INTRODUCTION

The Theta Rhythm

Theta activity is one of the most prominent oscillatory patterns in the EEG of animals and humans. The mechanisms and functional role of theta oscillations have long been debated within a relatively narrow field, and this interest has recently spread to encompass a large portion of the neuroscience community (see Buzsáki, this volume). Theta provides a convenient bridge between behavior and cellular physiology, since it is correlated with behavior and also occurs in anesthetized animals and slice preparations, in which its cellular physiology and pharmacology can be explored. Theta is most easily recorded from the hippocampus of rodents but occurs in other cortical and subcortical structures as well. Several functions have recently been suggested for hippocampal theta, including roles in binding together the activity in different cortical areas, providing the temporal context for long-term potentiation and long-term depression, and acting as a clock signal against which single spikes in pyramidal cells can be timed. In particular, these oscillations, and the associated neuronal machinery, represent one of the most promising avenues for understanding the mechanism of temporal coding and its relationship to plasticity in the mammalian brain. The relationship between the firing of single spikes and theta recorded from the hippocampus of freely moving rats provides the clearest and most robust example of phase-coding of a cognitive variable (location, in this case) in the mammalian cortex. The cellular mechanisms by which the theta rhythm is generated are also becoming better understood. It is clear that pyramidal cells have intrinsic properties that can cause them to oscillate given the appropriate synaptic and modulatory inputs. Furthermore, recent work has suggested a role for the inhibitory interneuronal networks in the generation and synchronization of theta. Finally, it has recently been demonstrated that theta can be recorded from the human brain using implanted electrodes or magnetoencephalography. Despite all of this, the functional role of theta has been relatively little-studied as compared with, for example, gamma oscillations.

In September 2004 we organized a workshop on "Theta Oscillations in the Brain: Neural Mechanisms and Functions" in Queen Square, London, supported by The Gatsby Charitable Foundation. The meeting brought together international experts from the fields of Neuroanatomy, Biophysics, Physiology, Pharmacology, Behavioral Neuroscience, Computational Neuroscience, and human EEG and MEG studies. The meeting concentrated on EEG theta activity and attempted to provide a framework in which the viewpoints of the various disciplines present could be united in an attempt to uncover its physiological and pharmacological bases, and its role in the neural computations carried out by cortical networks. After the meeting there was a consensus that a special issue reviewing the current state of the field would be of use to the wider neuroscience community. The field is still small enough for a reasonably comprehensive review to fit into a single volume, although this will not be the case for much longer, given the current explosion of interest in it. In addition, we thought that a special issue might serve to consolidate the field, particularly the related perspectives from currently disparate disciplines, and possibly serve to alert others to the potential importance of theta. For example, recent investigations of EEG and single unit correlates of human memory using subdural and depth electrodes have raised the prospect of developing neuronal models of human memory. In this regard, insights from models of phase-coding of spatial location by hippocampal neurons in the rat provide useful but relatively unexplored ideas and constraints for models of human memory.

This issue of *Hippocampus* results from the aforementioned meeting: authors were asked either to provide related new experimental data or to review their current thinking on the generation and functional use of theta. The issue starts with a historical review of the discovery of theta and how thinking regarding its functional role has evolved, by Buzsáki. The following papers move from electrophysiology in freely moving rats, through intracranial recording in epilepsy patients and magnetoecephalography in healthy volunteers, to theoretical accounts of the generation and function of the theta rhythm. Other relevant recent work, not represented in this issue, includes study of the interneuronal mechanisms (Rotstein et al., 2005; Somogyi and Klausberger, 2005) and intrinsic properties of pyramidal cells (Pike et al., 2000) relating to hippocampal theta.

Starting with electrophysiology in freely-moving rats, Maurer and colleagues from McNaughton's laboratory report that the increase in the spatial scale of the place cell representation of location along the septo-temporal axis of the hippocampus may result from a decreasing intrinsic oscillation frequency of pyramidal cells compared with theta. O'Keefe and Burgess review the evidence that, beyond the "clocking" or synchronizing roles suggested for both theta and gamma rhythms, dual coding by firing rate and firing phase might exist in place cells, possibly reflecting interference between theta and a slightly faster intrinsic oscillation, and relate this possibility to the recent observation of "grid cells" in entorhinal cortex (Hafting et al., 2005). Theta-related firing activity has been found in several extra-hippocampal brain areas. The implications of hippocampal phase coding are

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extended to medial prefrontal cortex by Jones and Wilson, who relate the temporal firing characteristics of neurons there to the hippocampal theta rhythm, while Pape and colleagues look at the coupling between hippocampal and amygdalar theta in long-term fear memory.

