Variations in task difficulty dissociate activity in prefrontal cortex and medial temporal lobe during working memory encoding

Wesley C. Clapp, Michael T Rubens, Jonas Karlsson, Theodore Zanto, Adam Gazzaley
Depts. of Neurology and Physiology, University of California San Francisco

Introduction

- Traditional models of memory suggest that information must pass through short-term memory in order to enter a long-term memory store.[1,2]
- This idea is refuted by evidence such as anterograde amnesia, which suggests that working memory (WM) and long-term memory (LTM) are distinct systems that act independently of each other under certain circumstances.[3]
- Previously, our group incidentally discovered that a double dissociation between WM and LTM may exist based upon subtle manipulations of a delayed match to sample task; WM performance increased as LTM performance decreased, and vice versa [6]
- The role of the MTL in the formation of memories and consolidation of information has been thoroughly investigated, yet the top-down factors that lead to its recruitment are relatively unknown.[7]

EXPERIMENTAL GOAL: To elucidate whether different manipulations of a working memory task, broadly reflecting difficulty, may increase engagement of the MTL resulting in a double dissociation between WM and LTM.

Behavioral Methods

Three different behavioral datasets were collected (20 different participants in each) to determine whether certain task manipulations might cause a double dissociation between WM and LTM. In each of the experiments, the participants were cued to which WM they were performing. Upon completion of the WM task, participants were given a surprise incidental LTM recognition test, where stimuli from the experiment as well as novel stimuli were shown. Participants rated recognition of stimuli on a scale of 1-4 (4 = definitely remember).

Stimuli: The stimuli used were grayscale images of faces, which had hair and ears removed.

Pairing Manipulation: Faces were paired according to two methods. **Loose pairings** were made by grouping together faces based upon fewer criteria: race, gender, age, resolution and head orientation, this condition is referred to as "Baseline". **Tight Pairings** were tediously created manually based upon several parameters of the images including: race, gender, age, head orientation, luminance, resolution, and salient facial features.

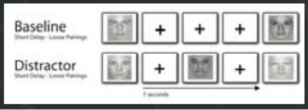
Delay Manipulation: All trials consisted of a single cue image followed by a single probe image, both of which were presented for a duration of 800ms. The delay between these two images was either 7 seconds (**short delay**) or 18 seconds (**long delay**).

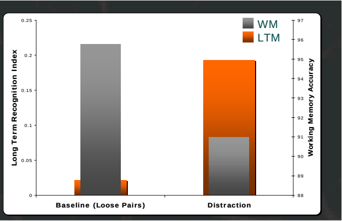
Conditions: Each experiment consists of two interleaved blocks of the two conditions (25 trials/block).

Experiment 1:

Baseline (Loose Pairing) – **Loose pairings** were used along with the **short delay** in this condition.

Distractor – **Loose pairings** were used along with the short delay in this condition. In addition, in the middle of the delay an irrelevant **distracting face** appeared for 1 second.

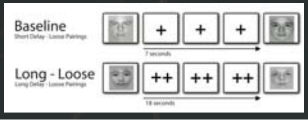


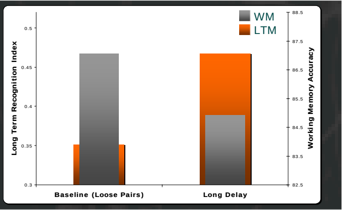


Experiment 2:

Baseline (Loose Pairing) – **Loose pairings** were used along with the **short delay** in this condition.

Long Delay – **Loose pairings** were used along with the **long delay** in this condition.

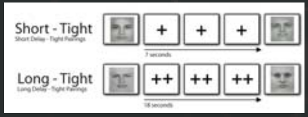


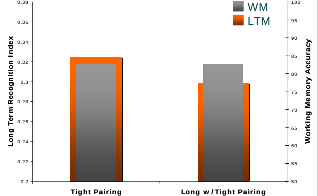


Experiment 3

Tight Pairing– **Tight pairings** were used along with the **short delay** in this condition.

Long-Delay with Tight Pairing – **Tight pairings** were used along with the **long delay** in this condition.



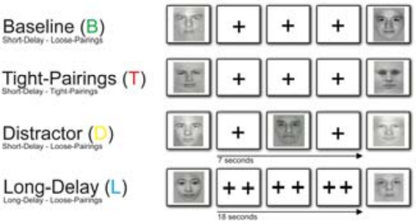


fMRI Methods

Participants: 22 subjects were run in the fMRI portion of this experiment.

fMRI Acquisition and Processing: All images were acquired on a Siemens 3T MAGNETOM Trio. EPIs were collected with a 2 second TR and 1.8 x 1.8 x 3.5 mm voxel size. Images were corrected for slice-timing, motion artifacts, and gaussian smoothed to 5mm FWHM. Data were modeled using a GLM in SPM5 in subject-native space. Group whole-brain maps were calculated from MNI-normalized data. In addition, high resolution T1-MPRAGE, T2-FLAIR, and Diffusion-Tensor-Imaging (DTI) data-sets were collected.

fMRI Network Analysis: Whole-Brain maps were created by extracting the trial-wise variability from each subjects ROIs and correlating this with each voxel's variability across the entire brain.



