

elte | ppk

Eötvös Loránd University
Faculty of Education and Psychology

ELKH | Eötvös Loránd
Research Network

A Strong Test of Content-Specific Pattern Separation via Distinct Medial Temporal Pathways

Zsuzsanna Nemecz^{1,2,3}, István Homolya^{3,4}, Alex Roland Ilyés^{1,2,3}, Anna Kispál², Tianyao Zhu⁴, Attila Keresztes^{3,2}

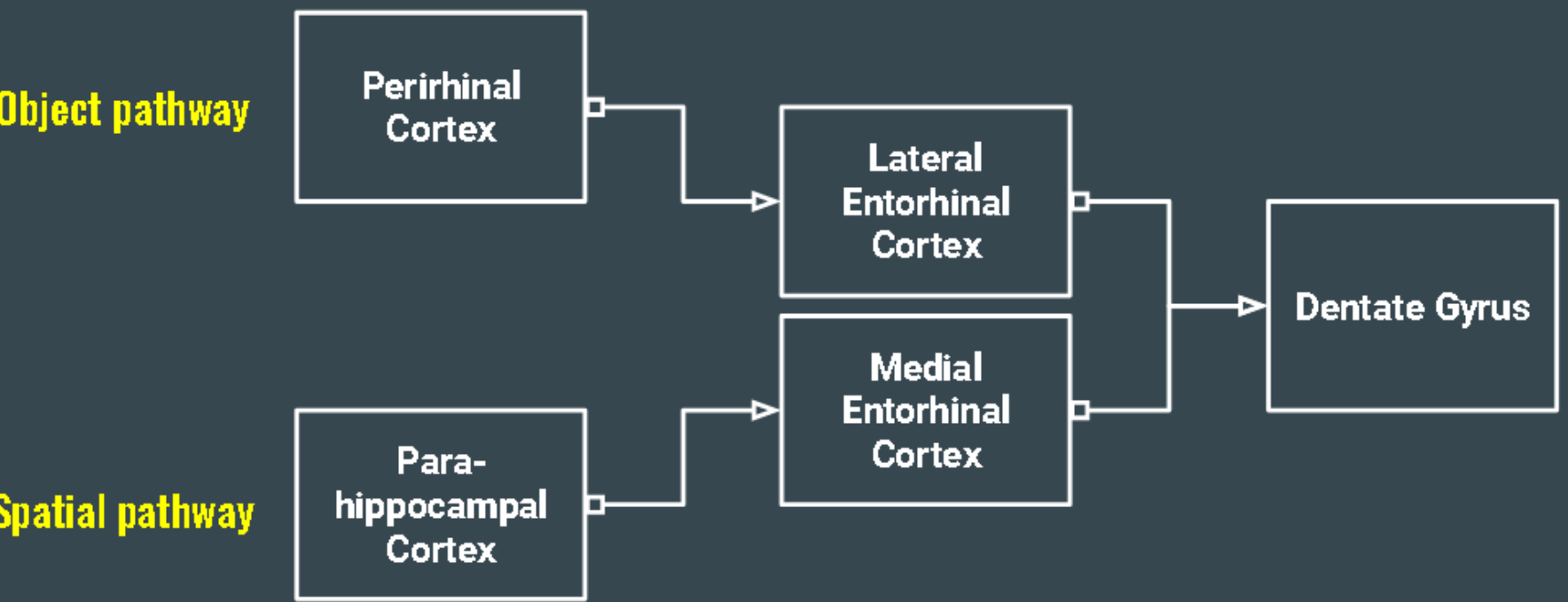
1. Doctoral School of Psychology, Eötvös Loránd University, Budapest, Hungary, 2. Institute of Psychology, Eötvös Loránd University, Budapest, Hungary, 3. Research Centre for Natural Sciences, Budapest, Hungary, 4. Budapest University of Technology and Economics, Hungary, 5. Queen's University, Ontario, Canada

