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TRAP2 model for studying activated structures during Paradoxical (REM) Sleep

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Introduction

As postulated by Michel Jouvet as a paradoxal state, REM sleep exhibits EEG activities in cortical structures similar to those observed during wakefulness (W). However, for over a decade now, our results shows that only a few limbic cortical structures are activated during REM sleep in contrast to wakefulness. It confirms our hypotheses that REM sleep exhibit a pattern of neuronal activity state-related. Here, using TRAP2-red mice we propose to identify neurons activated during REM sleep. With this novel approach regarding sleep, we propose to broaden the avenue in the study of the REM sleep function(s).

Aims : Taking advantage of the genetic engineering applied to animal models we propose in this study to identify neuronal populations activated during wakefulness and REM sleep using the TRAP2 mice. This knock-in strain allow us to get different time points in the same animal, and to obtain two fluorescent markers of neuronal activity: tdtomato and cFos. Corroborating our last findings, we identified a few structures exhibiting high cFos activity during REM sleep compared to wakefulness.

Conclusion

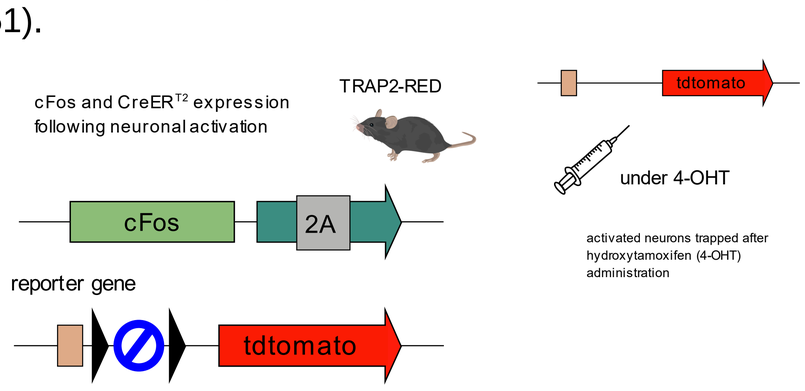
TRAP2-Red mice combined with automatic counting (NeuroInfo - MBF Bioscience) seems to be a suitable approach for identifying neuronal activity during REM sleep. Based on our last results we could identify structures differently activated during REM sleep (cFos+ neurons) compared to wakefulness (tdtomato+ neurons) such as **retrosplenial cortex (RSP) and dentate gyrus (DG)**

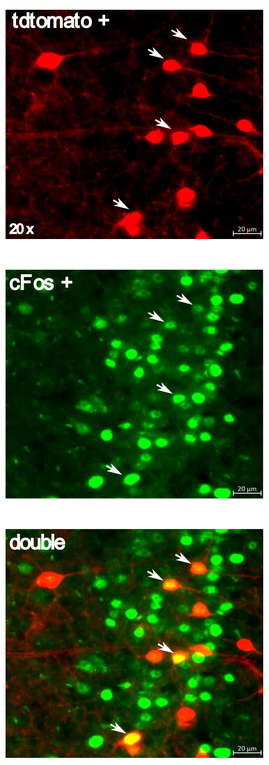
Next steps :

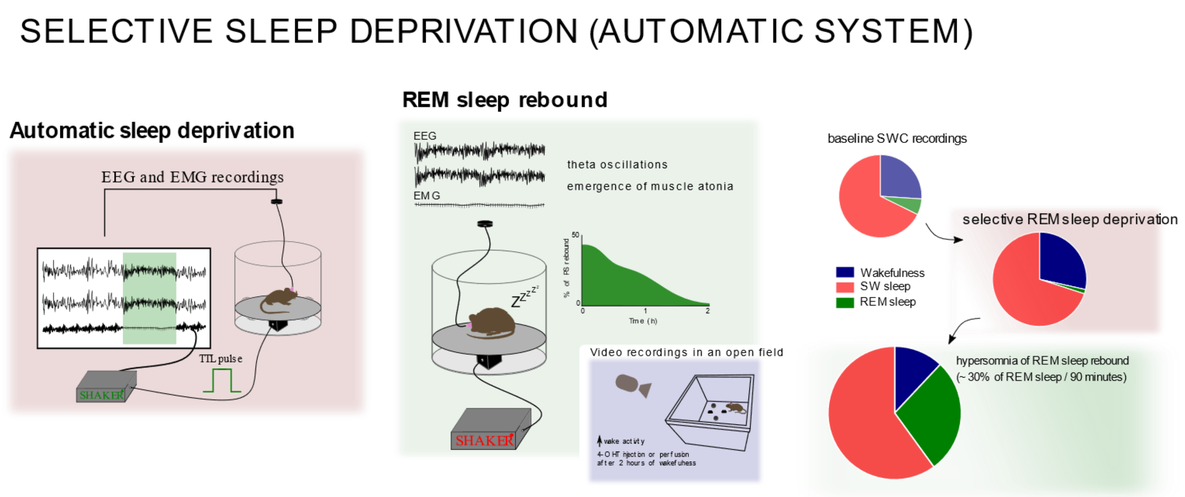
- Analyze all structures and percentages of double-labelled neurons.
- Inactivate or activate TRAPed-neurons to determine their function in REM-sleep (chemogenetic and optogenetic).

