shows that ECoG recordings provide a temporally precise indication of neuronal spiking, which may complement techniques such as fMRI that measure neuronal activity with less precision [8,17,47].

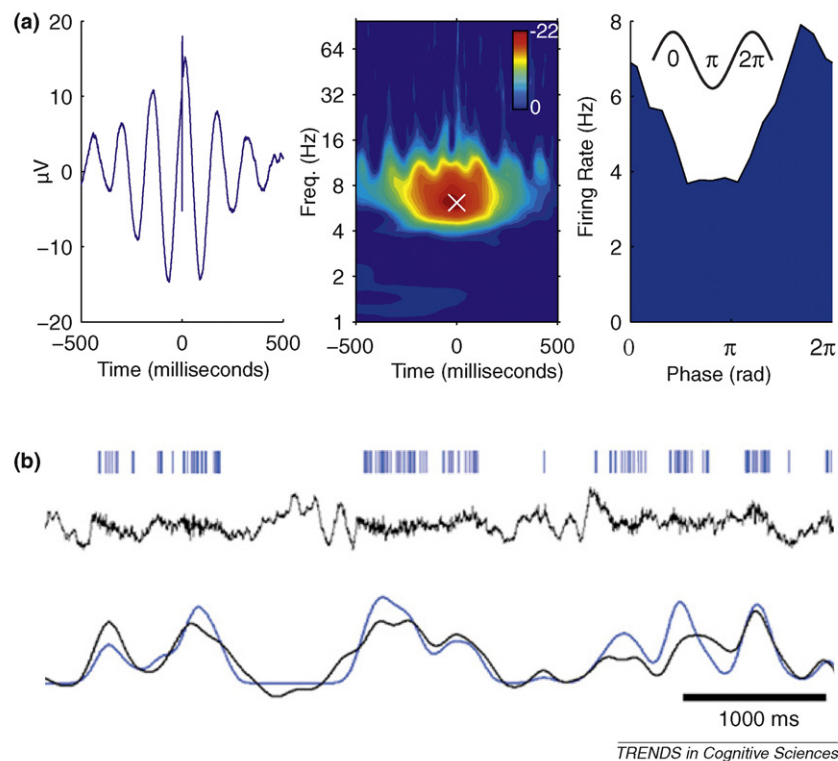


Figure 1. Relation between oscillatory brain activity and neuronal spiking. (a) Activity of a neuron from the right superior temporal gyrus that spiked just before the peak of the oscillation. Left panel, average local-field potential (LFP) computed relative to each spike. Middle panel, z score from a Rayleigh test, which measured LFP phase uniformity at the time of each spike, as a function of frequency and time offset. White \times indicates the frequency of peak phase locking. Right panel, firing rate of this cell as a function of instantaneous theta phase at the frequency of peak phase locking. Adapted, with permission, from Ref. [30]. (b) Activity of a neuron from one patient's auditory cortex for which spiking was tightly coupled to the amplitude of simultaneous gamma oscillations ($r=0.84$). Ticks in the top row indicate individual action potentials. The middle row depicts the LFP signal filtered to include only frequencies below 130 Hz. The bottom row indicates LFP gamma power (black) and the neuronal firing rate (blue), showing that these two measures are closely related. Adapted, with permission, from Ref. [17].

concerning oscillations rather than ERPs because more is known about how oscillations relate to the activities of individual neurons [8,17,30].

Early ECoG work focused on measures of amplitude and phase that were separately computed at each frequency and electrode. However, it soon became evident that the neural patterns that support cognition also involve complex interactions between oscillations at

different frequencies and brain regions. One of these phenomena is phase–amplitude coupling [31–33], in which the amplitude of a fast oscillation varies with the phase of a slower oscillation. In addition, human ECoG data, like animal recordings, exhibit phase synchrony between oscillations at different sites [34–36]. Phase–amplitude coupling and phase synchrony have important roles in various cognitive processes, including

Box 2. Brain oscillations reveal neuronal correlates of specific cognitive representations

Research into human brain oscillations has generally sought to identify broad cognitive processes that are correlated with the properties of different neural signals. For example, research into hippocampal theta oscillation has characterized oscillatory activity that increases in amplitude during memory and navigation [49,88]. However, gamma oscillations can be used to reveal specific cortical network states and an examination of oscillatory activity in sensory cortices revealed that the identity of a percept was encoded in the landscape of gamma-band activity [59]. This indicates that cortical recordings of brain oscillations can predict sensory inputs, because individual stimuli were associated with distributed patterns of gamma activity that had different spatial topographies. These stimulus-specific patterns are important theoretically because they suggest that gamma oscillations can identify neuronal patterns that underlie specific cortical network states.

