Neural Bases of the Development of Relational Memory

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Introduction

Even though behavioral studies of memory in children have shown that declarative/episodic memory continues to develop into young adulthood, very little is known about the neural systems mediating this development. Using fMRI and the subsequent memory paradigm, greater activity during encoding for subsequently remembered items than for subsequently forgotten items has been reported in bilateral prefrontal cortex (PFC) and bilateral medial temporal lobes (MTL). The PFC does not reach adult levels of structure or function until late adolescence and little is known about the functional development of the MTL. The extant fMRI studies of memory development examined recognition memory instead of recall, and memory for items rather than association between items. Both MTL and PFC are particularly involved in memory for contextual details, or relational encoding.

Goal: To examine contributions of MTL and PFC to successful memory encoding and recall for picture pairs across development

Participants

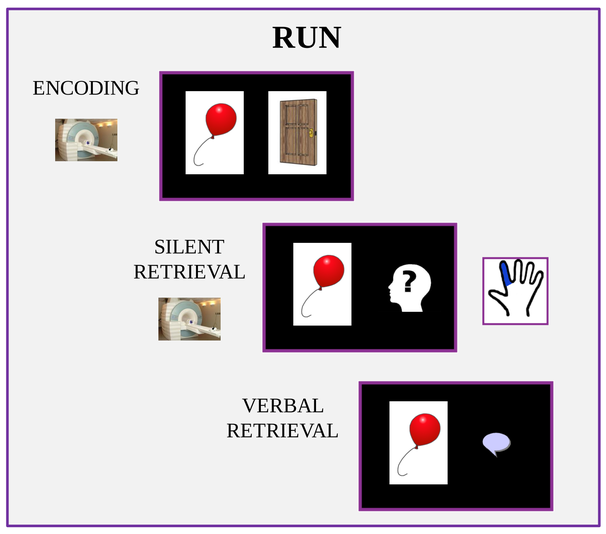
Typically developing children, 2 age groups:

Younger Children	Older Children
8- to 9-year-olds	12- to 13-year-olds
N = 13 (6 females)	N = 12 (6 females)
mean = 8 years, 8 months	mean = 12 years, 8 months
range= 8y, 3m – 9y, 4m	range = 12y, 2m - 13y, 3m

** An additional 13 children were tested but excluded due to motion artifact (n=8) or insufficient trials (n=5)

Procedure

Paired-Associates Cued-Recall Task



Event-Related Design

4 Runs
20 pairs/Run
Stimulus Duration = 4000 ms
ISI = average 2000 ms
(jitter 1500-2500 ms)
TR =2000 ms

Fixation = 6 TRs
2 before each block

Imaging:

3T Siemens Trio

Structural: MPRAGE, T1-weighted, 240 sagittal slices (1x1x1 mm voxel)
[TR=2530, TE=3.65, Flip = 7°, Matrix = 256 x 256, FOV = 256, Slice thickness = 1 mm, Scan duration= 10 min, 49 sec]

Functional: Gradient echo EPI, T2*-weighted, 34 axial slices (3.125 x 3.125 x 3 mm voxel)
[TR=2000, TE=28, Flip = 80°, Matrix = 64 x 64, FOV=200, Slice thickness = 3 mm, Repetitions = 131, Scan duration = 4 min, 26 sec]

Image Data Processing:

BrainVoyager QX (version: 2.0.8)

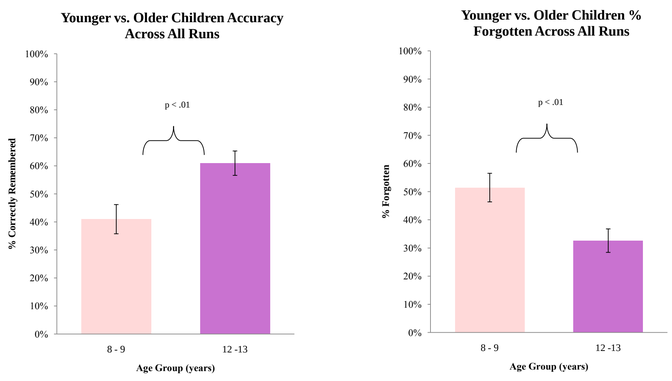
Preprocessing: slice scan time correction, linear trend removal, high-pass temporal filter for non-linear drifts, spatial smoothing with a 9mm Gaussian kernel, and 3D motion correction

