Exploring the neural mechanisms underlying pattern separation in preschool-aged children: an fMRI paradigm

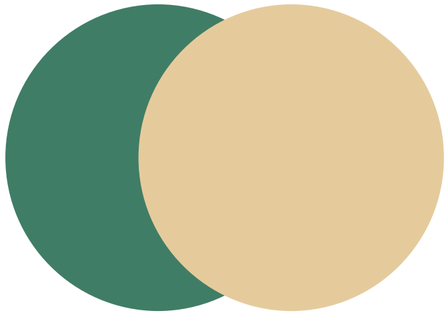
Jade Dunstan

March 25, 2023

Society for Research on Child Development

Salt Lake City, Utah

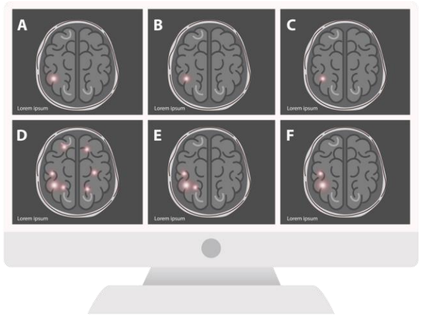
Overview



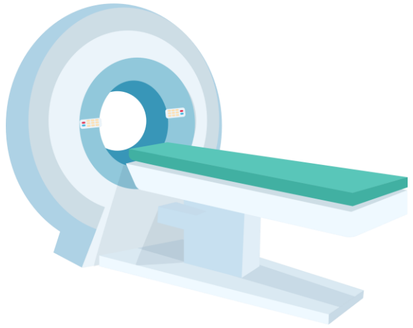
Introduction

What is Pattern Separation?

The current study



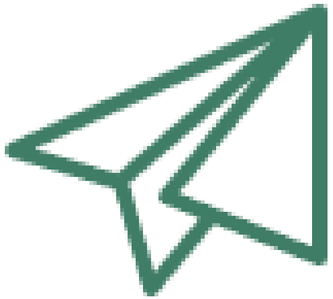
Results



Methods

Participants

Task procedure



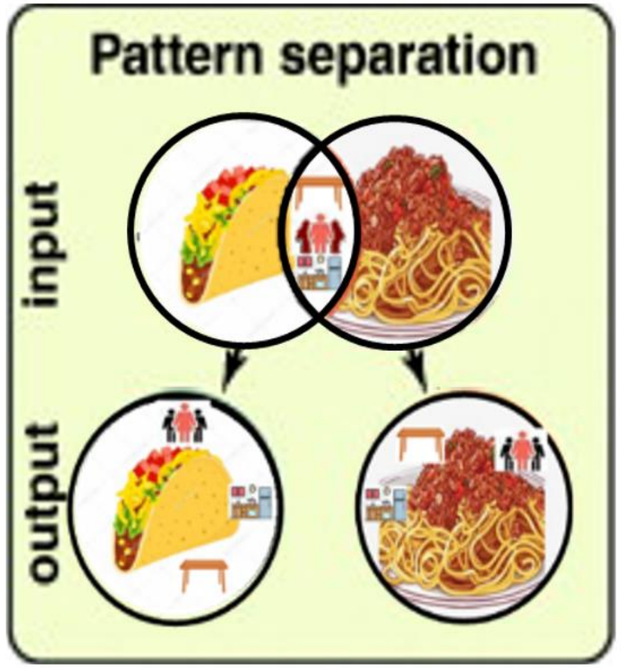
What we've learned

Limitations

Where should we go next?

What is Pattern Separation?

Pattern separation is a computational process by which patterns of neuronal activation underlying similar memories are made distinct to counteract interference during retrieval (Norman & O'Reilly, 2003)

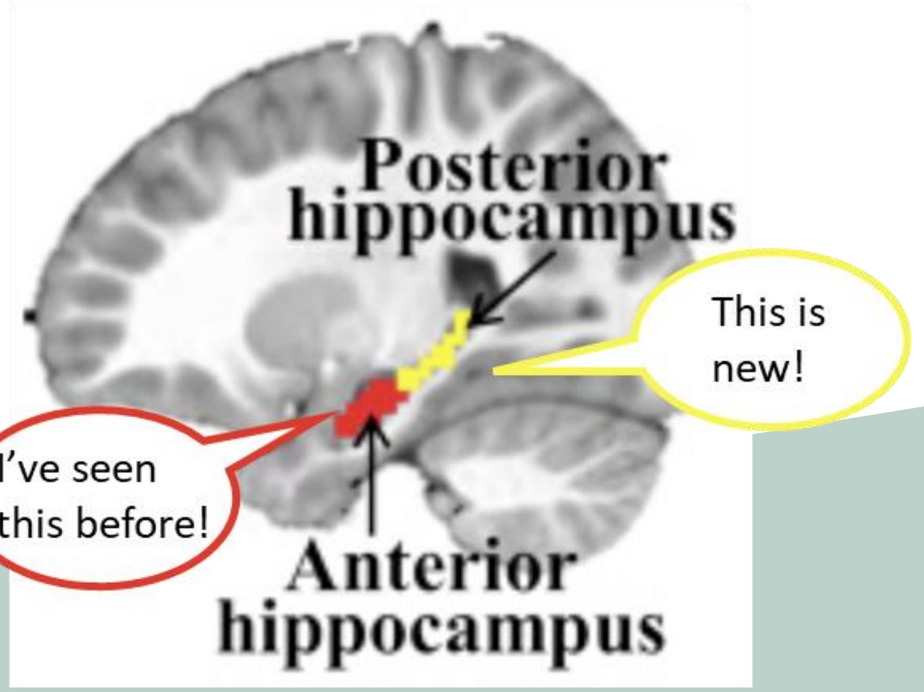


Pattern separation allows us to separate out events with overlapping features (Yassa & Stark, 2011)

How does our brain do this?