1. Background

- Hippocampal pattern separation (PS) is a neural process of orthogonalizing similar inputs into independent neural representations. This is considered to be a key process of interference reduction in episodic memory. (Leal & Yassa, 2018)
- Little is known about the role of other medial temporal areas in mnemonic interference reduction (Nash et al., 2021).
- The perirhinal (PRC) and the parahippocampal (PHC) cortices have been implicated in content-selective processing of objects and spatial information, respectively (Ranganath and Ritchey, 2012).
- Tasks relying on mnemonic interference reduction in the object and spatial domain have been shown to selectively engage the lateral entorhinal cortex (LEC) and PRC, and the medial entorhinal cortex (MEC) and PHC (Reagh & Yassa, 2014).
- The validity of the two-pathway theory of the medial temporal lobes (MTL) has been recently questioned (Lawrence, Cardoza, Ryan, 2020).
- Behaviorally, pattern separation is usually studied with the Mnemonic Similarity Task (MST, Stark, Kirwan & Stark, 2019), presenting similar everyday objects to the participant. This could induce retrieval of existing memory representations, obscuring PS processes.

2. Objectives

- Investigate interference reduction in the medial temporal lobe in the object and spatial domains in healthy young adults.
- Assess neural pattern separation without the confounding influence of prior knowledge.

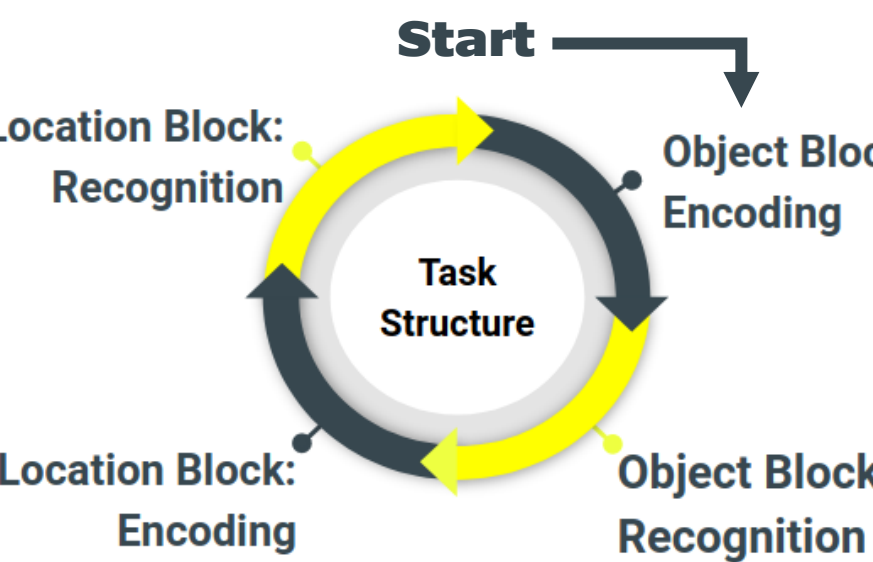


References

Bender et al. (2018). *Hum. Brain Mapp.* 39(2), 916-931.
Lawrence, Cardoza & Ryan (2020). *Hippocampus*, hipo.23203.
Leal & Yassa (2018). *Nat. Neuro.*, 21(2), 163-173.
Nash et al. (2021) *Hippocampus*.
Ranganath, C., & Ritchey, M. (2012). *Nat. Rev. Neuro.* 13(10), 713-726.
Reagh & Yassa (2014). *PNAS*, 111(40), E4264-E4273.
Stark, Kirwan & Stark (2019). *TICS*, 23(11), 938-951.
Yushkevich et al. (2014). *Hum. Brain Mapp.*, 36(1), 258-287.
Kriegeskorte, Mur & Bandettini (2008). *Front. Syst. Neurosci.* 2, 4.

3. Methods

- High-resolution structural and functional magnetic resonance imaging
- Modified version of the Mnemonic Similarity Task with unfamiliar fractals as stimuli during fMRI to reduce bias of previous knowledge
- Resting-state fMRI for connectivity analysis
- Wide-range of behavioral covariates measuring long-term memory, working memory, visual discrimination and processing speed



Task design

- Modified version of MST
- Object and Spatial trials in 6 blocks
- Encoding and recognition phase in each block

Encoding Phase

Object block

Would you display this image in the gallery?