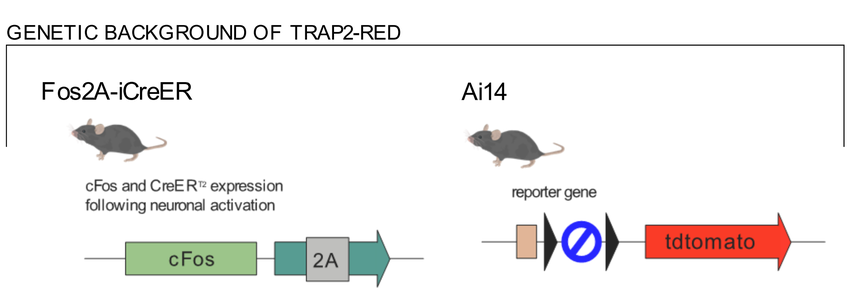
Methods

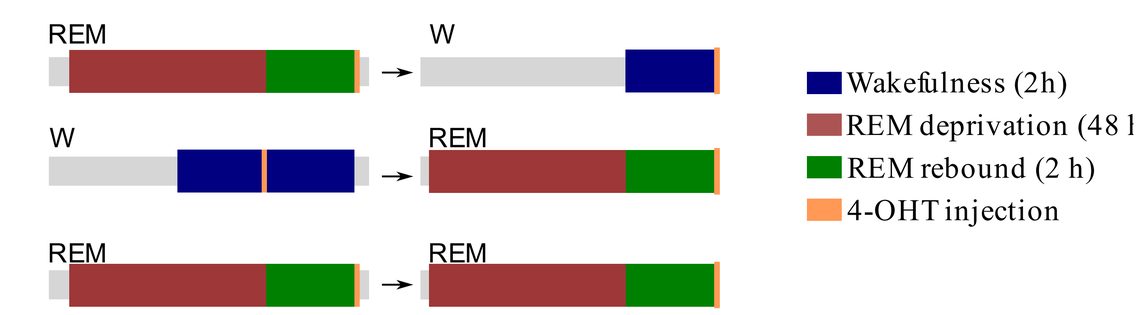
Seven TRAP2 mice were analysed in REM-W (n=1), W-REM (n=2) and REM-REM (n=4) conditions 1 week apart. Basal sleep wake cycle recordings were performed 24h / day (10 - 10 am) in order to generate the automatic detection of REM sleep as we previously described (Arthaud et al, 2015). Mice underwent automatic REM sleep deprivation during 48h and received hydroxytomaxifen (4-OHT) 2h after the first epoch of REM event, in the first condition; or perfusion, in the second condition. Brain sections (30 µm; cFos, Alexa 488; tdtomato, spontaneous fluorescence ~555 nm wavelength) were obtained every 240 µm. The experiments were approved by the Ethics Research Committee of University Lyon 1 in accordance with the European guidelines for care in animal research (#21351).

