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

Methods
Participants
Task procedure

Results

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) \(\rightarrow\) 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)
Lacy et al. (2011) had participants complete an incidental encoding task involving a "Indoor"/"Outdoor" concept.

- Inside/outside button response
- No memory test administered
- Event-related design (longer runs)
- Significant differential activation for Targets relative to Lures
- Lures treated like novel stimulus (Foils) in posterior hippocampus

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)

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

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

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

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

- Predicted Activation Levels
  - Target > Lure
  - Target > Foil
  - Lure > Foil
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

<table>
<thead>
<tr>
<th></th>
<th>Age 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td># of Scheduled visits</td>
<td>17</td>
</tr>
<tr>
<td># of kids who went in scanner</td>
<td>16</td>
</tr>
<tr>
<td># of kids who attempted scans</td>
<td>16</td>
</tr>
<tr>
<td># of successful task-based functional scans</td>
<td>13</td>
</tr>
<tr>
<td># of successful structural scans</td>
<td>13</td>
</tr>
<tr>
<td>% of successful task-based functional scans</td>
<td>81%</td>
</tr>
<tr>
<td>% of successful structural scans</td>
<td>81%</td>
</tr>
</tbody>
</table>
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.
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.
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!

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