Following this line of work, a recent study examined stimulus-specific activity in human ECoG recordings [53]. This study measured gamma-band oscillatory brain activity in 37 patients

memorizing lists of letters. After each letter was presented, the amplitude of oscillatory activity at many sites varied according to the identity of the viewed letter. As an example of this phenomenon, Figure 1 depicts the amplitude of high-gamma activity observed at a site in left temporal cortex. At this site, an overall increase in gamma activity occurred ~ 100 ms after the letter appeared and the amplitude of this signal subsequently varied with the identity of the viewed letter. Significant numbers of electrodes exhibiting stimulus-specific activity were located in occipital and temporal regions. Furthermore, at some sites in occipital cortex these patterns encoded visual features of the shape of the viewed letter, which is consistent with previous observations that activity in sensory regions encodes perceptual features of stimuli [17,22,48]. This work shows that human ECoG recordings can reveal detailed information about the state of a cortical network. Because gamma-band activity appears in widespread brain regions [9,54], stimulus-specific gamma patterns may be used to map the neural basis of various specific cognitive states in the future.

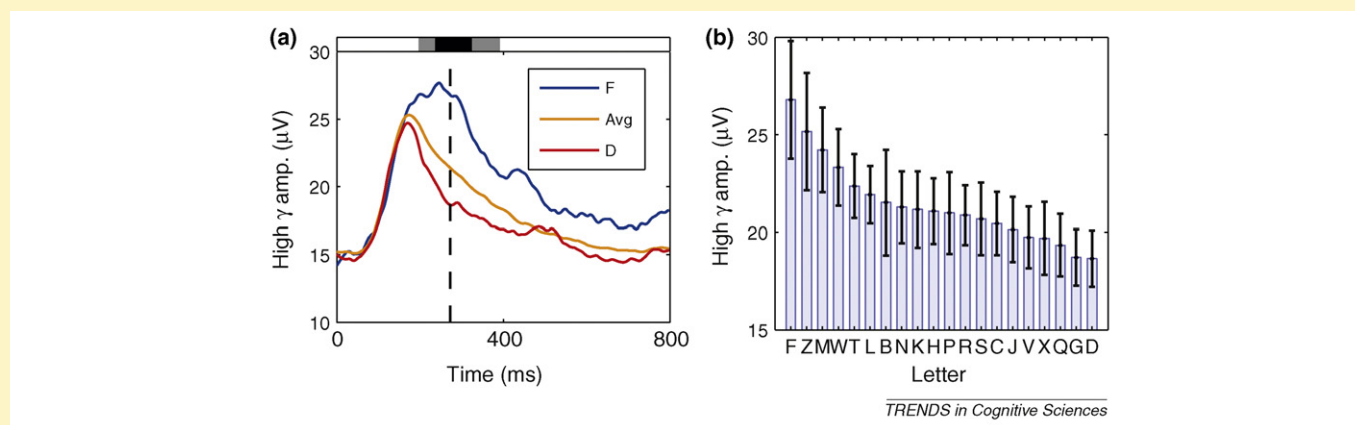


Figure 1. Gamma-band correlates of specific cognitive representations. (a) Activity of an electrode in left temporal cortex that exhibited significant variations in high-gamma (65–128 Hz) amplitude according to the identity of the stimulus that was viewed. The blue line indicates the gamma amplitude after viewing ‘F’, red indicates the gamma amplitude after viewing ‘D’, and orange indicates the mean gamma power across all letters. Shaded rectangles indicate time points at which this effect is significant (gray indicates $p < 0.05$, black indicates $p < 10^{-5}$). (b) The mean high-gamma power for each letter at the time point corresponding to peak letter-related differences (indicated by the black dashed line in (a)). Modified, with permission, from Ref. [53].

working and episodic memory [31,37,38], as reviewed below.