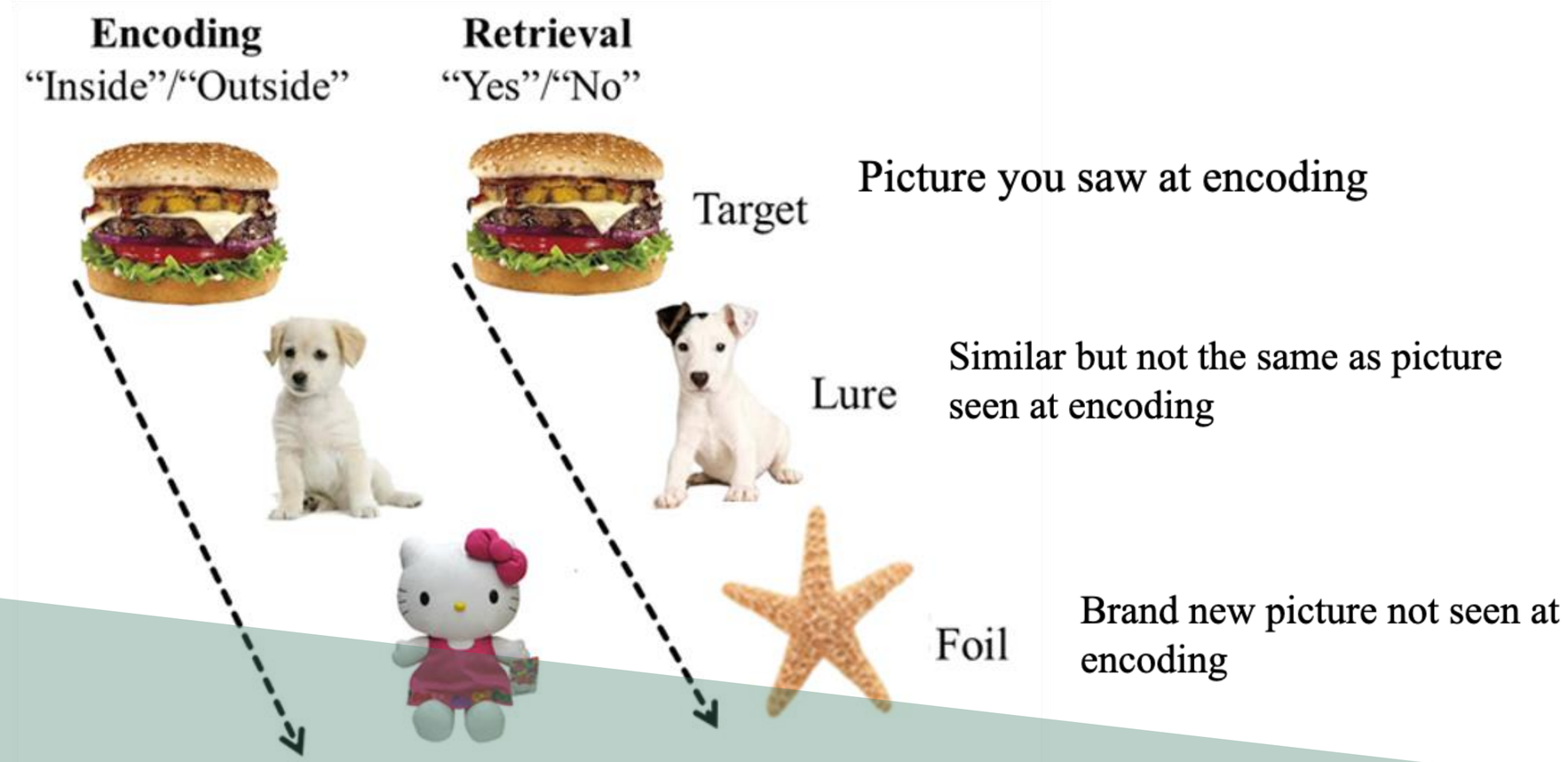
The Hippocampus

Pattern separation in dentate gyrus (DG) ⟶ hippocampal subfield located primarily in posterior hippocampus (Malykhin et al., 2010)



Caveat: We Cannot Directly Measure Pattern Separation

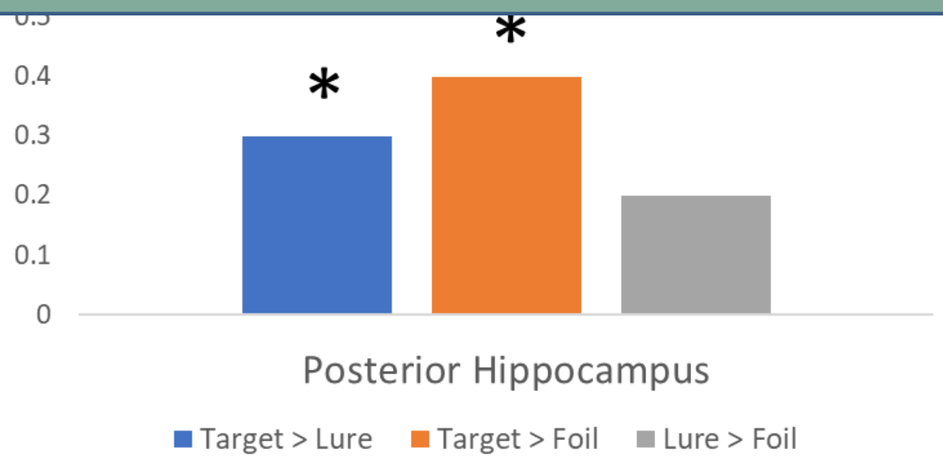
Behavioral tasks that require mnemonic discrimination of similar stimuli serves as an index of this process (e.g., Kirwan & Stark, 2007; Lacy et al., 2011)



Adult Literature on Functional Activation and Pattern Separation

Lacy et al. (2011) had participants complete an incidental "Indoor"/"Outdoor"

Do you think a preschooler could do this task in the scanner?



