

Locus coeruleus reactivity during wakefulness is associated with REM sleep intensity

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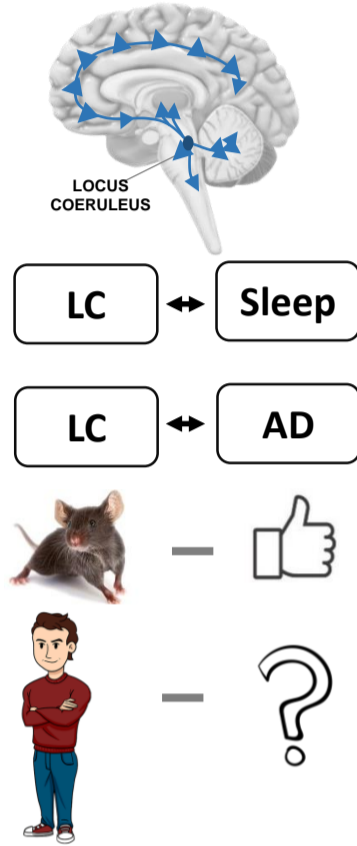
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Introduction

- Sleep is variable across individuals and changes over the lifespan.
- These changes contribute to pathophysiological mechanisms of neurodegenerative diseases including Alzheimer's disease (AD)

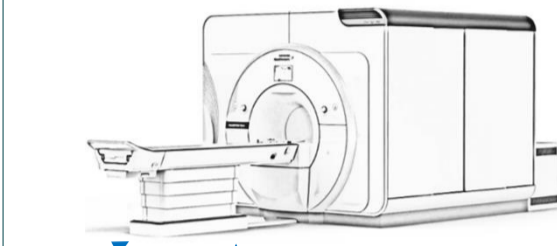
- **Locus coeruleus (LC):** small nucleus in brainstem: 15*2,5*2 mm³
- LC is the main source of norepinephrine (NE) and is involved in **sleep regulation**
- LC = 1st site of **Alzheimer's disease** neuropathology
- LC – sleep: based on **animal / lesions**
- The contribution of the LC-NE system to the regulation of **sleep and wakefulness in humans** is unclear.



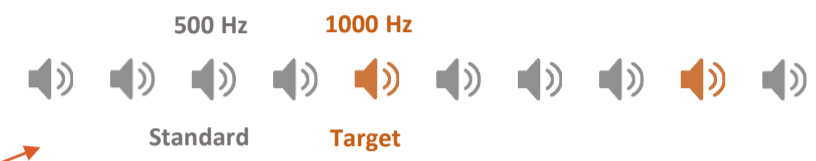
Is LC activity related to sleep variability, including in aging ?

Methods

7T MRI high resolution / sensitivity



An attentional task ('oddball') that mimics novelty detection and recruits the LC-NE system:



fMRI

Oddball task

LC activity

sMRI

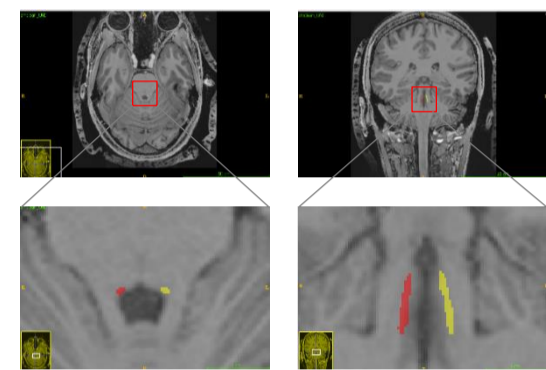
MT-TFL sequence

Individual LC

Night of sleep

EEG recording

Sleep metrics

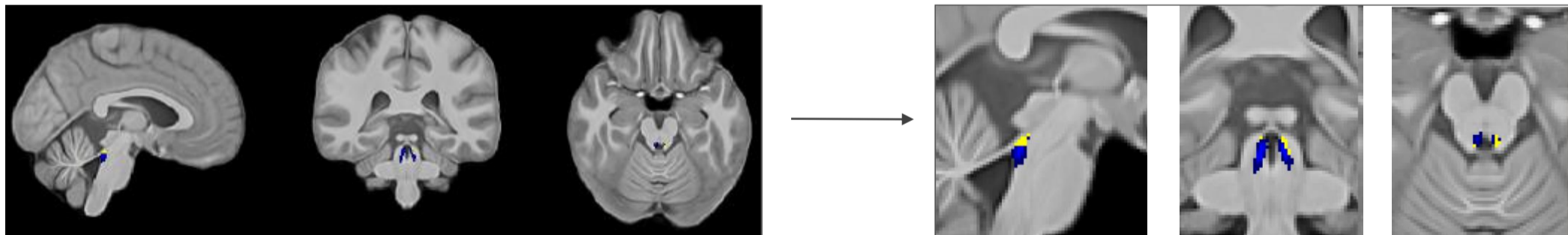


- Overall architecture [REM Percentage]
- Intensity of REM (theta power) and NREM sleep (SWE)
- Sleep continuity [arousal number] and duration
- Sleep efficiency