In addition to oscillations that appear only at specific frequencies, researchers recently observed that ECoG recordings contain broadband signals that exhibit power changes at many frequencies simultaneously [1,39,40]. It has been suggested that these broadband power changes are caused by an increase in the spiking rate of nearby neurons [41]. Consistent with this is the observation that neuronal spiking positively correlates with broadband power [42] and the prediction from computational models that spiking appears at various frequencies in ECoG recordings [4,43]. Together, these findings raise the intriguing possibility that standard ECoG electrodes can measure the rate of neuronal spiking that is nonoscillatory, even though these electrodes are much larger than those typically used to record action potentials. To this end, an important area of future research is the development of improved methods to distinguish broadband signals from narrowband oscillations.

Finally, a different set of studies examined the relation between ECoG data and other types of neural recordings. Examination of simultaneous recordings of ECoG oscillations and neuronal spiking revealed that neuronal spik-

ing is correlated with the phase and amplitude of ECoG oscillations [17,30,44,42] (Box 1). Furthermore, research in humans and animals has shown that ECoG gamma oscillations correlate with the blood-oxygenation signal observed with functional magnetic resonance imaging (fMRI) [8,17,45–47]. Scientists have shown that fMRI reveals how the brain encodes diverse types of perceptual and conceptual information [48]. The correlation between fMRI data and ECoG gamma oscillations suggests that ECoG recordings can elucidate neural oscillations that underlie various cognitive representations (Box 2). Together, these findings indicate that ECoG is an important link between noninvasive human brain recordings (scalp EEG, MEG, and fMRI) and the direct brain recordings commonly made in animals.

Oscillations and cognition

Over the past decade, researchers examining ECoG recordings of human brain oscillations identified neural correlates of various perceptual, motor and cognitive processes [1,2]. Below, we review how ECoG data have informed our understanding of the neural basis of four cognitive domains: working memory, episodic memory, language, and spatial cognition.

Review

Working memory

Working memory – the process of remembering a stimulus temporarily for immediate processing – is critical for many common tasks. Experimentally, researchers often examine working memory using a task in which a participant views a short list of items and, after a short delay, is asked to indicate whether a probe item appeared in the list (Figure 2a). Thus, a trial in this task has three phases: stimulus encoding, memory retention and memory retrieval.

Examining ECoG activity during stimulus encoding, researchers observed patterns of theta and gamma oscillations that help to illustrate how the brain encodes memories. After each stimulus presentation, theta oscillations at widespread regions undergo a phase reset (Figure 2b) [27]. Because individual neurons spike at different theta phases (Box 1) [30], these phase resets cause the spiking of widespread neurons in precise temporal patterns. In addition to theta, after stimulus presentation there is an increase in the amplitude of gamma activity at many electrodes in temporal and occipital cortices [40,52]. This indicates that temporal and occipital cortices are involved in stimulus encoding, because elevated gamma activity indicates that nearby neurons are especially active [9,17]. Furthermore, this gamma activity has greater amplitude at the trough of simultaneous theta oscillations [37,53], which supports the view that theta-gamma phase-amplitude coupling is important for memory encoding [31,50]. One study described a site in ventral temporal cortex that exhibited elevated gamma activity after viewing images of animals compared to images of tools [40]. Other ECoG studies also reported analogous patterns in which gamma activations were specific to certain stimulus classes [52,54–58]. These selective activations indicate that specific regions, especially in the ventral temporal lobe, encode different categories of cognitive representations [48]. Furthermore, recent work showed that gamma activity encodes the identities of specific stimuli (Box 2) [53]. Thus, ECoG gamma oscillations are a rich information source, revealing specific cortical network states [59,60].

ECoG recordings of gamma activity can distinguish brain regions that process low-level visual percepts from areas that encode richer representations of consciously attended stimuli. One study examined recordings while patients were shown stimuli for different durations [61]. When a stimulus was presented rapidly and could not be recognized or attended, gamma activity appeared only in primary sensory regions. By contrast, when stimuli were presented for longer durations, high-amplitude gamma activity appeared for a long duration throughout ventral temporal cortex. Thus, when a stimulus is recognized and consciously attended, it ‘ignites’ neural assemblies in high-level regions. A different study provided complementary evidence of the effect of attention on human brain oscillations by showing that gamma activity appears at many sites only when a patient actively attends to a stimulus (Figure 2c) [62]. Together, these findings indicate that much of the gamma activity of the brain is a correlate of conscious recognition of and attention to stimuli, rather than low-level perception.