Challenges Associated with Scanning Preschool-Aged Children

How can we promote successful child scans?

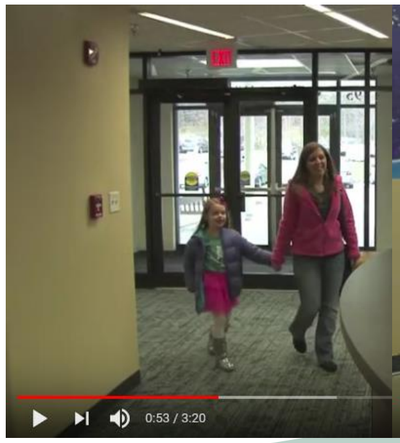
Children may not want to get into the scanner (anxious/defiant)

Children may struggle to stay engaged during the scan

Children may struggle to stay still during the scan

Scanning preschool-aged children: before the session

- Tunnel w/ scanner noises
- MRI book
  - Brain camera
  - 3Ss: Still, Soft & Super-duper
- MRI video
  - https://www.youtube.com/watch?v=HvJSXxFUpZg

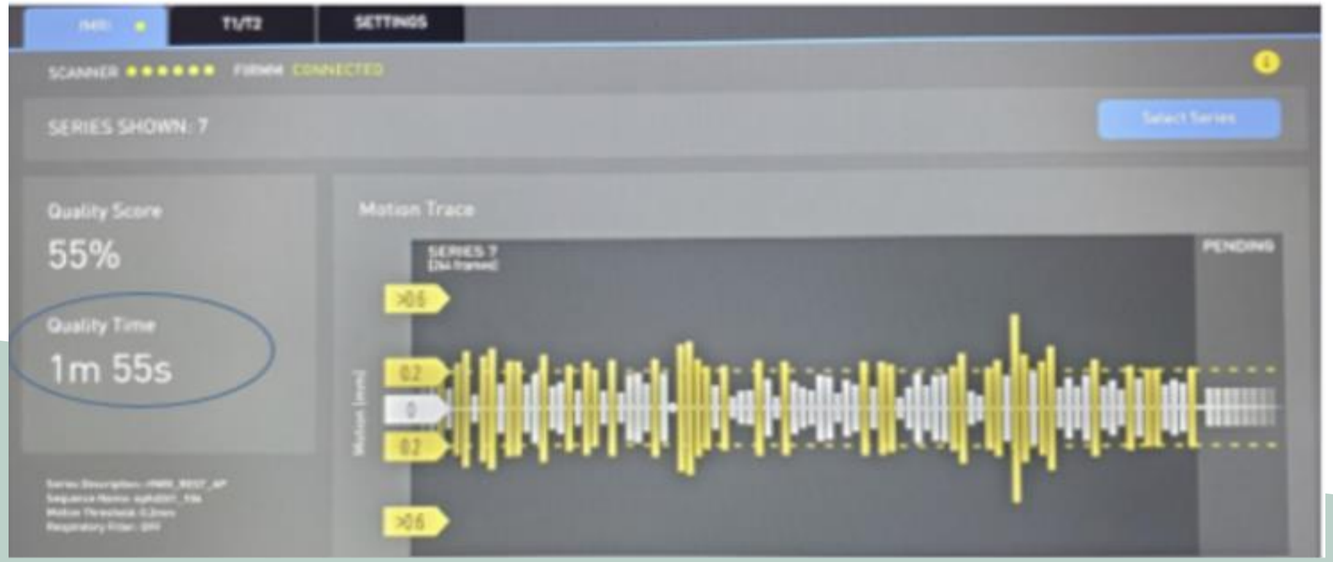


Scanning preschool-aged children: Mock MRI

- Our lab uses a space-themed mock MRI to train participants on the in-scanner functional tasks and get them comfortable with the machine itself
  - Can show them on Mom/Experimenter or Stuffed animal first
  - Outside scanner – scanner noises
  - Metal detector/Magic wand – “poses”
  - Scanner bed
  - Headphones
  - Movie
  - Motion “feedback” -> Squeeze foot, don’t look down, answer verbally – don’t nod your head

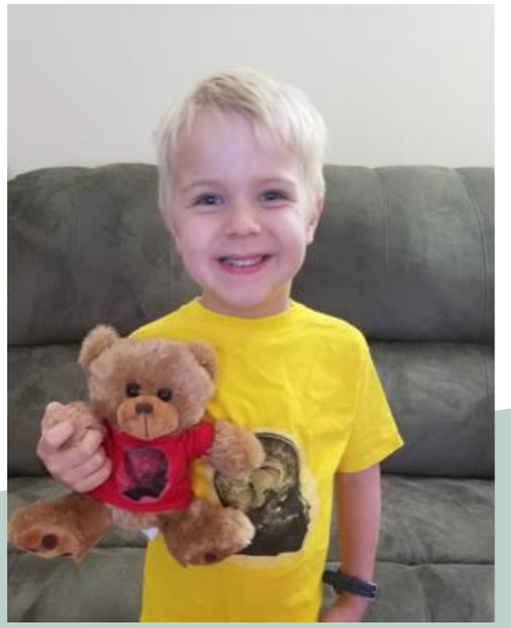
Scanning preschool-aged children: Motion Correction

- Framewise Integrated Real-Time MRI Monitoring (FIRMM)
- MRI “buddy” stays in the room with the child to provide motion feedback



Scanning preschool-aged children: Brain Prizes!

