Time is represented by global changes in entorhinal and hippocampal whole-brain functional connectivity patterns

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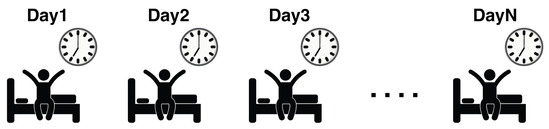
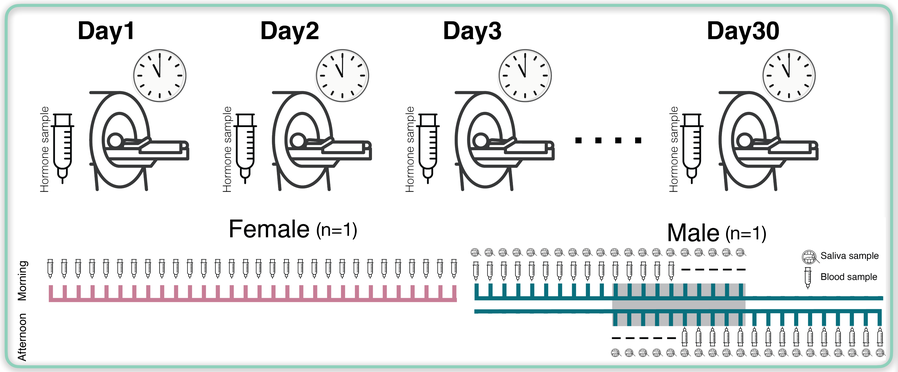
Background & Aims



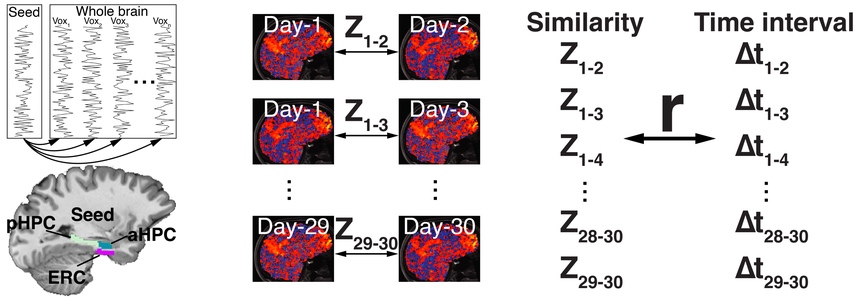
- Multivariate neural activity patterns in the hippocampus (HPC) and entorhinal cortex (ERC) represent conjunctive spatial-temporal context information [1, 2, 3].
- In rats, hippocampal place cell firing patterns become increasingly *dissimilar* when a task is performed over progressively longer **temporal intervals**, suggesting **temporal context** representation in the hippocampus [4].
- In humans, the similarity of regional<—>whole-brain functional connectivity patterns has been found to reflect changes in global states (e.g., arousal) [5].

(1) Do HPC/ERC <-> whole brain resting state functional connectivity (rsFC) patterns reflect temporal context?
(2) Do time-dependent rsFC pattern changes in HPC show differences along the long-axis?
(3) Are HPC/ERC time-dependent rsFC pattern changes network specific?

