Coherent oscillations and learning-related reorganization of spike timing

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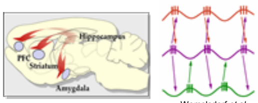
Introduction

The parcellation of the brain into a large number of functionally distinct cytoarchitectonic areas presents a problem for understanding the integrative processes that underlie cognitive functions. How do brain areas with distinctive functional properties cooperate synergistically to accomplish complex operations? A mounting body of evidence points to oscillatory activity as an integrative operation for higher brain functions.

In addition to facilitating binding of synchronously active neurons into assemblies presumably corresponding to experiences, rhythmic oscillations would also create regularly occurring temporal windows for signal transmission between different structures. This would assure that appropriate signals arrive when the receiver is most excitable (Fries, 2005). Moreover, oscillation-induced synchronous activation of neurons improves temporal precision of spike generation and facilitates synaptic plasticity through spike timing dependent plasticity (STDP) (Markram et al., 1997). Oscillations have thus been supposed to be involved in memory formation and consolidation by mediating active communication between hippocampus and neocortex to transform newly formed memories in the hippocampus into more permanent traces in the cortex (Marr, 1971). This process has been supposed to occur in two parts, online (awake) encoding during hippocampal theta rhythmic activity and off-line replay and consolidation during hippocampal ripples (slow-wave sleep, SWS) (Buzsaki, 1989)

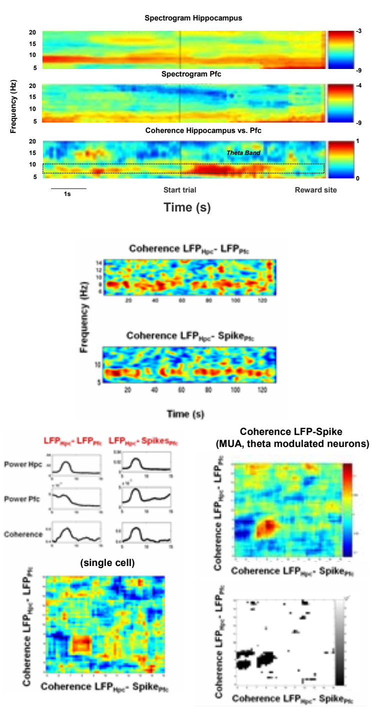
Many experimental data support the two-stage model of memory proposed by Buzsaki in 1989, however, our knowledge is incomplete about how oscillations modify neuronal network activity and enable long term changes in synaptic strength between co-oscillatory brain areas.

This study addresses these issues by examining the hippocampal-prefrontal (Hpc-Pfc) pathway. Coherence in the theta band has been suggested to mediate the communication between Hpc and Pfc (Jones, 2007) (as well as striatum and amygdala, DeCoteau, 2007, Seidenbecher, 2003). Indeed, both structures show LFP oscillations within the theta frequency range (5-10 Hz) and these are coherent during spatial working memory tasks (Jones 2007). Hence, first we examine the relation between learning and Hpc-Pfc-θ-coherence, we further analyze the impact of oscillatory coherence on the excitability of prefrontal neural ensembles and local processing therein.



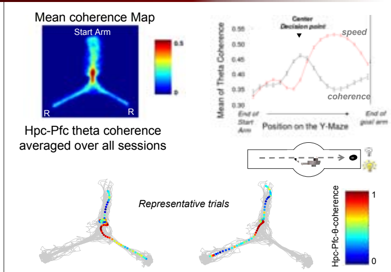
Womelsdorf et al., Science, 2007.

Hpc-Pfc-θ-coherence

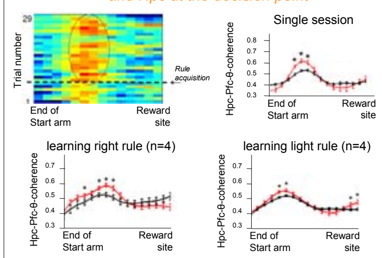


LFP-LFP and LFP-Spike Hpc-Pfc coherence show similar profile

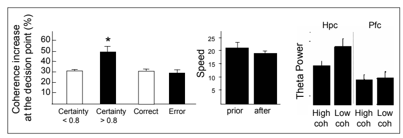
Hpc-Pfc-θ-coherence and learning



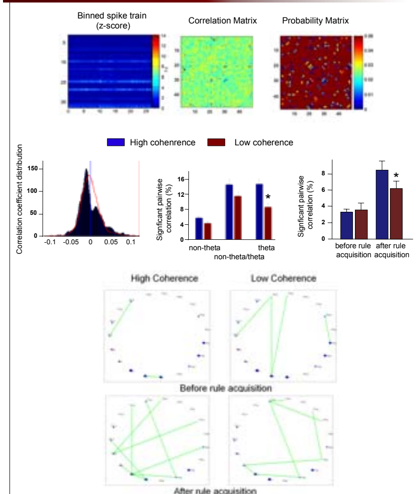
Coherence in the theta band between Pfc and Hpc at the decision point



