

Whole-brain network dynamics informed by locus coeruleus activity: Associations with sleep and mood

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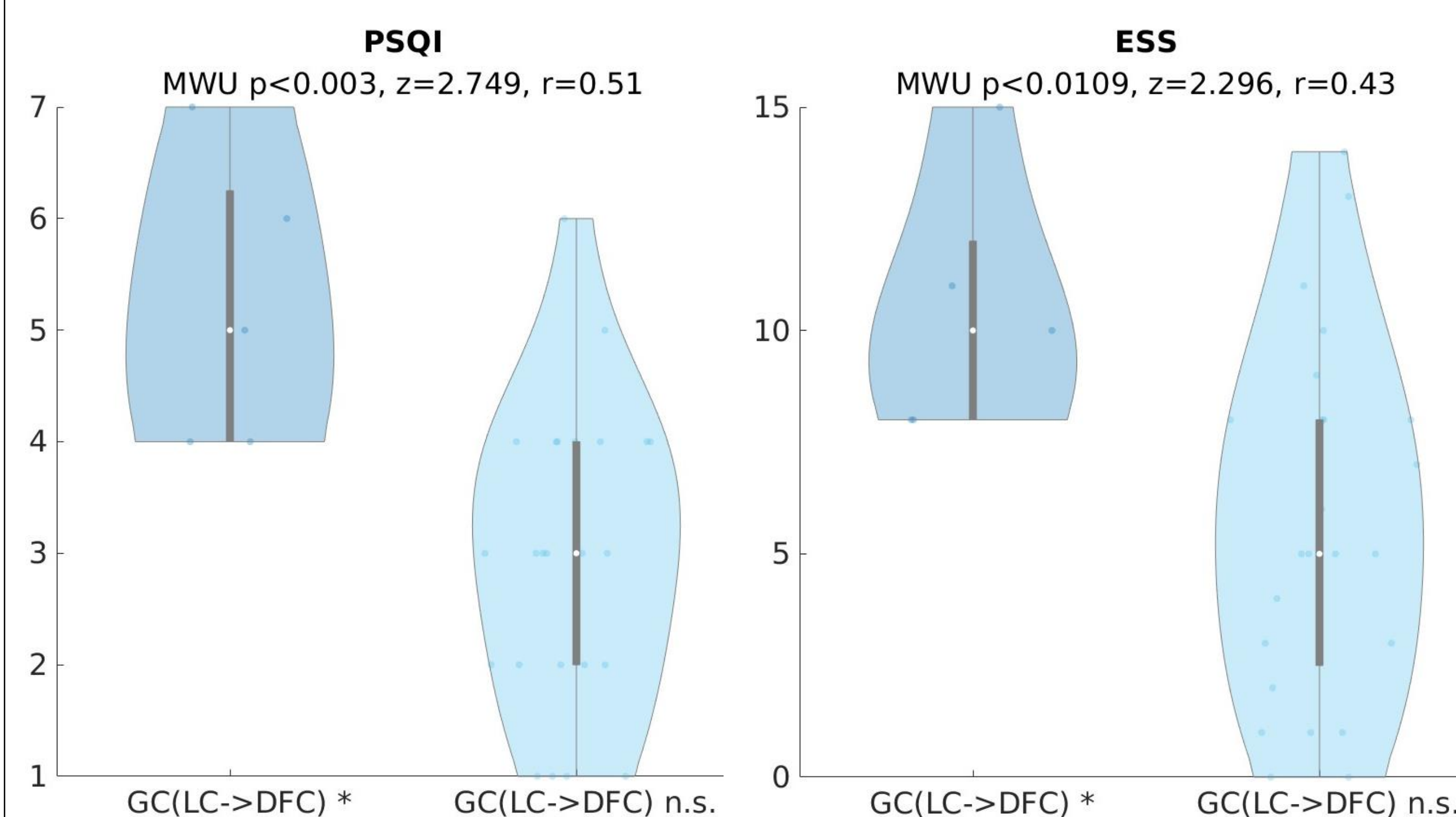
Introduction

- **Arousal shapes brain networks:** The locus coeruleus (LC) is suggested as a central hub, dynamically modulating global functional topology, through direct projections and slower acting NA modulation [1, 2]
- **The missing link:** How LC-NA activity causally drives resting-state connectivity—and how this relates to sleep and mood—remains largely unknown
- **Our approach:** UHF (7T) resting-state fMRI, exploratory investigation of LC-whole-brain coupling in healthy individuals
- **Validation of LC role in sleep, arousal, mood:** LC->DFC coupling strength associations with sleep quality (PSQI), sleepiness (ESS), depression (BDI), anxiety (BAI)

Results

- PSQI: **P**ittsburgh **S**leep **Q**uality **I**ndex, mean=3.45 (SD=1.57, range=1-7)
- ESS: **E**pworth **S**leepiness **S**cale, mean=6.48 (SD=4.22, range=0-15)
- BDI: **B**eck **D**epression **I**ndex, mean=4.62 (SD=4.65, range=0-16)
- BAI: **B**eck **A**nxiety **I**ndex, mean=2.48 (SD=2.63, range=0-10)

Delay = 1 TR:



GC(LC->DFC): **G**ranger **C**ausality log ratio, *: significant causal relationship, true for 5/29 (delay=1TR) or 8/29 (delay=2TR), MWU: **M**ann-**W**hitney **U** test

