BRAIN CIRCUITS OF MEMORY: QUALITY *VERSUS* QUANTITY?

Giulia Torromino, Fellow Seminar Abstract
Italian Academy for Advanced Studies
Zuckerman Brain Mind Behavior Institute
Columbia University

Memory is a complex system that since antiquity fascinated philosophers, scientists and scholars from different disciplines. The term "memory" comes from Latin *memoria*, which is the faculty of remembering events from the past.
As a brain process memory can be studied from many perspectives, but is generally referred as the ability to retain and recall facts and information acquired through experience. However, this definition is only partial, several distinctions have been made for memory based on type, duration and its neurobiological aspects. Besides the taxonomy of memory, over time many efforts have been addressed to localize the memory trace in the brain, or the *engram*. From a neurobiological perspective, the prevailing view is that memories are codified by enduring physical changes in synaptic connections between groups of neurons (neuronal ensembles) that are activated during a specific event (Josselyn, Köhler, and Frankland 2015). According to this model the formation of a memory is a process that can be divided in three main temporal stages: *acquisition* (learning), *consolidation* (storage) and *retrieval* (recall).
The consolidation process has been proposed to occur after learning, during periods of rest or sleep. Greatly anticipating the current idea of memory consolidation, Muller and Pilzecker in 1900 proposed the *perseveration-consolidation hypothesis*, holding that "neural activity initiated by a learning trial continues and recurs for some time after the original stimulation has ceased and that this perseveration aids the consolidation of a stable memory trace" (Muller and Pilzecker 1900; Rosenzwaig 2007). Seminal works in 90s (Pavlides and Winson 1989; Wilson and McNaughton 1994; Skaggs and McNaughton 1996) have shown how experience-induced *replay* in neuronal ensembles, the recapitulation of patterns of activity from previous wakeful experience, occurs after learning in a time-compressed form. Since that, the neurophysiological mechanisms that occur in the phases following learning has been deeply explored, giving support to the idea that the electrical activity of neuronal ensembles after learning can underlie system-level memory consolidation (Lansink and Pennartz 2015; Foster 2017). Through replay activity, newly encoded memory representations (presumably in the hippocampus) are thought to be transferred to broader neuronal network for long-term storage.
In my previous research activity at Sapienza University of Rome in Prof. Andrea Mele's laboratory, we characterized the contribution of two anatomically connected brain regions in the consolidation of spatial memory: the *hippocampal formation* (HF) and the *ventral striatum* (VS). Our results demonstrated that the post-learning communication between the HF and VS, through the ventral subiculum, is a biological mechanism required for memory consolidation and for learning-related synaptic plasticity. Our data integrate in the framework of memory consolidation theories and pose the attention on the role of sub-cortical structures in long-term memory stabilization, suggesting that a more diffused brain network, including also the HP/VS pathway, may contribute to the formation of an engram. However, an issue rises from data

obtained through brain network manipulation techniques, which is the difficulty of elucidating the dependence of a downstream target on the information provided by an upstream brain region (Wiegert et al. 2017). Indeed, when the inhibition of a pathway cause an effect on a cognitive process we mostly conclude "that pathway is involved in that function". However, the fact that the blockade of the information coming from one input structure to a target structure cause a detrimental effect on performance leave us to assert that this information is necessary, but we cannot infer whether that input is *instructive*, it may be just *permissive*. In other words, we need to discern between *quality or quantity* of inputs acting in a brain network for memory consolidation.

BIBLIOGRAPHY

Foster D. J. 2017. "Replay Comes of Age." Annual Review of Neuroscience 40(1): 581–602.

Josselyn S. A., Köhler S. and Frankland P. W. 2015. "Finding the Engram." *Nature Reviews Neuroscience* 16 (9): 521–34.

Müller G.E. and Pilzecker A. 1900. "Experimentelle Beiträge zur Lehre vom Gedächtnis." Z. Psychol. Ergänzungsband (1):1–300.

Pavlides C. and Winson J. 1989. "Influences of Hippocampal Place Cell Firing in the Awake State on the Activity of These Cells during Subsequent Sleep Episodes." *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* 9 (8): 2907–18.

Lansink C. S. and Pennartz C. M. A. 2015. "Associative Reactivation of Place-Reward Information in the Hippocampal-Ventral Striatal Circuitry." In M. Tatsuno, & J. Knierim (Eds.), "Analysis and modeling of coordinated multi-neuronal activity" (Springer series in computational neuroscience (12): 81-104. New York: Springer.

Rosenzwaig M.R. 2007. "Historical Perspectives, in Neurobiology of Learning and Memory." by Kesner, P. and Martinez, Jr., 2nd edition, *Elsevier*.

Skaggs W. E., and McNaughton B. L. 1996. "Replay of Neuronal Firing Sequences in Rat Hippocampus during Sleep Following Spatial Experience." *Science* 271 (5257): 1870–73.

Wiegert J. S., Mahn M., Prigge M., Printz Y., and Yizhar O. 2017. "Silencing Neurons: Tools, Applications, and Experimental Constraints." *Neuron* 95 (3): 504–29.

Wilson M. and McNaughton B. L. 1994. "Reactivation of Hippocampale Ensemble Memories during Sleep." *Science* 265: 676–79.