- Our lab offers participants different prizes that use the child's brain images
- This encourages children to stay still during the scan to get the best possible picture

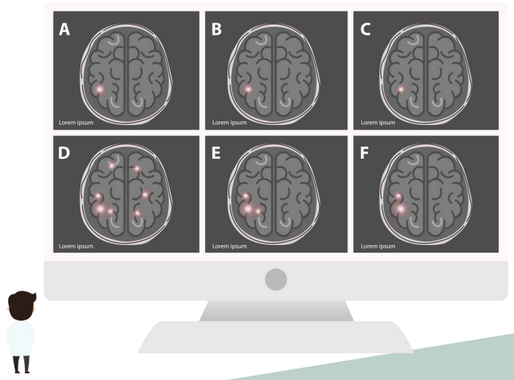

Riggins Lab Success Rates (as of 2021)

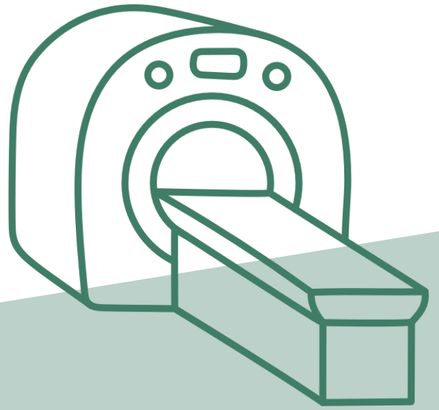
	3yrs	4yrs	5yrs	6yrs	7yrs	8yrs		Total
# of Scheduled visits	25	90	49	41	30	31		266
# of kids who went in scanner	25	84	49	41	29	31		259
# of kids who attempted scans	25	83	49	41	29	31		258
# of successful “task-free” functional scans (>5min of data at <.3mm)	22	65	18	31	25	23		184
# of successful structural scans	21	78	43	41	29	31		243
% of successful “task-free” functional scans (at least 5min of data at <.3mm)	**88%**	**72%**	**37%** *	**76%**	**83%**	**74%**		**69%**
% of successful structural scans	**84%**	**87%**	**88%**	**100%**	**97%**	**100%**		**91%**

*Our lab started out scanning 5-year-olds (we’ve gotten much better since then!)

The Current Study: Developing a Child-Friendly fMRI MST Paradigm

- Goal: Use our child neuroimaging experience to develop and validate child-friendly assessment of hippocampal activation and pattern separation
- Replicate Incidental Encoding/active retrieval findings in adults
- Replicate event-related design results with a block design

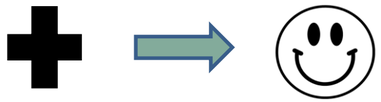




Adapting the Adult MST fMRI Paradigm for Children

Changes made to Lacy et al. (2011):

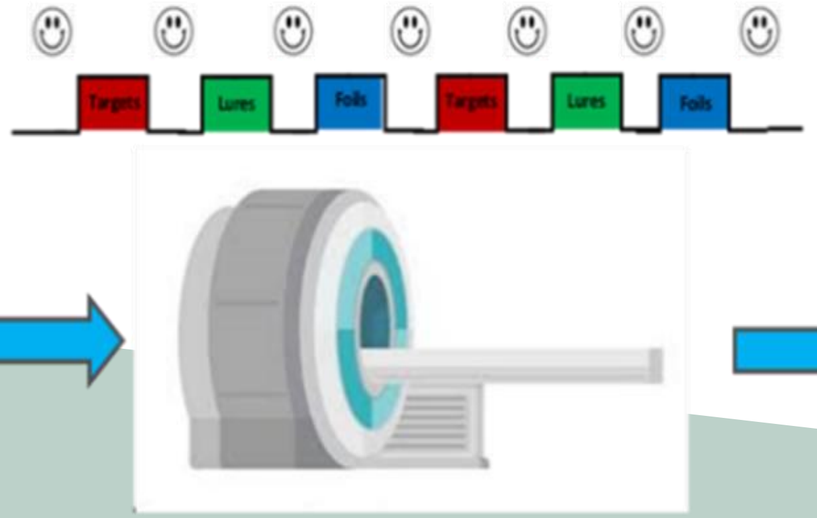
- Event-related Design → Block Design
  - Higher power, shorter runs



- Smaller voxel size (0.75 mm isometric) → larger voxel size (2.2 mm isometric)
  - Resolution/Motion Tolerance tradeoff
- No in-scanner behavioral response

Out-of-scanner incidental encoding

In-scanner passive retrieval: "Pay attention to the pictures"

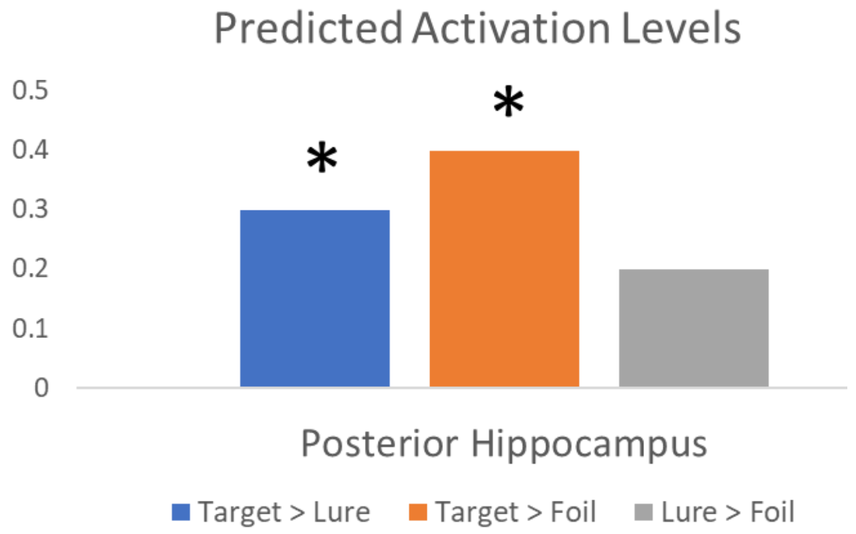


Out-of-scanner active retrieval

Research Questions & Hypotheses

Can we replicate the Lacy et al. (2011) findings in an adult sample?