Paradigm

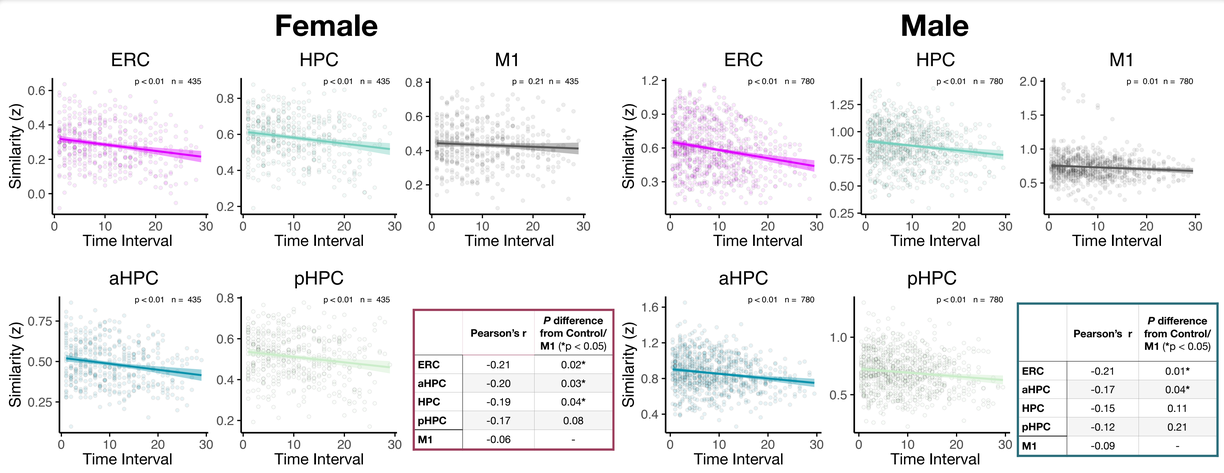


Data analysis



fMRI Data Preprocessing: fMRI data were processed using FSL (www.fmrib.ox.ac.uk/fsl) and AFNI (https://afni.nimh.nih.gov). Preprocessing steps included motion correction, high&low-pass filters, and white matter/CSF/motion noise removal. Each day participants' EPIs were registered to T1 space using FLIRT. HPC/ERC masks: automatic segmentation of hippocampal subfields using ASHS [6]. Network masks: Yeo et al. 17-network registered to subjects' T1 space using FNIRT [7]. Multivariate functional connectivity patterns: The rsFC pattern similarity between pairs of sessions was computed and Fisher-z-transformed. We correlated Z-transformed similarity (correlation) coefficients for session pairs with the Δ time interval between session pairs. The correlation between multivariate rsFC pattern similarity and time interval for each seed was tested against a control region (M1) to determine regional specificity. Change in hormone levels between session pairs was also controlled. [8]. Age: female (23yr), male (26yr).

The similarity of ERC & HPC whole-brain functional connectivity patterns significantly decreases over time

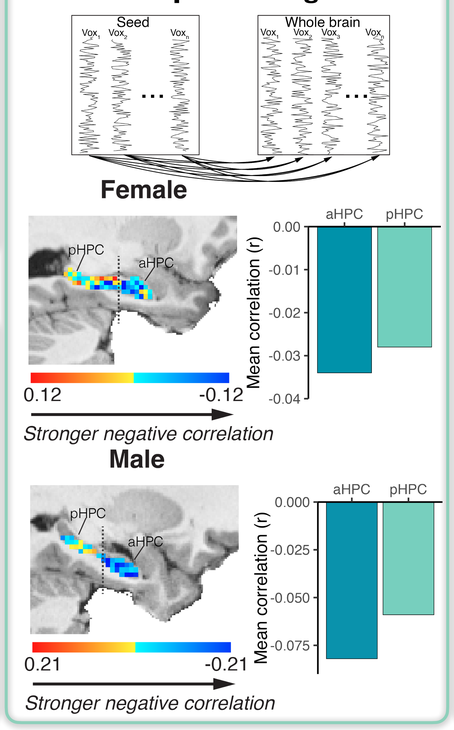


	Pearson's r	*P* difference from Control/ M1 (*p < 0.05)
ERC	-0.21	0.02*
aHPC	-0.20	0.03*
HPC	-0.19	0.04*
pHPC	-0.17	0.08
M1	-0.06	-

