The neuronal networks activated during paradoxical (REM) sleep and their functions

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Rapid eye movement (REM) sleep (also known as paradoxical sleep; PS) is characterized by EEG rhythmic activity resembling that of waking with a disappearance of muscle tone and the occurrence of REMs. It will be proposed that the entrance from SWS to PS is due to the activation of different subpopulations of PS-on hypothalamic GABAergic, Lhx6 and MCH neurons. These neurons would inhibit during PS a population of mesencephalic PS-off GABAergic neurons inducing the disinhibition of the glutamatergic neurons generating PS localized in the pontine sublaterodorsal tegmental nucleus (SLD). The exit from PS would be induced by the inhibition of the PS-on neurons by waking systems such as the pontine and medullary noradrenergic neurons and the hypothalamic hypocretin. In addition, recent data using functional neuroanatomy showed that only a small number of limbic structures are activated during PS in contrast to waking. Among them, the hippocampal dentate gyrus (DG) is the only cortical region that display more activated neurons during PS hypersomnia than waking. Further, combining retrograde tracing, neurotoxic lesion and FOS immunostaining, it has been demonstrated that neurons from the lateral part of the supramammilary nucleus (SuML) projecting to DG, are responsible for the activation of DG granule cells during PS. In addition, it has recently been shown that the few other limbic cortices activated during PS like the retrosplenial and medial entorhinal cortices are activated by a projection from claustrum. More recently, using TRAP mice, we showed that different neurons are activated during wakefulness and PS. We propose that such specific cortical activation during PS might play a key role in generation of dreaming, the setting of complex motor tasks and the previously reported beneficial effect of PS on learning and memory. Indeed, several recent studies clearly indicate that PS is instrumental for memory consolidation. In particular, it has been recently demonstrated that activation of adult born granule cells during PS play a key role in the formation of the contextual component of fear memories. In summary, original new converging data strongly suggest that PS is generated by populations of excitatory and inhibitory neurons located from the hypothalamus to caudal brainstem while the cortical activation during the state of PS is limited to a few limbic cortical structure. Taking into account these new data, we will discuss whether PS is indeed a "Paradoxical state". We will also show that the identification of the function (s) of the pathways identified is now accessible using new genetic tools such as the TRAP mice.

Dr. Pierre-Hervé Luppi is internationally recognized for his current work on the mechanisms responsible for the genesis of the sleep-waking cycle, the cognitive role of sleep and the studies of sleep pathologies like narcolepsy and REM sleep behavior disorder. In particular, he described the brainstem network responsible for generating muscle atonia during paradoxical sleep and discovered the role of MCH in controlling the state. He also more recently described at cellular level the state of the cortex during paradoxical sleep, showing that only a few limbic cortical structures are activated by the claustrum and the supramammillary nucleus.