Statistical contrasts tested with GLM
Age group included in a second level
All group-level analyses with random effects modeling (DV = % change in signal)
Significance criteria: 10 contiguous functional voxels; $p < .05$ for group-level analyses

Behavioral Results

"Remembered" items were defined as items for which the participant indicated recall with button press during the silent retrieval phase *and* gave correct response during the verbal retrieval phase.

"Forgotten" items were defined as items for which the participants did not press the button during the silent retrieval phase *and* failed to give a response during the verbal retrieval phase.



Older children showed significantly better performance in the paired-associates cued-recall task compared to the younger children.

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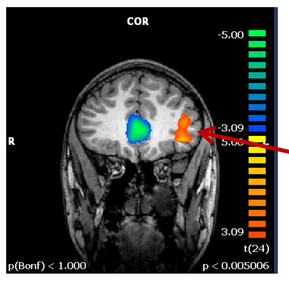
fMRI Results: Encoding & Subsequent Memory Effects

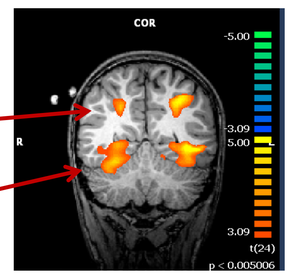


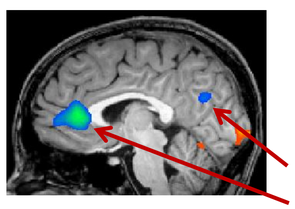
Both age groups showed increased *activation* for subsequently remembered pairs compared to subsequently forgotten pairs in left prefontal, bilateral parietal, and ventral temporal cortex.

Left Inferior Prefrontal
xyz = -41 31 6

Bilateral Parietal
Left xyz = -29 -51 35
Right xyz = 24 -54 34

Bilateral Posterior Parahippocampal & Fusiform Gyri
Left xyz = 27 -39 -7 Right xyz = -34 -43 -9

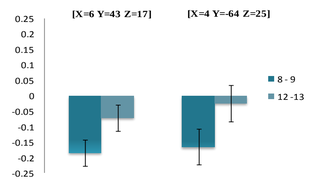




Both age groups also showed increased *deactivations* in medial prefrontal and parietal cortex for subsequently remembered compared to subsequently forgotten pairs.

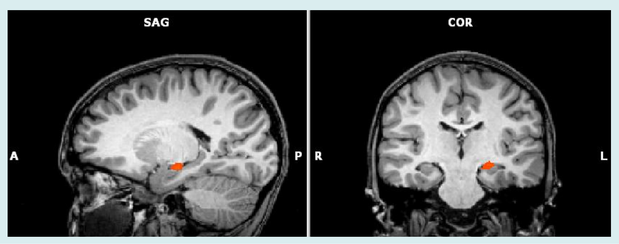
Left Precuneus xyz = -5 -65 27

Medial Prefrontal & Anterior Cingulate Gyrus
xyz = 6 40 10



Within a subset of these two regions that showed deactivation, younger children showed significantly more signal change than older children.

fMRI Results: Developmental Effects on Hippocampus

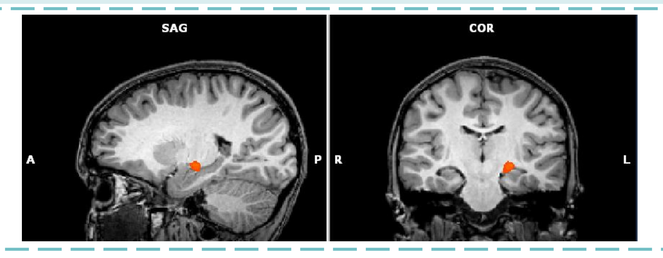


Successful Encoding > Baseline

Left Anterior Hippocampus (xyz = -20 -21 -10)

Older children activated this region significantly more for successfully encoded pairs.