- 48 images: new, exact repetition, lure

Spatial block

Would you display this image at this location?

- 48 stimuli: new, exact repetition, close location

Recognition Phase

Object block

Have you seen exactly this image?

- Response options: Yes (Old image), No (New image)
- 24 images: target, foil, lure

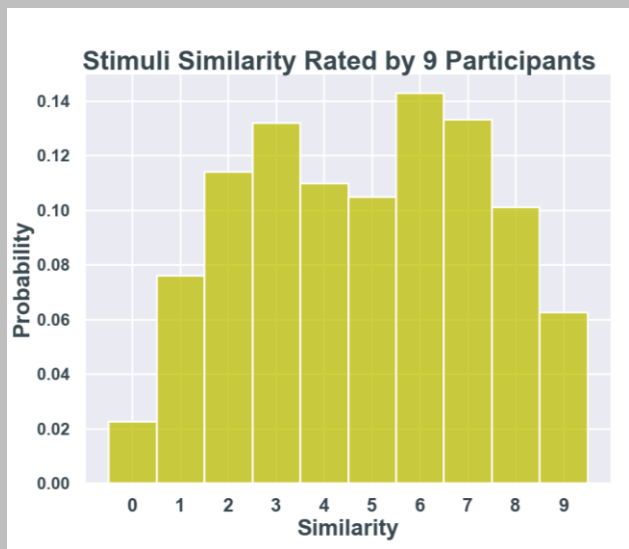
Spatial block

Have you seen this image at this location?

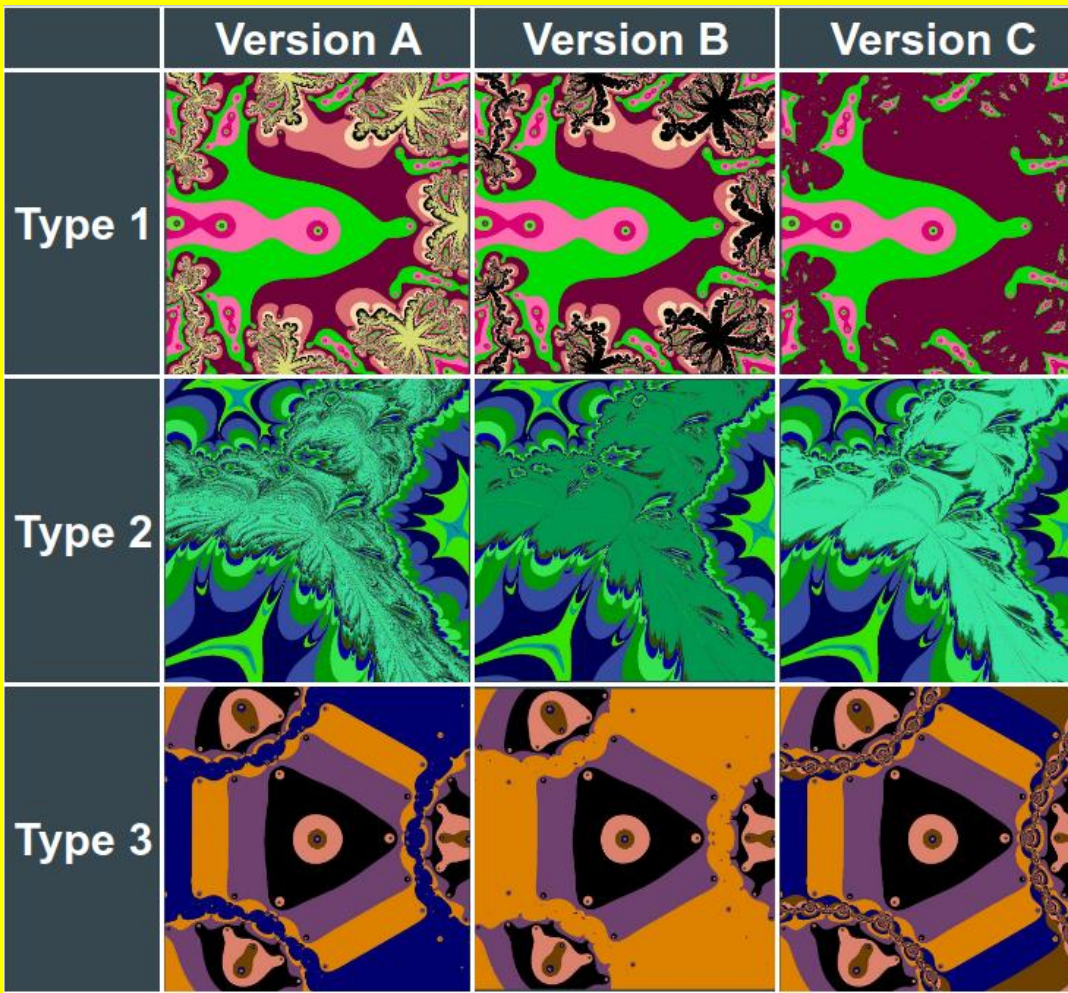
- Response options: Yes (Old location), No (New location)
- 24 stimuli: new, exact repetition, lure