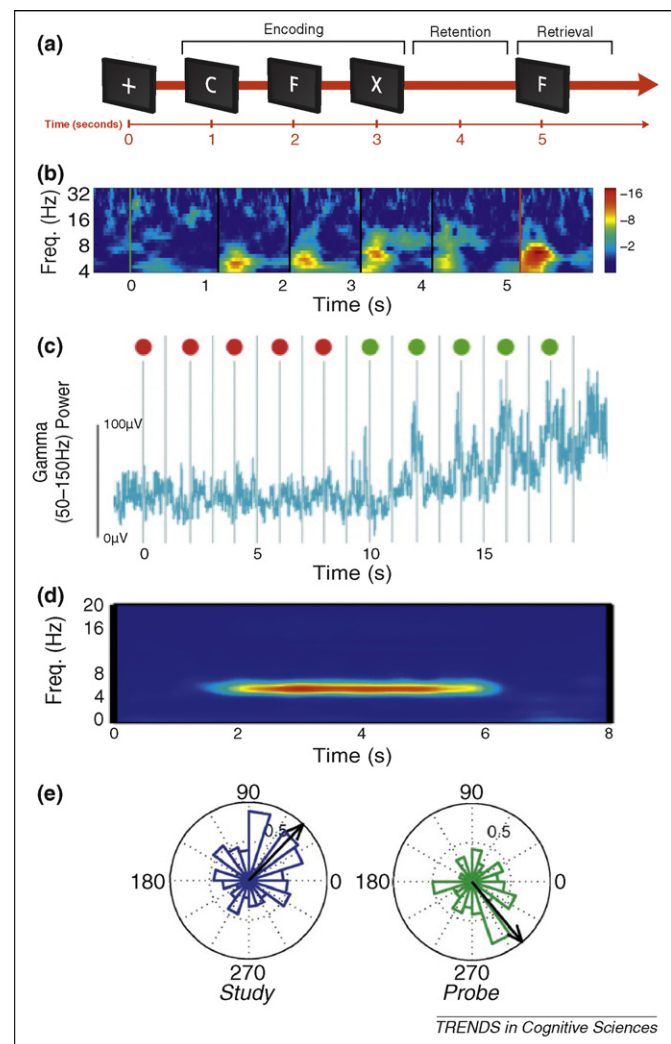


Figure 2. Oscillatory brain activity in human working memory. (a) Schematic of a working memory task. (b) Phase-reset analysis of ECoG activity from an electrode in one patient’s right subcallosal gyrus during this task. The color at each frequency and time point indicates the z score from a Raleigh test to evaluate the uniformity of the ECoG phase distribution (computed across trials). Warm colors indicate significant phase resetting. Modified, with permission, from Ref. [27]. (c) Gamma power from an electrode in Broca’s area in a different patient performing a variant of this task in which each stimulus is preceded by an indication of whether the item should be attended (green dot) or ignored (red dot). The gamma power of this electrode is correlated with memory load, as this activity increases following stimuli that are remembered. Modified, with permission, from Ref. [62]. (d) Normalized oscillatory power at a site in one patient’s parahippocampal gyrus that exhibited elevated theta activity during memory retention. Red coloring indicates elevated oscillatory power relative to the baseline. Modified, with permission, from Ref. [97]. (e) Electrode in a patient’s right frontal cortex that resets to different phases between viewing study items (left) and viewing cues (right). Each plot is a circular histogram that indicates the number of trials in which different theta phases were observed 100 ms after stimulus onset (0 indicates the peak phase of theta, and 180 is the trough). The black arrow indicates the mean theta phase. Modified, with permission, from Ref. [66].

After a person encodes a stimulus, their next task is to retain it in memory. ECoG recordings indicate that the set of brain regions that support working-memory maintenance is different from the areas involved in perception and involves some areas that were traditionally thought to support language [62]. One study observed that during memory retention oscillatory phase synchrony in the beta band (~16–30 Hz) occurs between sites in extrastriate cortex [34]. Notably, other human studies also reported phase synchrony in the beta range [35,36] rather than in

the gamma band, where cortical phase synchrony typically appears in animals [11,22]. The different frequencies of cortical phase synchrony represent an important difference between the brains of humans and animals. Researchers have also examined the neural basis of memory retention by identifying electrophysiological patterns that correlate with memory load (the number of simultaneously remembered stimuli; Figure 2c). In particular, the amplitude of gamma activity correlates with memory load in both neocortex [62–64] and hippocampus [65]. This widespread phenomenon indicates that various brain regions support memory maintenance and that gamma oscillations help to maintain persistent neural activations [9,11,23]. In addition to gamma, theta oscillations are also linked to memory maintenance. During memory maintenance, widespread neocortical sites exhibit increased theta power (Figure 2d) [19] and the hippocampus exhibits phase-amplitude coupling between theta and gamma oscillations [38].