Changes in Hpc-Pfc coherence coincides with new rule acquisition

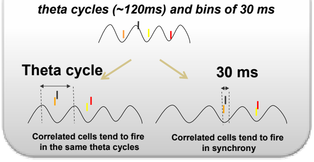


Coherence and Pfc neuronal network



Modification of Pfc neuronal network activity during high coherence periods

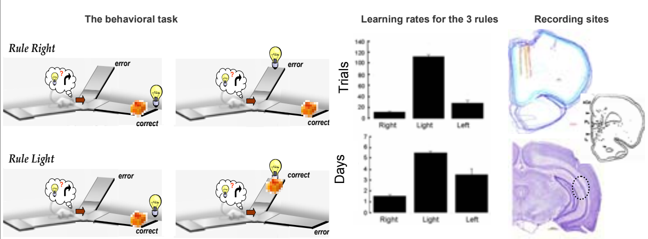
Increased correlations triggered with theta cycles (~120ms) and bins of 30 ms



Methods and Analyses

Recordings: In four rats, recordings of hippocampal local field potentials (LFP) and prefrontal prelimbic and infralimbic (PL/IL) LFPs and single units were made with single electrodes and tetrodes respectively (42 sessions). Data were processed offline with Klusters and our custom software.

Behavioral protocol: On a Y maze, one of the choice arms was lit randomly. These rats learned four successive reward contingency strategies for liquid rewards. Their rules were: go right (ignoring the light), go to the lit arm, then go left. Rats returned to the start arm after each trial. All four rats learned the 'Right' and 'Light' rules, but only two also learned the left rule. At the end of the recording sessions, the animals were sacrificed, and brains prepared for standard histological procedures.



Coherence analysis: The coherence of two time series, $s_1(t)$ and $s_2(t)$, for the frequency f, is given by the product of their Fourier transforms, $F_{1;2}(t)$, at the frequency f. (Note that $F_{1;2}(t)$ are complex numbers)

$$F_{1,2}(f) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} s_{1,2}(t) e^{-i2\pi f t} dt$$

$$\gamma(f) = \frac{F_1^*(f) F_2(f)}{|F_1(f)||F_2(f)|}$$

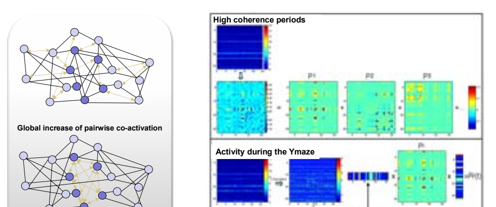
where $F^*_1(t)$ is the conjugate of $F_1(t)$.

Theta modulation analysis: The spike phase distribution relative to the theta oscillation is hypothesized to follow a Von Mises distribution. This is given by:

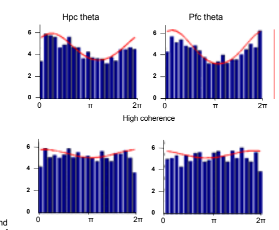
$$f(x|\mu,\kappa) = \frac{e^{\kappa\cos(x-\mu)}}{2\pi I_0(\kappa)}$$

with I_0 the modified Bessel function of order 0. κ (concentration factor, a measure of phase dispersion) and μ (preferred phase) are computed with standard methods detailed in Fischer (2000).

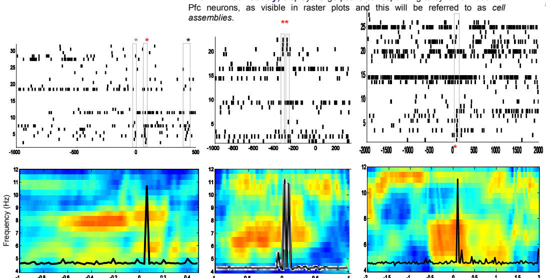
Theta modulation of coherence–related cell assemblies



PCA was applied to the binned spike trains during high coherence periods, and the strongest components were retained. Thus, the PC score for the vectors of population activation at each time bin described the temporal evolution of the activation of these groups. The resulting time course (**see Poster Peyrache 225.12 Wednesday**) displays large peaks corresponding to synchronization of Pfc neurons, as visible in raster plots and this will be referred to as *cell assemblies*.