Stimuli

540 fractal images: 180 image types, 3 versions from each type



- Similarity calculated by
- pixel-wise difference of colorful images based on RGB value
 - pixel-wise mean standard error between grayscale images
 - rated on a 0-9 scale (0: same, 9: very different)



Magnetic Resonance Imaging

Whole Brain T1-weighted Sequence

Resolution: 1mm isotropic

Partial FoV Proton Density Sequence

Resolution: 0.4*0.4*2mm

Functional Echo Planar Sequence

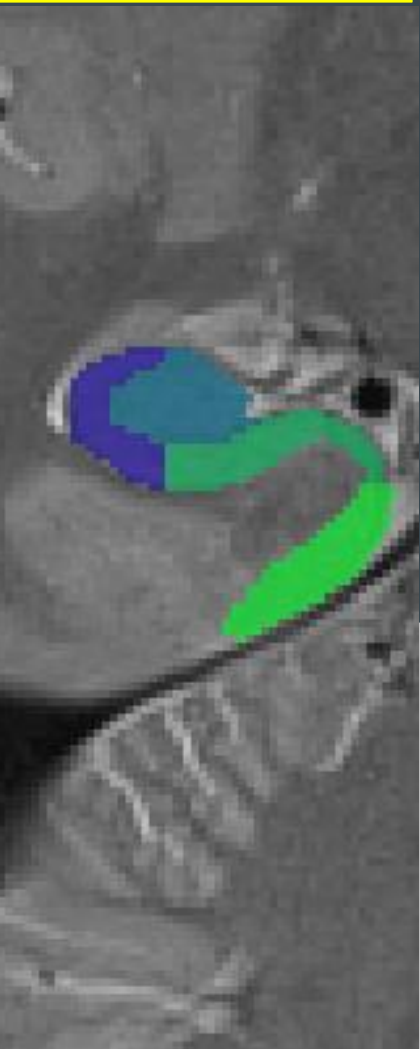
Resolution: 2mm isotropic

Repetition Time: 0.71s

Multiband Factor: 6

Echo Time: 0.031s

Scans aligned with the longitudinal axis of the hippocampus.



Planned Analysis

- Segmentation of the hippocampus
- ASHS (Yushkevich et al, 2014)

Functional analysis

- Across conditions
 - Spatial/Object
 - Target/Lure/Foil
- ROIs: PHC, PRC, LEC, MEC, DG/CA3