The final phase of each trial is the retrieval interval, in which the participant determines whether a probe stimulus matches one of the remembered list items. ECoG recordings during this interval are informative about the types of neural computations that support memory retrieval. After a probe is viewed, theta oscillations at many sites again exhibit phase resets (Figure 2b,e). However, between the probe and the list items, some sites reset to different phases [66], with varying levels of precision [27]. These phase resets occur in an arrangement [66] that is consistent with the peak and trough phases of theta supporting memory encoding and retrieval, respectively [51]. ECoG recordings also reveal the nature of the neural computations involved in comparing a stimulus to the contents of memory. For example, in one study the amplitude of frontal activity in the delta band (1–4 Hz) correlated with the similarity between the probe and the items held in memory [67]. This establishes electrophysiological support for psychological theories that humans recognize stimuli by computing a graded measure of the similarity between a percept and the contents of memory [68,69].

Episodic memory

An issue of significant practical and theoretical interest is why people remember some events easily whereas they are unable to remember others despite much effort [70]. This issue is a core topic in the study of episodic memory (i.e., memory for autobiographical events). One technique for probing the neural basis of episodic memory is the free-recall task. In this task, a person is presented with a list of items and is later asked to recall the items in any order.

Analysis of ECoG recordings while patients performed the free-recall task revealed theta and gamma oscillations in widespread brain regions that varied in amplitude according to whether a viewed stimulus was recalled successfully [20]. Later studies showed that these oscillations were especially prominent at gamma frequencies in the left inferior frontal gyrus [71], which is consistent with neuroimaging studies implicating this region in memory formation [72]. The high spatial resolution of ECoG was critical for identification of this phenomenon, which had not been observed previously with noninvasive recordings.

Furthermore, during memory retrieval, theta and gamma activity appeared in the same set of brain regions as during encoding [73]. This supports the view that memory retrieval involves reinstatement of the pattern of brain activity that appeared during learning [70].

A broad body of literature shows that the hippocampus underlies long-term memory [49,74], so it is important to characterize the electrophysiological activity in this region during memory formation. This research revealed that humans and animals exhibit different patterns of memory-related hippocampal activity. In animals, hippocampal theta oscillations increase in amplitude during memory encoding [49,75]. By contrast, human memory formation is associated with decreased hippocampal activity at many frequencies [71]. A subsequent study further illustrated the complex role of the hippocampus in human memory, showing that hippocampal activity (measured via slow ECoG voltage shifts) is positively correlated with successfully remembering stimuli that are retained for long durations and negatively correlated with remembering stimuli that are retained for short durations [76]. These differing patterns suggest that humans use different physiological processes to remember items that must be retained for different lengths of time [77].

ECoG data indicate that distinct patterns of cortical activity support memory formation during periods of high and low attention. Remembering the viewing of a common word requires more attention than memorizing a novel stimulus. Accordingly, memorizing common words elicited a larger N400 ERP response compared with memorizing rare words. This pattern appeared in rhinal cortex but not hippocampus [78]. Scalp EEG also showed that successful memory formation when attention is high is associated with greater gamma activity in posterior cortices compared with memory formation during low attention [77]. Importantly, this research indicates that attention-related differences in the neural correlates of memory formation are limited to neocortex rather than hippocampus [78].

A body of research indicates that episodic memories are initially encoded in hippocampus and later consolidated into neocortex [74]. This theory predicts that there is communication between hippocampus and neocortex during memory encoding [79]. Supporting this prediction, several ECoG studies report synchronous oscillations between hippocampus and neocortex. When a stimulus is successfully memorized, there is increased gamma-band coherence (a similar phenomenon to phase synchrony) between rhinal cortex and hippocampus [13]. Furthermore, during memory retrieval there is increased gamma activity in the layers of entorhinal cortex that project to hippocampus [80]. Cortico-hippocampal communication also appears outside of controlled experiments, as demonstrated by the finding that increased rhinal-hippocampal coherence during sleep predicts that dreams would be remembered [81]. These findings show that cortico-hippocampal interactions play an important role in human memory and, more broadly, demonstrate that neuronal oscillations are not only informative about the activity within individual brain areas, but also show how information is transferred between regions.