Younger children did not show a significant signal change in this region.



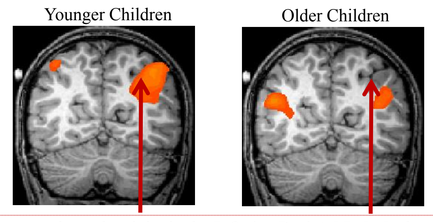
Successful Recall > Baseline

Left Anterior Hippocampus (xyz = -22 -19 -10)

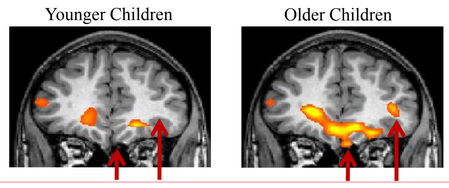
This region was activated in the whole group during successful recall. However, *neither* group showed a significant signal change when analyzed separately.

Notes: 1) Regions of activation outside of hippocampus have been masked. 2) Additional activity in posterior hippocampus but contiguous with visual stream activity.

fMRI Results: Developmental Effects of Recall Success

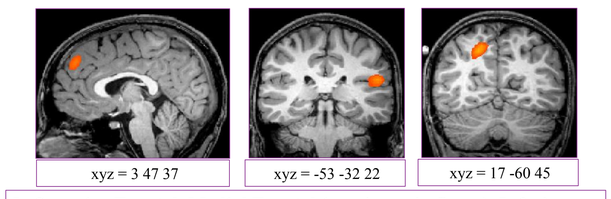


Both age groups showed activity in the **Inferior Parietal Lobule,** however, younger children activated a significantly larger region (xyz = -32 -60 37) on the left compared to older children during successful recall.
(Successful Recall v. Baseline > Unsuccessful Recall v. Baseline)



Compared to younger children, older children showed additional regions of activity in the Left **Inferior Frontal Gyrus** (xyz = -38 38 10) and **Ventromedial Prefontal Cortex** (xyz = -5 39 -16) during successful recall.
(Successful Recall v. Baseline > Unsuccessful Recall v. Baseline)

fMRI Results: Comparing Encoding to Retrieval



xyz = 3 47 37 | xyz = -53 -32 22 | xyz = 17 -60 45

In **Superior Frontal**, **Medial Frontal** (not shown in figure), **Inferior Parietal** and **Superior Parietal** regions, older children showed greater activity for successful recall than for successful encoding. Younger children showed no difference in these regions for this comparison.
(Successful Recall v. Baseline > Successful Encoding v. Baseline)

Right posterior **Hippocampus** (xyz = 25 -38 -1)
Right **Parahippocampal Gyrus** (xyz = 25 -40 -4)

Younger children showed greater activity for encoding than retrieval; however, the older children showed the opposite pattern, with greater posterior hippocampal activity for retrieval than for encoding.

Note: Regions of activity outside of shown regions have been masked.

Conclusions

- Behavioral accuracy in the paired-associates cued-recall task was significantly worse for the 8- to-9-year-old children than the 12- to- 13-year-old children.
- We observed an activation pattern for the subsequent memory effect that was similar to what was previously reported in the literature for adults. Both age groups also showed memory related deactivations (stronger effect for the younger group) in regions that were previously reported as being part of the default mode network.
- Older children activated the left anterior hippocampus for successful encoding (compared to fixation baseline).
- During successful recall, younger children demonstrated greater activation in the parietal regions, whereas older children showed greater activity in the prefrontal regions.
- The two groups differed in the way they recruited regions in the frontal cortex, parietal cortex and the posterior hippocampus/parahippocampal regions during encoding versus recall.

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