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Coupling of mesoscopic brain oscillations: Recent advances in analytical and theoretical perspectives

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ABSTRACT

Oscillatory brain activities have been traditionally studied in the context of how oscillations at a single frequency recorded from a single area could reveal functional insights. Recent advances in methodology used in signal analysis have revealed that cross-frequency coupling, within or between functional related areas, is more informative in determining the possible roles played by brain oscillations. In this review, we begin by describing the cellular basis of oscillatory field potentials and its theorized as well as demonstrated role in brain function. The recent development of mathematical tools that allow the investigation of cross-frequency and cross-area oscillation coupling will be presented and discussed in the context of recent advances in oscillation research based on animal data. Particularly, some pitfalls and caveats of methods currently available are discussed. Data generated from the application of examined techniques are integrated back into the theoretical framework regarding the functional role of brain oscillations. We suggest that the coupling of oscillatory activities at different frequencies between brain regions is crucial for understanding the brain from a functional ensemble perspective. Effort should be directed to elucidate how cross-frequency and area coupling are modulated and controlled. To achieve this, only the correct application of analytical tools may shed light on the intricacies of information representation, generation, binding, encoding, storage and retrieval in the brain.

Contents

Abbreviations: MPO, membrane potential oscillation; FPO, field potential oscillation; DFT, discrete Fourier transform; DCOH, directed coherence; PDC, partial directed coherence; DTF, directed transfer function; nDTF, normalized directed transfer function; ffDTF, full-frequency directed transfer function; dDTF, direct directed transfer function.

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1. Introduction

To understand the brain, one has to understand how hundreds of billions of neurons actually code and transmit information in an efficient manner. Brain oscillations appear to be prime candidates to facilitate information transmission through input filtering (Hutcheon and Yarom, 2000), spike-timing (Jacobs et al., 2007; Schaefer et al., 2006; Somogyi and Klausberger, 2005), phase coding (Mehta et al., 2002; O'Keefe and Recce, 1993; Varela et al., 2001) and information binding (Engel et al., 1992; Fries et al., 2007; Singer, 1999) to execute processes such as perception (Basar et al., 2000) and memory formation (Jensen and Lisman, 2005; Steriade, 2006). However, it is extremely difficult to demonstrate a causal relationship between oscillatory activities in the brain and overt behaviour output. Consequently, many believe that recordable brain oscillations are merely an epiphenomenon (Koch, 1993; Pareti and De Palma, 2004) and maybe a product of volume conduction from other distant areas (Bland and Whishaw, 1976; Sirota et al., 2008).

This review has two major goals: (1) to discuss convincing data supporting the idea that brain oscillations are indeed functional and (2) how linear (i.e. within a single frequency) and cross-frequency coupling of brain oscillations is central to their proposed functions with some suggestions of how they should be further explored. Additionally, the studies reviewed here will mainly focus on recent advancements in animal research in the study of brain oscillations. Similar reviews in the human literature have recently been published elsewhere (Sauseng and Klimesch, 2008; Sauseng et al., 2008).

1.1. Neural oscillations

Since the word "oscillation" merely describes the periodic upward and downward deflections of a time series, the premise and terminology used in this review should be discussed. Brain oscillations can roughly be divided into two classes: (1) single neuron oscillations such as membrane potential oscillations (MPOs) and oscillatory spike trains (Llinas, 1988); (2) field potential oscillations (FPOs) that are recorded as the sum of inhibitory and excitatory currents in brain space, and depend on the dynamic interactions between many neurons and their electrophysiological constituents (Freeman, 1992). We consider MPOs as microscopic oscillations, whereas local FPOs are considered mesoscopic, and scalp or epidural recorded FPOs as macroscopic. To a certain extent, the problem posed by how MPOs are generated is less daunting than those considered in FPOs. In many cases, MPOs can be eliminated or facilitated by selectively manipulating membrane potential (Amitai, 1994; Bland et al., 2005; Bracci et al., 2003; Chapman and Lacaille, 1999; Dossi et al., 1992; Gutfreund et al., 1995; Hu et al., 2002; Kamondi et al., 1998; Leung and Yu, 1998; Pare et al., 1995; Zhu et al., 1999) and blocking specific ionic currents (Agrawal et al., 2001; Amitai, 1994; Bracci et al., 2003; Chapman and Lacaille, 1999; Dickson et al., 2000; Fry and Ferguson, 2007; Klink and Alonso, 1993; Sanhueza and Bacigalupo, 2005; Yoshida and Alonso, 2007). With these manipulations, the causal role of MPOs in spike generation can be succinctly addressed within the system of a single cell.

In order to provide strong evidence for the importance of studies in FPOs, what exactly is being recorded should be clarified. Recordable FPOs are by no means a direct reflection of local spiking activity. It is known that FPOs represent relatively slow current fluctuations in the extracellular matrix, not the action potentials themselves. These slow currents include synaptic currents, voltage-dependent membrane oscillations, calcium spikes, spike afterpotentials and currents associated with spike backpropagation (Buzsaki, 2002; Buzsaki and Kandel, 1998; Creutzfeldt et al., 1966; Eccles, 1951; Watanabe et al., 1966). However, this means that the FPOs can reflect local action potential generation, as their deterministic role in neuronal membrane excitability ultimately determines firing probability in the immediate area (Eeckman and Freeman, 1990; Eggermont and Smith, 1995; Murthy and Fetz, 1996; Rasch et al., 2008; Ray et al., 2008; Young et al., 1992). This means that FPOs serve as second order measurements of neuronal excitability in the immediate brain space. By this definition and the fact that FPO is a composite property dependent on interaction of local currents, FPOs are indeed epiphenomenal—at the level of single neuron physiology—for they are generally considered not to cause subsequent events, but it is clear that they reflect excitability state changes in the microenvironment.

Cortical layer dependence of the FPOs can be studied by using a current source density (CSD) analysis. A CSD can be measured by recording simultaneously or sequentially at depths, d, of say 100 μm intervals perpendicular to the cortical surface and subtracting half of the FPO waveform amplitude recorded at depths $d - 100$ and $d + 100$ from the FPO recorded at depth d. The CSDs calculated for sequential depths correspond to the projection of the passive and active currents, i.e., sinks and sources, onto the direction perpendicular to the electrode track. The amplitudes of the CSD signals depend on the orientation of the currents and on the impedances within the dendritic tree. Note that not all directions of the current spread are reflected in this linear estimate of the CSD. This method has been applied in the neocortex of the rat to study the synaptic sources of sleep spindles and spike-and-wave patterns (Kandel and Buzsaki, 1997).

At the level of neuronal ensemble physiology, or how loosely compartmentalized neuronal populations receive inputs and generate outputs, FPOs should be considered as the primary phenomenon. As mentioned above in brief, FPOs can reliably predict action potential generation owing to their representation of neuronal excitability. In some examined systems, FPOs have even proven to be as accurate in the prediction of behaviour as activities recorded from single neurons (Mehring et al., 2003; Pesaran et al., 2002). Action potentials can be coupled with ongoing FPOs in a periodic or aperiodic manner, as observed in medium spiny neuron entrainment to high voltage spindles or hippocampal theta oscillations (Berke et al., 2004). One of the best-studied examples of brain oscillations is the rodent hippocampal theta rhythm. Theta rhythm is a robust, high amplitude voltage