Moving to humans, both Ekstrom and colleagues from Kahana's laboratory and Mormann and colleagues from Fernández's laboratory present data from intracranial recordings in epilepsy patients. Ekstrom et al. report increased theta in both hippocampal and neocortical locations during navigation in virtual reality, while Mormann et al. report indications that correct retrieval from memory corresponds to modulation of hippocampal gamma activity by theta. Guderian and Düzel use magnetoecephalography to suggest that recollection is associated with an induced activity increase in a distributed synchronous theta network including prefrontal, mediotemporal, and visual areas.

In the next three papers, Lisman, Vertes, and Hasselmo separately review their own broad-ranging theories regarding the functional role of theta. Lisman, in particular, raises the possibility of functionally relevant coordination between the theta and gamma rhythms. The 40-Hz gamma rhythm has been postulated to provide the basis for binding together different neocortical representations (Singer and Gray, 1995) but in Lisman's models it functions to partition each theta cycle into approximately five subcycles. Together the theta and gamma waves provide the basis for the ordering and recall of behavioral sequences. Vertes notes that theta might sufficiently depolarize pyramidal cells to activate the NMDA receptor, and puts forward the hypothesis that theta is involved in the short-term tagging of information arriving at the hippocampus from the neocortex. The paper by Hasselmo also discusses the role of theta in the encoding and retrieval of memories, in particular the context-dependent retrieval of sequences. He focuses on the relationship of frontal and hippocampal theta activity in the formation of associations between hippocampal episodic memories and the motor plans for specific actions located in the frontal cortex.

In more detailed computational analyses, Huhn and colleagues analyze a dual oscillator model of phase precession, following the suggestion by O'Keefe and Recce (1993), and modeled at the cellular level by Lengyel et al. (2003). They show how their new two-compartment model accounts for many features of the phenomenon, including the better correlation of phase with position than with temporal variables and the independent coding of speed and position by firing rate and firing phase respectively. Sato and Yamaguchi present simulations of place-cell firing during phase precession and use these to account for the role of the human hippocampus in object–place associations, while Scarpetta and Marinaro relate a generalization of the Hopfield model which can store patterns of oscillatory activity to the phase coding of place cells relative to theta.

Overall, we hope that this collection of papers will come to serve as a useful starter to the topic of the possible functional correlates of the theta rhythm, and suspect that this special issue marks the last time in the expansion of the field that such a collection will be possible in a single volume.

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REFERENCES

Hafting T, Fyhn M, Molden S, Moser MB, Moser EI. June 19, 2005. Microstructure of a spatial map in the entorhinal cortex. Nature (Epub ahead of print).

Lengyel M, Szatmary Z, Erdi P. 2003. Dynamically detuned oscillations account for the coupled rate and temporal code of place cell firing. Hippocampus 13:700–714.

O'Keefe J, Recce ML. 1993. Phase relationship between hippocampal place units and the EEG theta rhythm. Hippocampus 3:317–330.

Pike FG, Goddard RS, Suckling JM, Ganter P, Kasthuri N, Paulsen O. 2000. Distinct frequency preferences of different types of rat hippocampal neurones in response to oscillatory input currents. J Physiol 529 (Part 1):205–213.

Rotstein HG, Pervouchine DD, Acker CD, Gillies MJ, White JA, Buhl EH, Whittington MA, Kopell N. April 27, 2005. Slow and fast inhibition and an h-current interact to create a theta rhythm in a model of CA1 interneuron network. J Neurophysiol (Epub ahead of print).

Singer W, Gray CM. 1995. Visual feature integration and the temporal correlation hypothesis. Annu Rev Neurosci 18:555–586.

Somogyi P, Klausberger T. 2005. Defined types of cortical interneurone structure space and spike timing in the hippocampus. J Physiol 562:9–26.