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EDITOR'S NOTE

Source: *La lettre*, no. 33, May 2012

- 1 **The teams led by Sidney Wiener (LPPA CNRS UMR-7152) and Laurent Venance (INSERM U667) received the *La Recherche* magazine's prize for the best publication in Neuroscience in 2010, for their article of collaborative research published in the journal *Neuron*¹.**
- 2 One of the theoretical underpinnings of this project stemmed from the discovery of the dopamine mesolimbic system and the characterisation of the pathway linking the hippocampus to the prefrontal cortex by the team of Dr Anne-Marie Thierry and Prof. Jacques Glowinski, Chair of Neuropharmacology. At the time of the experiments, the LPPA (Laboratory of the Physiology of Perception and Action) was directed by Prof. Alain Berthoz, Chair of Physiology of Perception and Action.
- 3 This research was motivated by the observation that neurological patients suffering from damage to a structure called the hippocampus cannot acquire new memories. The fact that they can remember only those events that occurred prior to but not after their accident, suggests that the memory traces are acquired through the hippocampus but are not permanently stored there. After learning, these traces appear to be transferred to the cerebral cortex and especially to the prefrontal cortex. A leading theory postulates that this transfer occurs during sleep, when the neurons activated during learning are reactivated, thus reinforcing the synaptic connections that are believed to be the neural bases of permanent memory traces.

- 4 In a first study, the LPPA team had recorded neurons in rats as they learned a decision-making task in a maze. They showed that suppressing neuronal reactivation during sleep strongly impaired learning (see *La lettre du Collège de France*, no. 27, p. 15).
- 5 The researchers then sought to understand how the brain encodes the information that will be reactivated during sleep and consolidated in long-term memory. With multi-site brain recordings, the team discovered that, while the rat learned to select the correct path in the maze (for example, turning right at an intersection to receive a reward), the excitation/inhibition cycles of the hippocampus and the prefrontal cortex oscillated in phase with one another as the rat was at the choice point, and this increased substantially from the moment the rat first understood the rule. This synchronization is hypothesized to be a mechanism to facilitate communication between those brain areas underlying appropriate behaviour in a given context. This would facilitate a reconfiguration of the local circuitry leading to formation of synchronously active groups of neurons in the prefrontal cortex. Very importantly, these same prefrontal neurons which synchronize upon learning are also reactivated together with hippocampal neurons during sleep.
- 6 Finally, thanks to the collaboration with the INSERM U667 team, the researchers were able to elaborate the analysis at the molecular level and to show that these phenomena are linked to dopamine. Sometimes considered as the neurotransmitter of pleasure, dopamine's operating mechanism is still poorly understood. We know that the brain releases dopamine in rewarding situations, or when a future reward is anticipated. This research shows that the synchronization of rhythms in the hippocampus and prefrontal cortex and the joint activation of groups of prefrontal neurons observed during learning could be replicated by dopamine injections in the prefrontal cortex. It thus suggests that a potential mechanism of action of dopamine is the reconfiguration of neuronal circuits in the brain during rewarded learning.
- 7 The interest of this study lies in its multidisciplinary and its links at different functional levels. Starting from the molecule, it extends to local neuronal circuits, then to the synchronization of different brain structures and finally to the global processes of learning and memory. In the future, the team will develop projects to implement these discoveries with a view to helping develop treatments for neuropsychiatric diseases.

NOTES

1. Benchenane K., Peyrache A., Khamassi M., Tierney P., Gioanni Y., Battaglia F., Wiener S. (UMR 7152, *Spatial Memory and Navigation Team and U667, Dynamics and Physiopathology of Neural Networks Team*), "Coherent Theta Oscillations and Reorganization of Spike Timing in the Hippocampal-Prefrontal Network upon Learning", *Neuron* no. 66: 6, June 2010, p. 921-936.

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