- We expect evidence of *pattern separation* in the posterior hippocampus
  - Targets will show significantly greater activation relative to both Lures and Foils → Lures being treated like novel stimulus rather than repeated stimuli



Can we use this novel paradigm to assess pattern separation in early childhood?

- We anticipate that young children will be able to complete the task

Participants

39 adults, ages 18-28 years (Mage = 23.30 ± 3.07 years; 27 females)

13 preschool-aged children (Mage = 4.15 ± 0.67 years; 5 females)

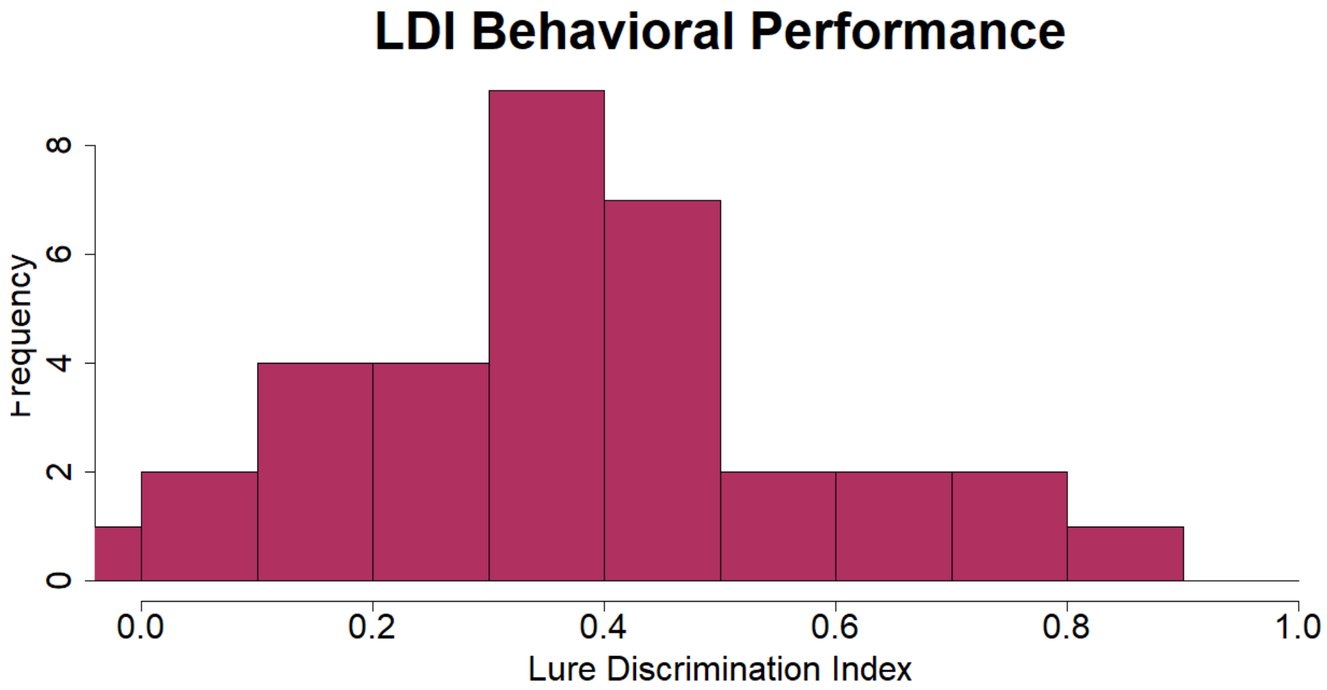
- Recruited through UMD
- No history of head or brain injury and no contraindications for MRI per self-report or parent-report

	Age 3-4
# of Scheduled visits	17
# of kids who went in scanner	16
# of kids who attempted scans	16
# of successful **task-based** functional scans	13
# of successful structural scans	13
% of successful task-based functional scans	**81%**
% of successful structural scans	**81%**

Adult Results: Behavioral Performance

Lure Discrimination Index (LDI)
→ # “Yes” Responses to Targets - # “Yes” Responses to Lures

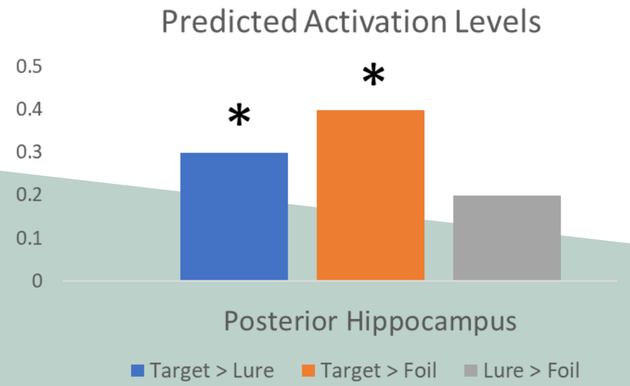
Participants showed variability in “precision” or memory for item details