N = 53 healthy: 34 younger (22 ± 3.27 y) and 19 older (61 ± 5.3 y)

Results

sMRI, fMRI: group-level activation inside the LC probabilistic template for the detection of the target sound:

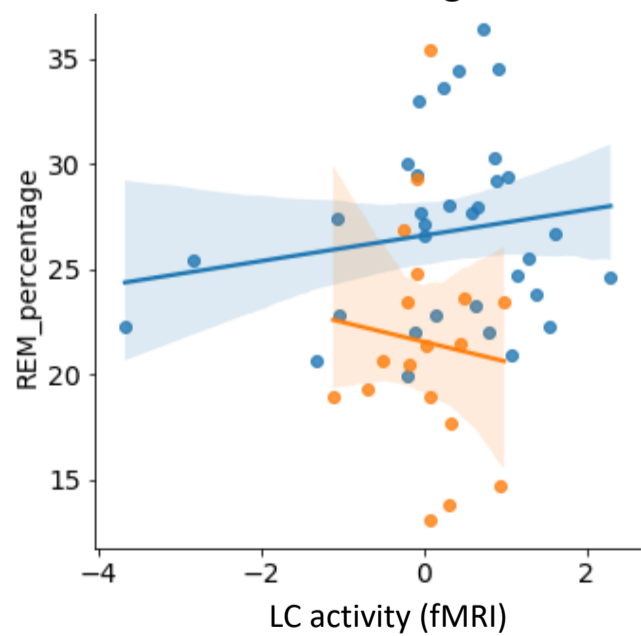


The LC activation at wakefulness is negatively associated with the percentage and intensity of REM sleep, but only in older individuals

Correlation between REM sleep percentage and the LC activation during wakefulness:

GLMM: sleep feature = LC activation*group sex BMI TST

Correlation between REM sleep intensity and the LC activation during wakefulness:



LC activation*group: p=.02

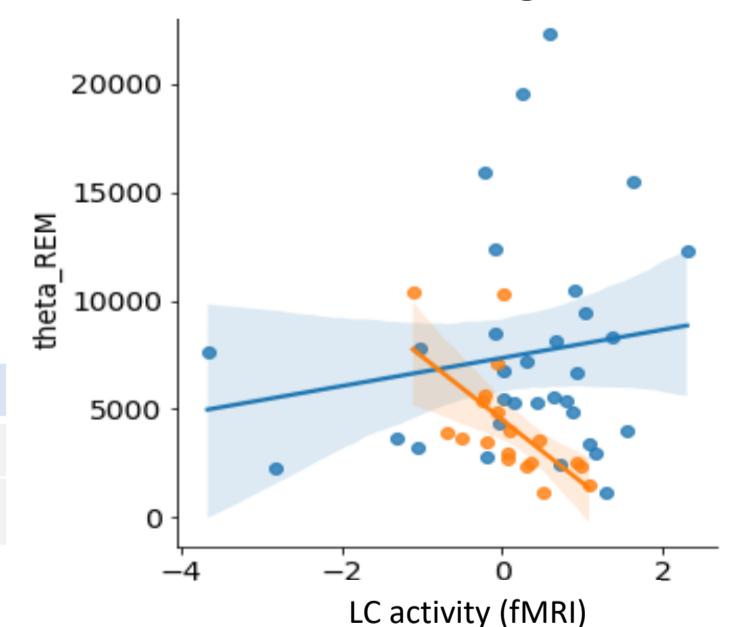
group	t Value	Pr > F
younger	0.61	0.54
older	-2.22	0.03*

Positive non-significant (in younger) and negative significant (in older) association between the percentage of REM sleep (relative to TST) during baseline night and the fMRI mean betas inside the left LC mask during oddball task

LC activation*group: p=.03

group	t Value	Pr > F
younger	0.38	0.70
older	-2.33	0.02*

Positive non-significant (in younger) and negative significant (in older) association between overnight cumulated power in REM sleep theta (4-8Hz) during baseline night and the fMRI mean betas inside the left LC mask during oddball task



Conclusion

- The variability in the LC activity during wakefulness is related to the overall architecture of sleep and to the intensity of REM sleep
- This seems particularly true in ageing
- Potential implication for sleep disorders (e.g. insomnia) and neurodegeneration (e.g. AD)