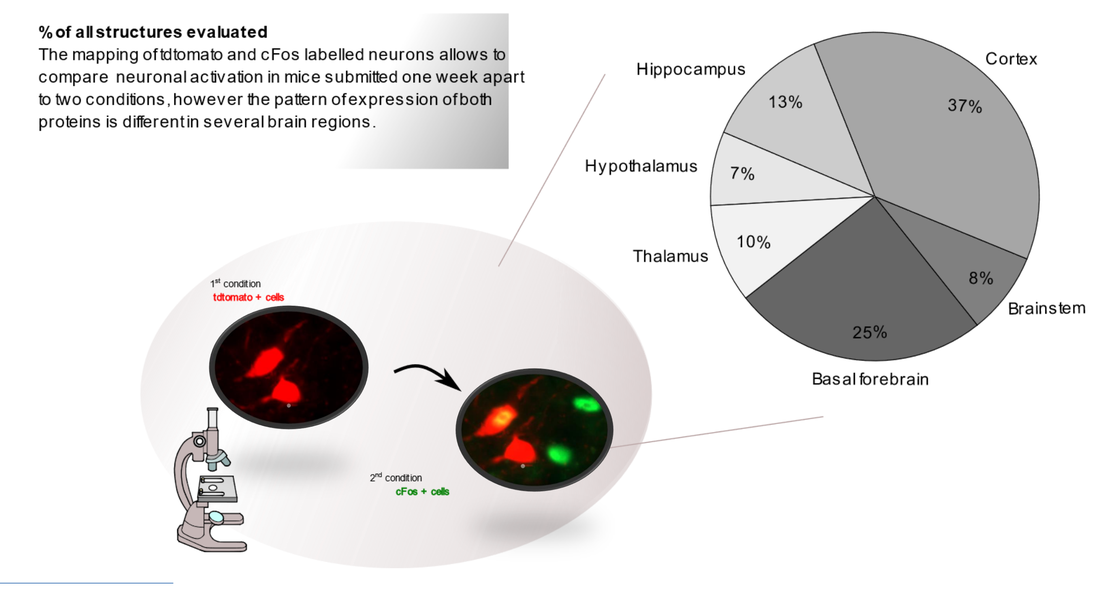




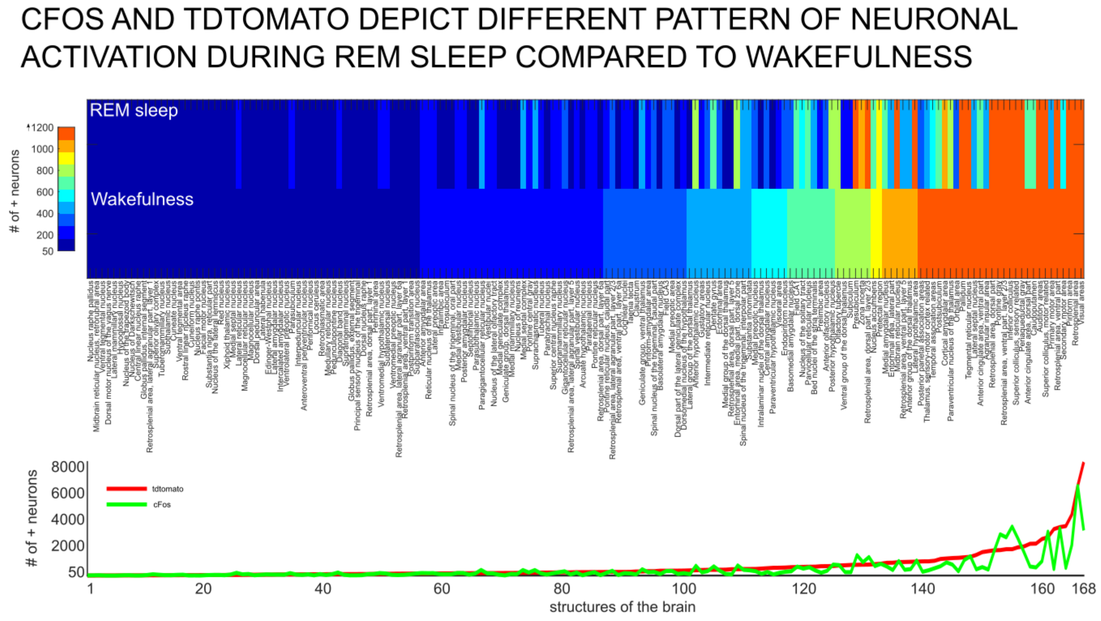


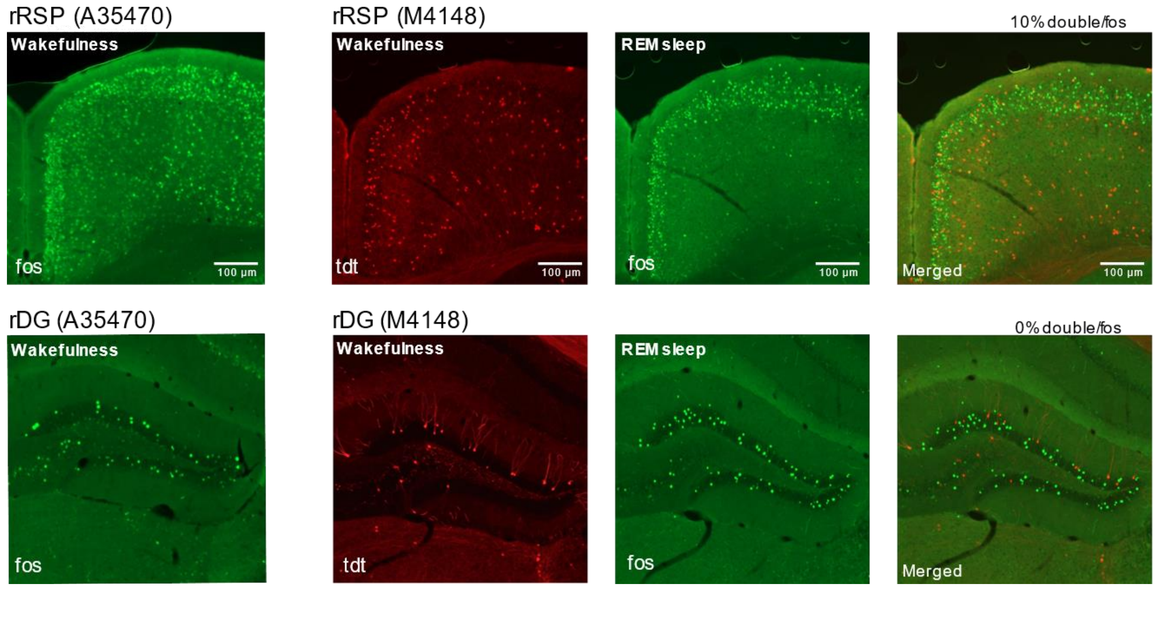






Results





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