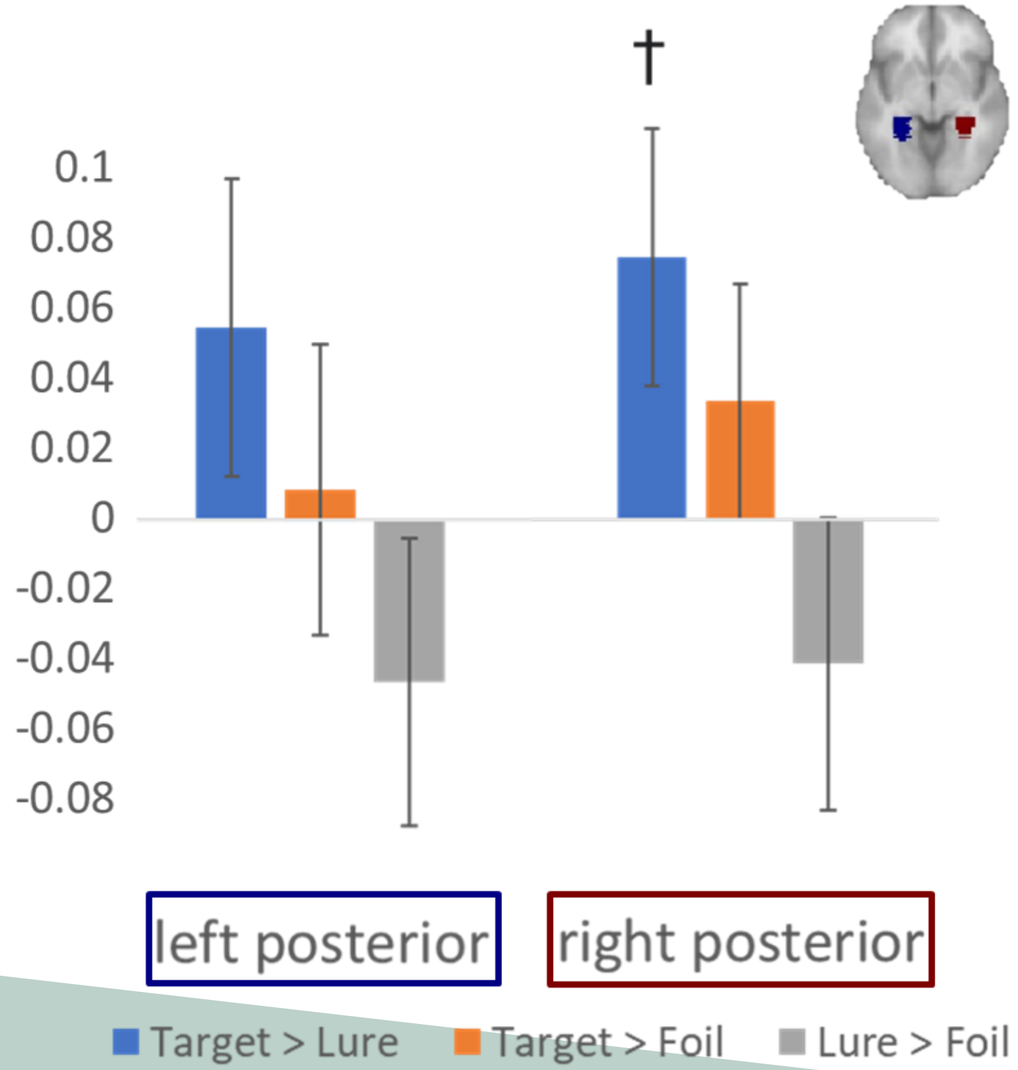


Does posterior hippocampus respond differentially to Targets and Lures in adults?

Activation for Targets was **marginally greater than activation for Lures** in right posterior hippocampus (t = 2.05, $p_{corrected}$ = 0.094).