Conditions: Each experiment consists of two pseudorandomly interleaved blocks of five conditions (15 trials/block).

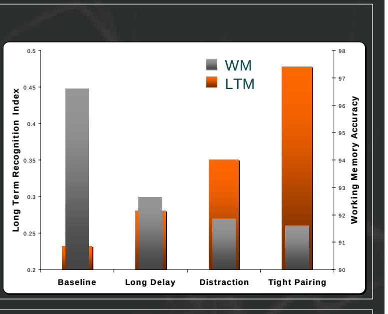
Baseline – **Loose pairings** were used along with the **short delay** in this condition.
Tight Pairing – **Tight pairings** were used along with the **short delay** in this condition.
Long-Delay – **Loose pairings** were used along with the **long delay** in this condition.
Distractor – **Loose parings** were used along with the **short delay** in this condition. In addition, in the middle of the delay an irrelevant **distracting face** appeared for 1 second.

In addition, a 1-back localizer task consisting of blocks of faces and blocks of scenes was run to aid in the independent identification of subject-specific Regions of Interest (ROI), which included left and right Fusiform Face Areas (FFA).

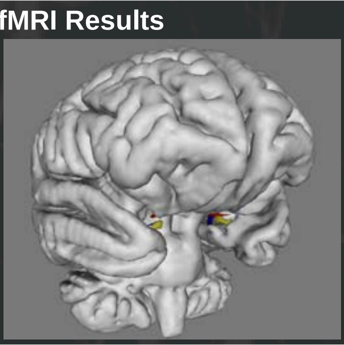
Long-Term Memory Test: At the completion of the WM task a surprise long-term memory test was administered.

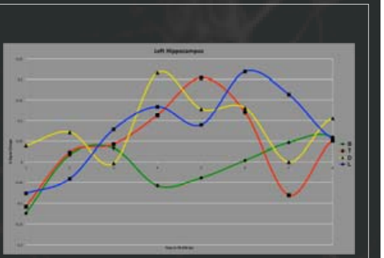
fMRI Behavioral Results

The WM results reveal that participants do best in the Baseline task. The other conditions all show a similar drop in WM performance (comparisons to Baseline p<.05). However, in the surprise incidental long-term recognition task, subjects show the opposite result, where they remember the faces from the Tight Pairing, Distractor, and Long Delay conditions best (comparisons to Baseline p<.05 for T and D, L Delay p=.39).



fMRI Results

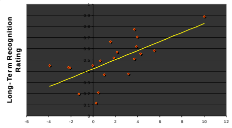




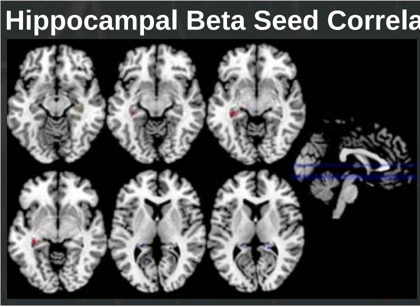
Results show medial temporal lobe (MTL), specifically hippocampus, is more active at encoding in Tight Pairing, Distractor and Long Delay conditions, but not in the Baseline.

Neuro-Behavioral Correlation

In the tightly paired condition, the magnitude of hippocampal activation during encoding strongly correlated with the incidental LTM recognition scores from this condition (p<.005).



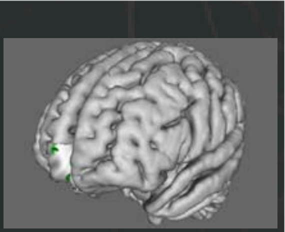
Hippocampal Beta Seed Correlation



These axial slices show regions within the hippocampus which correlate with the right FFA in experimental conditions greater than the baseline condition. The distractor condition (gold) appears in the right hippocampus. The tight pairing condition (red) appears in the left hippocampus. The long delay condition (blue) appears bilaterally in the dorsal part of the hippocampus.

Frontal Beta Seed Correlation

The activations in this image (green) represent regions in the ventro-medial prefrontal cortex which exhibit a greater correlation with the right FFA during the baseline condition compared to all other conditions. The frontal pole, Brodmann area 10, has been associated with activity in easier tasks[4] and has been shown to be active during WM encoding[5].



Conclusions

- Extending the length of delay, distraction during WM maintenance, and increasing the similarity of stimulus pairings causes a significant drop in working memory performance. Conversely, the stimuli from these conditions are better remembered via incidental long-term memory, providing a double-dissociation between WM and LTM.
- It seems that when task demands are low, participants rely solely on a prefrontal-visual association cortex loop to encode information. However, the MTL, specifically the hippocampus, is more active with increasing task difficulty, which may lead to increased LTM.
- During the WM task in which subjects performed the worst, hippocampal recruitment during encoding directly correlated with increased LTM.

References and Funding

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