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 mm^2 [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].

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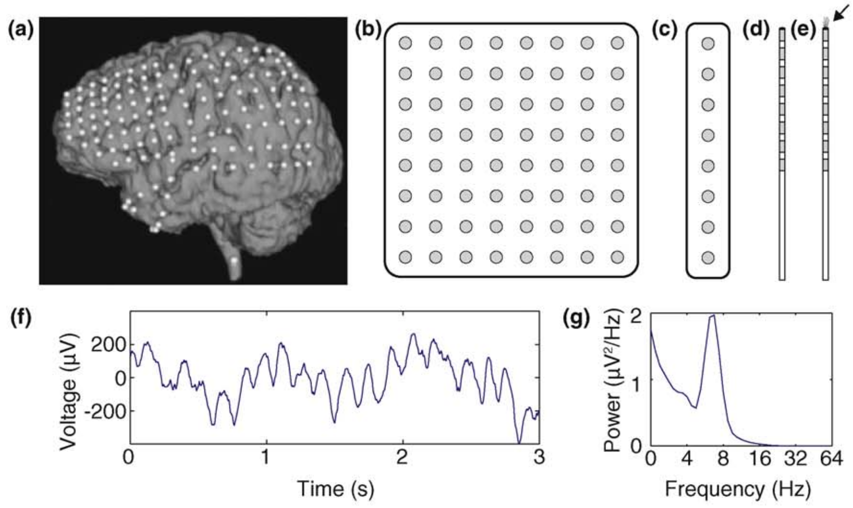

Figure 1. Performing electrocorticographic recordings in humans. **(a)** MRI image of one patient's brain with the locations of implanted ECoG electrodes indicated by white dots. Modified, with permission, from Ref. [56]. **(b)** Illustration of an 8 × 8 electrode grid; gray shading indicates the conductive 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