Some evidence of pattern separation processes in posterior hippocampus

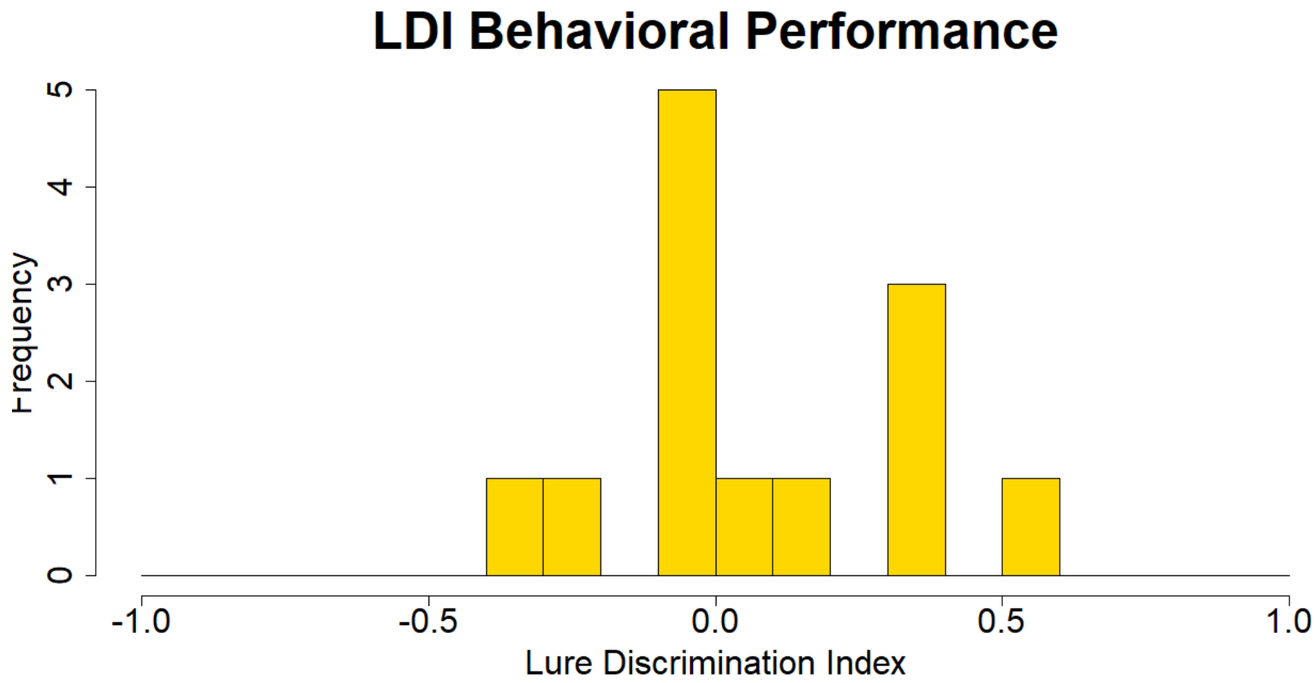




Preliminary Child Results: Behavioral Performance

Children show even more variability in precision memory than adults

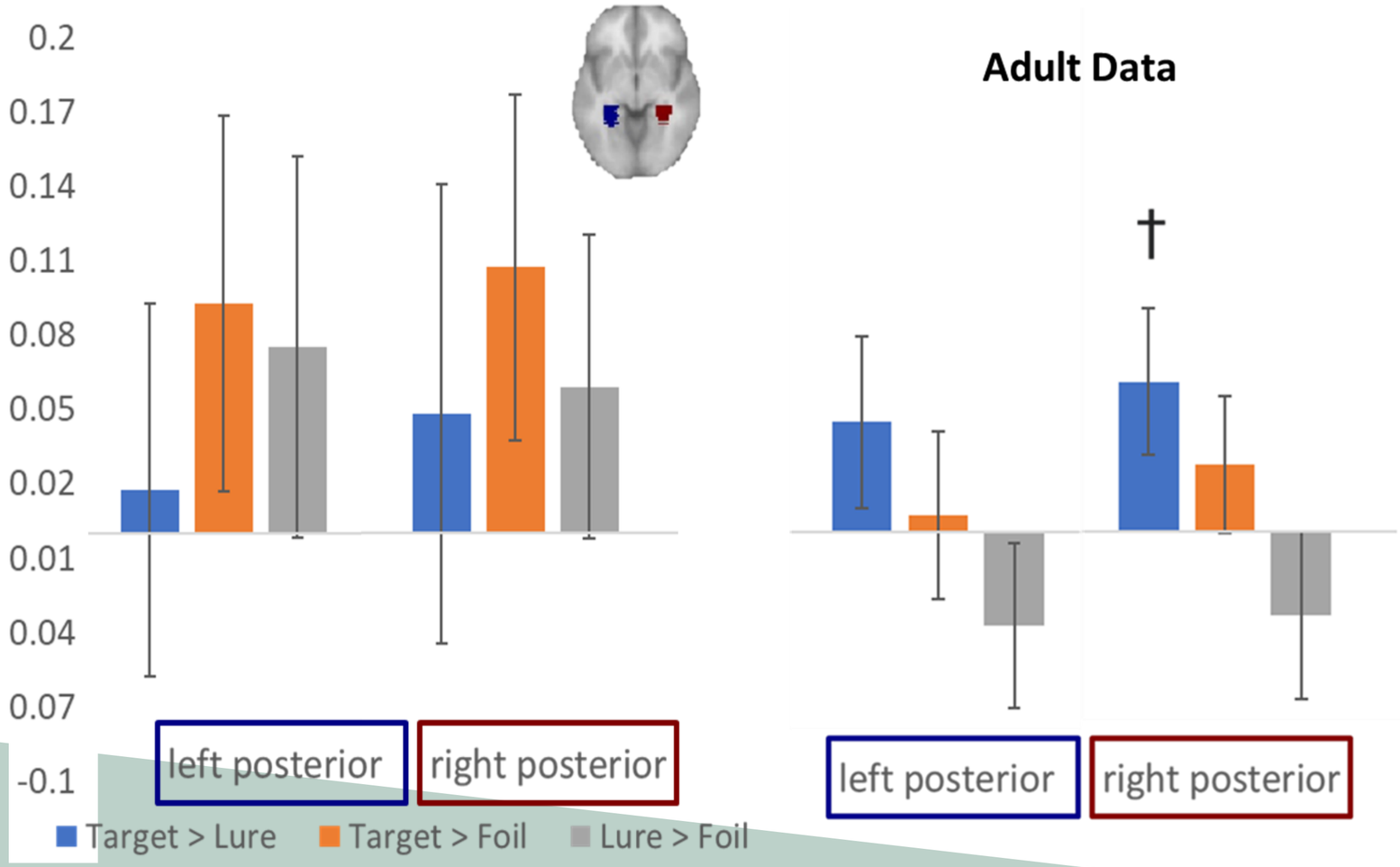
- Negative LDI indicates tendency to overgeneralize (treat Lures like Targets)



Preliminary Child Results: Does posterior hippocampus respond differentially to Targets and Lures?

