Sleep regulation by morpho-functional modulation of astrocytes

A. Rancillac[1], *A. Walter*[1], *F. Bellier*[1], *L. Lecoin*[1], *P. Ezan*[1], *F. Chauveau*[2], *N. Rouach*[1]
[1]Collège de France, Paris, France, [2]Institut de recherche biomédicale des armées, Brétigny-sur-Orge, France

---

Background: Sleep is an essential biological process for life. However, sleep disorders still affect a third of the Western population and represent a major public health problem by promoting the emergence of numerous other diseases such as diabetes, hypertension, or depression. Yet, sleep regulation mechanisms remain only very partially characterized. Recently, it has been suggested that astrocytes and Brain-Derived Neurotrophic Factor (BDNF) are involved in sleep regulation. But their modes of action within the ventrolateral preoptic nucleus (VLPO), a key structure in the regulation of slow sleep, remain largely unknown.
Methods: By combining immunolabeling, 3D cellular reconstructions, STED super-resolution microscopy, and sleep recordings in piezo-electric cages we investigated how the morphology of astrocytes was modulated during the circadian cycle, and what was its impact on synaptic coverage, neuronal activity and sleep regulation.
Results: We here show that during the rest period of mice, the astrocytes from the VLPO enlarge and complexify, reaching a maximum at ZT-8, that is 8 hours after the lights go on, and then shrink after ZT-12, when the lights go off and the activity period begins. Simultaneously, we have shown that at the beginning of the rest period, the synthesis of BDNF by sleep-promoting neurons progressively increases, as well as its maturation, from the proBDNF to the mBDNF by astrocytes. The perisynaptic astrocytic processes (PAP) then get closer to the synapses, up to ZT-8, where the activation of TrkB receptors to BDNF is maximal. BDNF could both play a trophic role on astrocytes and strengthen neuronal activity. We have indeed also shown that *in vivo* injection of BDNF consolidates sleep.
Conclusions: Altogether, these results suggest that VLPO astrocytes participate in sleep modulation by regulating the release of BDNF and their morphology, in order to modulate the coverage of synapses and consolidate sleep at the end of the rest period.