Review

Language

ECoG recordings are especially useful for studying the neural basis of auditory linguistic processes because electrodes are frequently implanted in regions that are critical for listening and speaking. ECoG recordings during listening and speaking support the traditional view that language comprehension is supported by Wernicke's area and that language production involves Broca's area [1,56,82]. However, these studies also implicate more widespread cortical networks in language.

After hearing a word, there is a dramatic increase in the amplitude of gamma activity in regions near Wernicke's area, including the superior temporal gyrus (STG) and the superior temporal sulcus (STS) [1,82]. ECoG recordings revealed that language-related gamma oscillations flow from the posterior STG to the middle STG and then to the STS. In the STG, gamma activity generally encodes low-level acoustic properties of a sound [82]. However, when this activity reaches the STS, its amplitude and duration encode lexical information [56,82]. This progression of gamma activity is consistent with a model proposing the sequential processing of linguistic information along the STG–STS pathway [83]. Language-related activity also appears outside the temporal lobe, as demonstrated by the finding that there is increased gamma activity in parietal and frontal cortices when a perceived syllable is consciously recognized [84]. The amplitude of gamma oscillations is greater when a person listens to external speech compared to hearing their own words [56]. This indicates that speech-related neuronal activity correlates with attentional demands, because greater attention is required to comprehend a different person's speech than one's own words.

ECoG studies provided data supporting theories that semantic information is represented throughout bilateral temporal regions [48], but that low-level linguistic information is represented only in the language-dominant hemisphere [83]. One study found that when a patient performed a lexical decision task, gamma activity appeared only in the temporal cortex of the language-dominant hemisphere. By contrast, a picture-naming task, which required access to deeper semantic information, elicited gamma activity in bilateral temporal regions [40]. Semantic information is also represented in frontal regions, as demonstrated by a study that examined ECoG recordings from patients who had to judge whether two words were semantically related. This study reported that some frontal sites exhibited gamma activity in a dynamic pattern that varied with the semantic properties of a word pair. Here, processing of two unrelated words immediately elicited brief high-amplitude gamma activity, whereas viewing of two related words induced lower-amplitude gamma activity that appeared only after a delay [1]. The detailed structure of these patterns indicates that neural activity in human frontal cortex exhibits important temporal variations.

A recent study investigated ECoG recordings in Broca's area to examine the role of this region in language comprehension and production [85]. Examining recordings while participants viewed words that they were asked to inflect and imagine speaking, the authors identified three

ERP components whose amplitudes correlated with different linguistic processes: The ERP component at ~200 ms encoded the lexical properties of the word (whether it was rare or common), the ~320-ms component reflected processes related to word inflection, and the ~450-ms component correlated with the phonological properties (number of syllables). These ERP components appeared at different recording sites, indicating that Broca's area contains a series of spatially distinct neuronal networks that sequentially perform different linguistic computations.

ECoG recordings revealed that speech production is associated with gamma activity in various brain regions, including not only Broca's area, but also other prefrontal and temporal cortices [1,56]. This extends the traditional view that Broca's area is the focus of speech production. Furthermore, analysis of the temporal dynamics of ECoG activity during speech has led to additional insights. Frontal gamma activity is elevated ~800 ms before speaking, which suggests that this area supports speech–motor planning in addition to direct motor output [56]. During speaking, gamma activity is synchronized between several cortical regions, including the mouth region of motor cortex, various frontal regions and Wernicke's area [86].

Spatial cognition

Spatial navigation is an essential behavior for nearly all humans and animals. Because navigation is such an innate function, understanding its neural basis can reveal important similarities and differences between human and animal neurophysiology. Although patients undergoing ECoG monitoring are confined to a hospital bed, researchers can examine neural correlates of spatial processing using computer-based virtual navigation tasks [87–89].