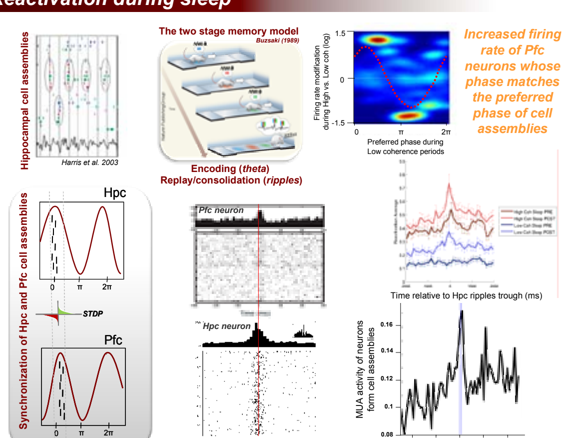


During high coherence periods, all the preferred phase of Pfc cell assemblies were concentrated at the trough of theta recorded either in CA1 stratum pyramidale or in Pfc, whereas during low coherence periods, the preferred phase were uniformly distributed



Spatial distribution in the Y-maze of cell assemblies obtained over all recordings days was restricted to the decision point.

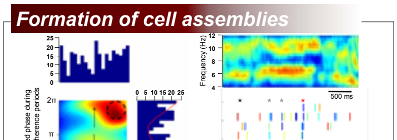
Long term modification of cell assemblies
Reactivation during sleep



Increased firing rate of Pfc neurons whose phase matches the preferred phase of cell assemblies

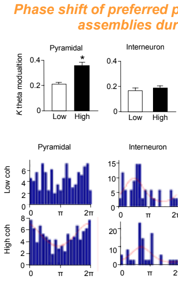
Theta-modulated cell assemblies formed during high coherence periods are reactivated during ripples

Formation of cell assemblies

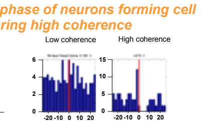


Raster display of neurons forming a cell assembly. Phase of each spike with respect to Hpc theta is indicated by its color. *Note that spikes' phases converge (black star and gray star) on the preferred phase of the assembly, finally active as an assembly (red star).*

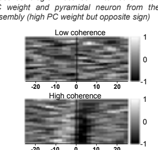
Phase shift of preferred phase of neurons forming cell assemblies during high coherence



Phase shift and increase in theta modulation is restricted to Pfc pyramidal neurons



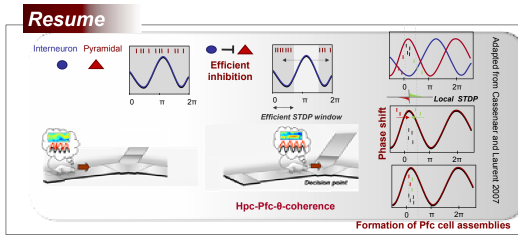
Cross correlogram between interneuron with high PC weight and pyramidal neuron from the cell assembly (high PC weight but opposite sign)



Mean cross-correlogram for all interneurons with high PC weight and pyramidal neurons

Efficient inhibition during coherent Hpc-Pfc oscillations

Resume



Formation of Pfc cell assemblies

Discussion

In this study we evidence that Hpc-Pfc-θ-coherence is enhanced at the decision point after rule acquisition.

During these high coherence periods, several modification of the PFc neuronal network occur:
- **Increased inhibitory activity from a subset of Pfc interneurons**
- **Increased theta modulation and phase shift of preferred phase of Pfc pyramidal neurons**
- **Formation of theta modulated cell assemblies**

The formation of theta modulated Pfc cell assemblies during high coherence periods will ensure them to be synchronized with Hpc cell assemblies. This will lead to Hebbian LTP between the two cell assemblies, as evidenced by the reactivation of Pfc cell assemblies during Hpc ripples in sleep after the task.

As a conclusion, our data detailed the mechanism of the increased inter-Brain-areas communication during high coherence periods. Overall, this suggests that theta and Hpc-Pfc theta coherence may serve as a brain mechanism for synchronization of cell assemblies between brain areas and then favoring specific functional pathways for decision making and mnesic consolidation.

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