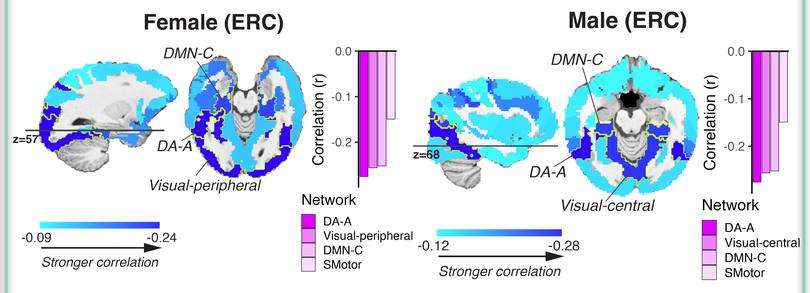
	Pearson's r	*P* difference from Control/ M1 (*p < 0.05)
ERC	-0.21	0.01*
aHPC	-0.17	0.04*
HPC	-0.15	0.11
pHPC	-0.12	0.21
M1	-0.09	-

Time dependent changes in ERC- and aHPC-whole brain rsFC patterns are significantly stronger than M1's (both sexes)

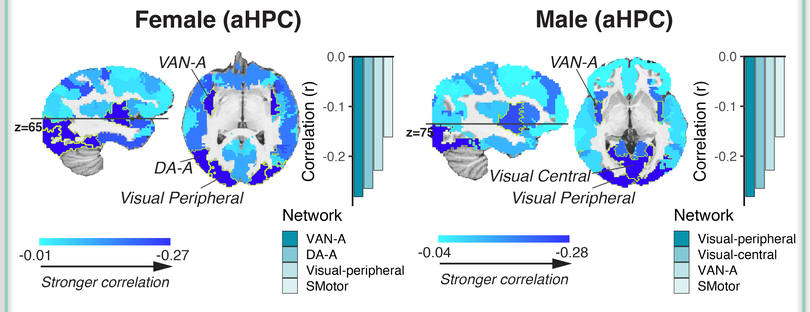
Time-dependent changes in HPC rsFC patterns show an anterior to posterior gradient



ERC time-dependent pattern changes primarily driven by DMN-C and DA-A networks

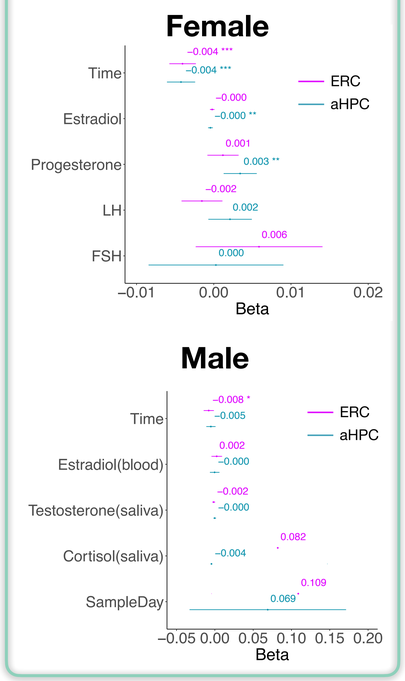


aHPC time-dependent pattern changes primarily driven by VAN-A and visual networks



Abbreviations: default mode network-C(DMN-C), dorsal attention network - A (DA-A), ventral attention network (VAN-A)

Time dependent changes in ERC rsFC patterns remain significant after controlling for hormonal fluctuation



Summary & Future Directions

- ERC and HPC-whole brain rsFC patterns track elapsed time, becoming increasingly dissimilar with longer temporal intervals
- Time-dependent changes in the similarity of ERC and aHPC rsFC patterns show regional specificity and remain significant after controlling for hormonal changes, suggesting that a **slow-drifting temporal context**—independent of spatial context—is represented in ERC- and aHPC-whole brain rsFC patterns
- The strength of time-dependent HPC-whole brain rsFC pattern changes varies along the hippocampal longitudinal axis
- We are running searchlight analysis to refine our results & examining emotional and temporal coding interactions

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