Children did not show significantly different activation levels for Targets and Lures in posterior hippocampus ($p > .05$)

Children and adults do not appear to show the same hippocampal functional activity during a pattern separation task



Discussion

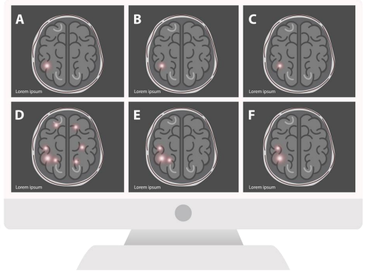
Adult results revealed some evidence of pattern separation processes in posterior hippocampus

- Marginal activation differences between Targets and Lures in right posterior hippocampus
- Partial replication of Lacy et al. (2011) findings

Child data collection was a success!

- Of 16 participants that attempted the MRI, 13 provided useable data (81.25% success rate)
- Children do not show differential activation for Targets relative to Lures

  → Consistent with worse behavioral performance



Limitations

- Investigation of anterior/posterior hippocampus is coarser than looking at subfields
- Only looked at mean activation/contrast estimates
- Weak signal to noise ratio
- Individual variability in mean activation for the hippocampal ROIs
- Small sample size for child data

Future directions

- Collect more child data
- Investigate role of hippocampal subfields on pattern separation using our fMRI paradigm
- Use the repetition sensitivity approach described by Klippenstein et al. (2020)
  - Identify regions sensitive to the task conditions and restrict analyses to those voxels
- Use local heterogeneity regression (Local-Hreg; Purcell & Rapp, 2018) to investigate the neural similarities (or differences) in response to Targets, Lures, and Foils across the voxels of the hippocampus

Thank you!

Neurocognitive Development Lab

Thank you to all of our families for participating in this study and the members of the Neurocognitive Development Lab for assistance with this project.

Special shoutout to Brooke Kohn for making these slides aesthetically pleasing (thank you)!

Jade Dunstan via e-mail at: jdunstan@umd.edu

www.ncdl.umd.edu/index.html

References

1. Bakker, A., Kirwan, C. B., Miller, M., & Stark, C. E. (2008). Pattern separation in the human hippocampal CA3 and dentate gyrus. *science*, *319*(5870), 1640-1642.
2. Botdorf, M. A. (2019). Development of the Episodic Memory Network in Early Childhood: Insights from Graph Theoretical Analysis (Doctoral dissertation, University of Maryland, College Park).
3. Canada, K. L., Ngo, C. T., Newcombe, N. S., Geng, F., & Riggins, T. (2019). It's all in the details: Relations between young children's developing pattern separation abilities and hippocampal subfield volumes. *Cerebral Cortex, 29*(8), 3427-3433.
4. Cansino, S., Maquet, P., Dolan, R. J., & Rugg, M. D. (2002). Brain activity underlying encoding and retrieval of source memory. Cerebral cortex, 12(10), 1048-1056.
5. Doxey, C. R., & Kirwan, C. B. (2015). Structural and functional correlates of behavioral pattern separation in the hippocampus and medial temporal lobe. Hippocampus, 25(4), 524-533.
6. Hannula, D. E., & Ranganath, C. (2009). The eyes have it: hippocampal activity predicts expression of memory in eye movements. Neuron, 63(5), 592-599.
7. Hay, L., Duffy, A. H. B., Gilbert, S. J., & Grealy, M. A. (2022). Functional magnetic resonance imaging (fMRI) in design studies: Methodological considerations, challenges, and recommendations. *Design Studies, 78*, 101078.
8. Hsieh, L. T., Gruber, M. J., Jenkins, L. J., & Ranganath, C. (2014). Hippocampal activity patterns carry information about objects in temporal context. Neuron, 81(5), 1165-1178.
9. Kirwan, C. B., & Stark, C. E. (2007). Overcoming interference: An fMRI investigation of pattern separation in the medial temporal lobe. *Learning & Memory, 14*(9), 625-633.
10. Lacy, J. W., Yassa, M. A., Stark, S. M., Muftuler, L. T., & Stark, C. E. (2011). Distinct pattern separation related transfer functions in human CA3/dentate and CA1 revealed using high resolution fMRI and variable mnemonic similarity. *Learning & memory, 18*(1), 15-18.
11. Malykhin, N. V., Lebel, R. M., Coupland, N. J., Wilman, A. H., & Carter, R. (2010). In vivo quantification of hippocampal subfields using 4.7 T fast spin echo imaging. *Neuroimage, 49*(2), 1224-1230.
12. Ngo, C. T., Newcombe, N. S., & Olson, I. R. (2018). The ontogeny of relational memory and pattern separation. Developmental Science, 21(2), e12556.
13. Norman, K. A., & O'Reilly, R. C. (2003). Modeling hippocampal and neocortical contributions to recognition memory: a complementary-learning-systems approach. *Psychological review, 110*(4), 611.
14. Prabhakar, J., Johnson, E. G., Nordahl, C. W., & Ghetti, S. (2018). Memory-related hippocampal activation in the sleeping toddler. *Proceedings of the National Academy of Sciences, 115*(25), 6500-6505.
15. Purcell, J. J., & Rapp, B. (2018). Local response heterogeneity indexes experience-based neural differentiation in reading. NeuroImage, 183, 200-211.
16. Riggins, T., Geng, F., Botdorf, M., Canada, K., Cox, L., & Hancock, G. R. (2018). Protracted hippocampal development is associated with age-related improvements in memory during early childhood. Neuroimage, 174, 127-137.
17. Riphagen, J. M., Schmiedek, L., Gronenschild, E. H., Yassa, M. A., Priovoulos, N., Sack, A. T., ... & Jacobs, H. I. (2020). Associations between pattern separation and hippocampal subfield structure and function vary along the lifespan: A 7 T imaging study. Scientific reports, 10(1), 1-13.
18. Yassa, M. A., & Stark, C. E. (2011). Pattern separation in the hippocampus. *Trends in neurosciences, 34*(10), 515-525.