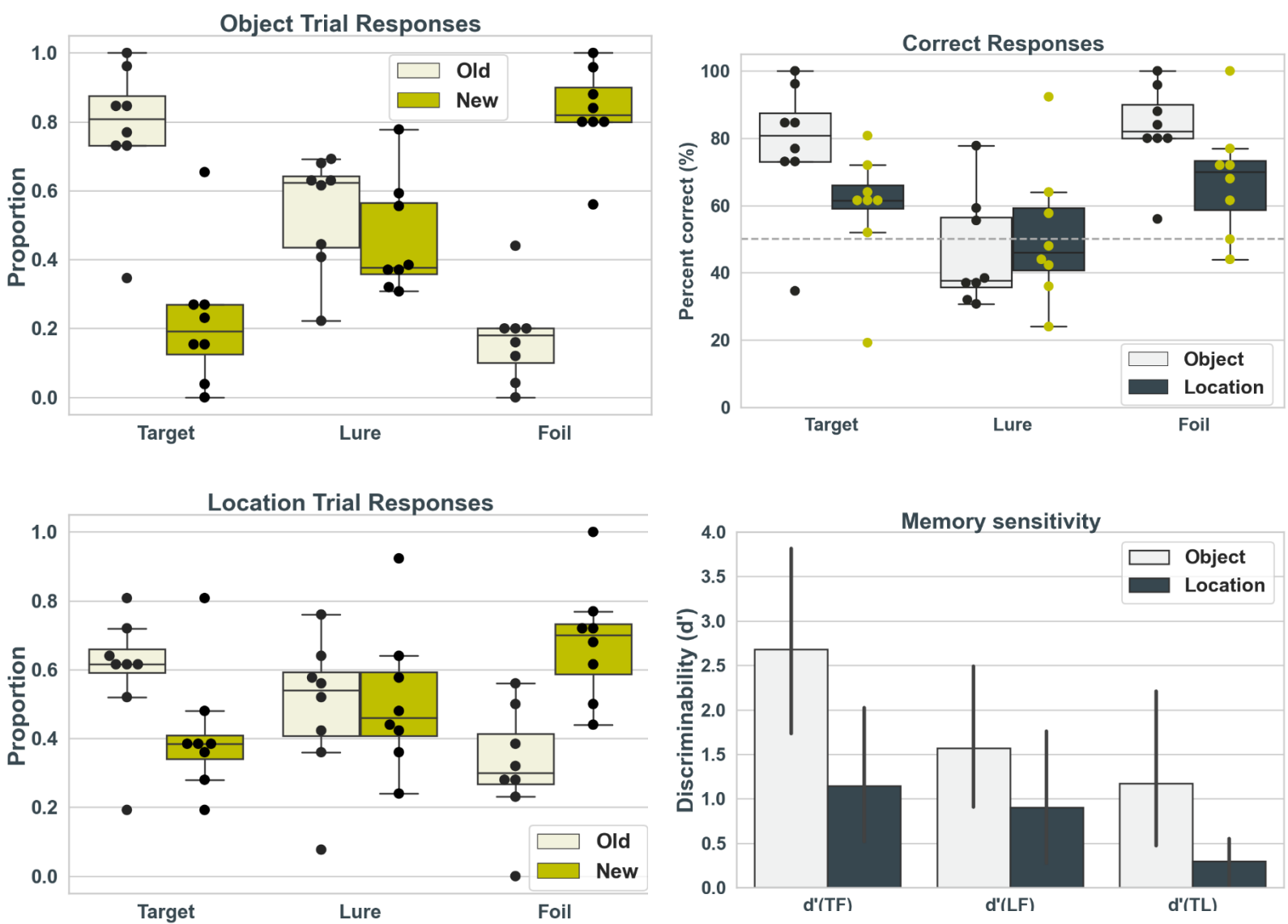
Univariate analysis

- Repetition suppression

Multivariate analysis

- Representational Similarity Analysis (RSA, Kriegeskorte et al., 2008)

4. Pilot Behavioral Results



5. Expected Results

- Repetition suppression in all MTL areas, except for PRC for object lures, and PHC for spatial lures.
- Negative correlation between object similarity and activity pattern similarity in the PRC & DG/CA3.
- Negative correlation between spatial similarity and activity pattern similarity in the PHC & DG/CA3.
- Within-pathway connectivity will predict discrimination of content-specific memories.

6. Outlook

Testing our predictions will contribute to the critical assessment of the two processing streams view of the medial temporal lobe.