Delay = 2 TR:

BAI: MWU $p < 0.0208$, $z = 2.038$, $r = 0.38$, BDI: Spearman $\rho = 0.4222$, $p < 0.0225$

Discussion

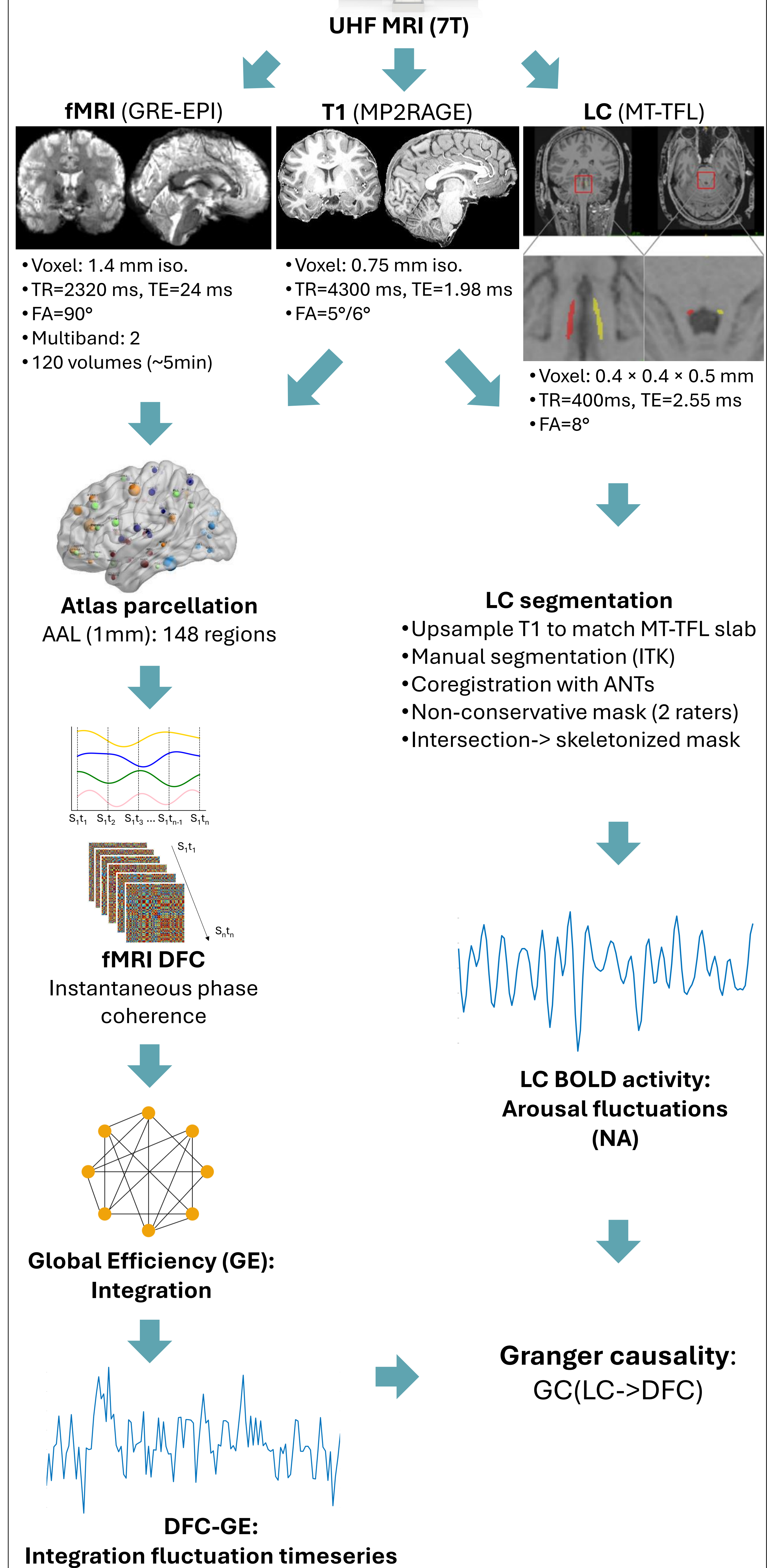
- **LC activity predicts changes in global integration;** GC(LC->DFC)* in sample subset
- People with stronger LC-driven integration have poorer subjective sleep quality and higher sleepiness (delay=1TR), higher depression and anxiety scores (delay=2TR)
- Potentially able to capture instantaneous (short delay) and diffuse, tonic [3] effects of the LC (longer delay)
- Baseline evidence to study cases of altered sleep, arousal and mood, all found in Insomnia Disorder, LC strongly implicated [4]

References

1. Aston-Jones G, Cohen JD. An integrative theory of locus coeruleus-norepinephrine function: Adaptive Gain and Optimal Performance. *Annu Rev Neurosci*. 2005
2. J. M. Shine et al. The Dynamics of Functional Brain Networks: Integrated Network States during Cognitive Task Performance. *Neuron*. 2016
3. Mortazavi N, Talwar P, et al. REM sleep quality is associated with balanced tonic activity of the locus coeruleus during wakefulness. *J Biomed Sci*. 2025
4. Van Someren. Brain mechanisms of insomnia: new perspectives on causes and consequences. *Physiological Reviews*. 2021

Methods

29 healthy sleepers
mean=39.17 (SD=18.13)
years
15 women



fnrs
FREEDOM TO RESEARCH

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