During navigation, the human brain exhibits several patterns of theta and gamma oscillations related to spatial processing. When a human moves through an environment, there is a widespread increase in the amplitude of theta activity [87,88]. This is similar to the movement-related theta oscillations observed in animals [49]. Furthermore, the amplitude of human theta oscillations positively correlates with navigation performance [90], adding to evidence that theta critically supports spatial processing [49].

The ability of human intracranial recordings to record from deep brain structures allowed researchers to compare the properties of hippocampal theta between humans and animals. As a result, researchers identified two important interspecies differences. In rodents, hippocampal theta oscillations reliably appear at 4–8 Hz [49]. However, in humans, hippocampal oscillations usually appear instead at 1–4 Hz [30,88,90–94]. Furthermore, whereas rodent theta oscillations are routinely sustained for over 10 s [18,49], human hippocampal oscillations usually appear only transiently [87,88] and sometimes not at all [95]. Despite these differences, it seems that human 1–4-Hz hippocampal oscillations are functionally analogous to rodent 4–8-Hz theta. During navigation, both of these oscillations increase in amplitude during movement [49,88,89] and the phase of both oscillations modulates neuronal spiking [15,18,30]. Unlike the activity in hippocampus, human neocortical

theta oscillations usually appear at 4–8 Hz [31,30,87]. However, a recent study reported significant 1–4-Hz coherence between hippocampus and neocortex [93], suggesting that the human neocortex also exhibits 1–4-Hz activity in addition to theta [32].

Beyond theta, navigation-related brain oscillations also appear in the gamma band [87,88]. Neuroimaging and lesion studies have shown that the right hemisphere plays a unique role in spatial cognition [96]. In agreement with the literature on hemisphere lateralization, a recent ECoG study compared the prevalence of navigation-related oscillations throughout the brain and found that navigation-related gamma activity was especially prevalent in the right hemisphere [89]. This supports the view that the right hemisphere is important for spatial processing and supplements research indicating that gamma oscillations and fMRI activations identify similar neuronal patterns [8,17].

Conclusions and future directions

Human ECoG recordings have implicated brain oscillations in various types of brain functions, including both cognitive and sensorimotor processes [1,2]. Although oscillations at many frequencies correlate with different cognitive processes, the theta and gamma bands most frequently correlate with task demands. Theta and gamma oscillations each have distinct physiological and computational properties (Box 1). Thus, these oscillations provide insight into the neuronal processes that underlie different human cognitive processes. Theta oscillations are more closely associated with temporally precise neuronal spiking, rather than changes in firing rate [17,30,45]. This suggests that cognitive processes that correlate with theta activity, such as movement during navigation [87] and working memory retention [19,97], are supported neurally by temporally precise spiking, rather than by firing-rate changes. By contrast, gamma-band activity is correlated with both elevated neuronal firing rates [8,11,17,41] and precisely timed spiking [9,30]. Thus, cognitive variables that relate to gamma activity, such as memory load [63,64], are probably associated with neuronal computations that involve both rate and temporal coding. Beyond theta and gamma, an ECoG signal of emerging interest is broadband power. Broadband power changes are an indication of cognitive processes that involve firing-rate changes but not temporally precise oscillatory spiking [4]. More generally, these signals show that ECoG recordings can be used to elucidate the neuronal patterns that support different human cognitive processes. Because ECoG reveals this information with greater precision than noninvasive techniques, it allows researchers to probe human brain activity with a rare level of detail. Thus, ECoG data have revealed unique human electrophysiological phenomena that do not appear in animals [34,30,85,89,97], as well as similarities between human and animal brain activities [5,8,17,45,49,87,88].

There are several exciting developments underway in the study of cognitive electrophysiology using ECoG data. Perhaps the most important of these is the study of oscillatory communication across regions [10,14,35,44,97,98] and of interactions between oscillations at different

frequencies within the same region [31,33,37,38]. To the extent that oscillations at different frequencies correlate with different functional processes, cross-frequency interactions seem to play a critical role in linking physically disparate neuronal networks [32]. Thus, an important area of future research is to identify how oscillatory interactions across both regions and frequencies relate to cognitive processes. Another emerging research trend is the use of real-time ‘closed loop’ systems that vary the parameters of an experiment according to instantaneous brain activity [99,100]. This research seeks to determine whether brain recordings can be used to alter human behavioral performance, and thus this work has the potential to distinguish the neural signals that have a causal role in behavior.

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