2012-02-11

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A thesis submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of

Master of Science in Neuroscience

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April 2012

ABSTRACT

A Parametric Investigation of Pattern Separation
Processes in the Medial Temporal Lobe

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The hippocampus is thought to be involved in memory formation and consolidation, with computational models proposing the process of pattern separation as a means for encoding overlapping memories. Previous research has used semantically related targets and lures to investigate hippocampal responses to mnemonic interference. Here, we attempted to define the response function of the hippocampus and its inputs during pattern separation by parametrically varying target-lure similarity in a continuous recognition task. We also investigated the effect of task demands (intentional versus incidental encoding) on pattern separation processes. We collected functional magnetic resonance imaging (fMRI) data while participants were shown a series of objects. In the intentional paradigm, participants identified objects as "new" (novel stimuli), "old" (exact repetitions), or "rotated" (previously seen objects that were subsequently rotated by varied degrees). In the incidental paradigm, participants were shown the same stimuli but identified objects as "toy" or "not toy". Activation in the hippocampus was best fit with a power function, consistent with predictions made by computational models of pattern separation processes in the hippocampus. The degree of pattern separation was driven by the information most relevant to the task—pattern separation was seen in the left hippocampus when semantic information was more important to the task and seen in the right hippocampus when spatial information was more important. We also present data illustrating that top-down processes modulate activity in the ventral visual processing stream.

Keywords: fMRI, hippocampus, pattern separation

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INTRODUCTION

The ability to remember, including consciously recalling the past and verbalizing previously stored memories, is one of humanity's defining characteristics. But memory fades with age, and scientific pursuits are actively trying to better understand memory in hopes of prolonging and enhancing it. The hippocampus has been shown to be involved in memory creation and consolidation (Squire et al., 2004) but how these processes actually take place is a topic of current investigation.

Questions arise as to how the hippocampus is able to store and retrieve distinct memory representations when inputs are similar or overlapping. Computational models propose the process of pattern separation as a means for encoding distinct memory representations and the process of pattern completion for retrieving previously stored memories (Marr, 1971; McClelland et al., 1995; O'Reilly and Rudy, 2001; Norman and O'Reilly, 2003).

Long-Term Declarative Memory

The hippocampus has been shown to be involved specifically in long-term declarative memory (Squire et al., 2004). In defining long-term declarative memory it is important to recognize that declarative memory is just one of multiple memory systems that exist in the brain. Declarative memory is defined as memory for facts and events (i.e. a memory that can be declared). All other memory systems are included under the category of non-declarative memory, and these systems include priming, reflexes, skeletal conditioning, fear conditioning, and procedural memory (Squire and Zola, 1996).

It is also important to recognize that long-term declarative memory is different from short-term memory (i.e. working memory). Working memory is anything that can be held in

mind at a given time (Baddeley and Hitch, 1974). If attention is given to something else, what is held in working memory is forgotten. In contrast, long-term memory is maintained even after attention has been diverted. Long-term memory is the process recruited when the working memory load is exceeded (i.e. if there are more things than can be held in mind at a given time). Thus, long-term declarative memory is memory for facts and events that is sustained over time.

Role of the Hippocampus

Since the case of patient H.M., the hippocampus and medial temporal lobe (MTL) have been proposed to play a role in long-term declarative memory (Scoville and Milner, 1957). Rodent, primate and human studies have all confirmed that the hippocampus is crucial for long-term declarative memory (Squire et al., 2004). At a synaptic level, long-term memory results from potentiated synapses in the hippocampus such that a given input results in a changed output upon subsequent presentation (Bliss and Collingridge, 1993). Computational models propose that the unique properties of the subregions of the hippocampus together with potentiated synapses allow for the encoding and retrieval of distinct memories even when the inputs are similar or overlapping (Norman and O'Reilly, 2003). The encoding of such memories has been termed pattern separation, with the complementary retrieval process being pattern completion.

Pattern Separation, Pattern Completion

Pattern separation occurs in the hippocampus as small changes in inputs are magnified in the dentate gyrus, and involves orthogonalizing the representing for stimuli such that stimuli with overlapping similarity are represented as dissimilarly as possible (Norman and O'Reilly, 2003). Pattern separation reduces interference and is an efficient way to retrieve memories from specific

inputs without recalling memories from similar inputs. Computational models of pattern separation propose that similar stimuli are treated more like novel stimuli than repeat stimuli.

Pattern completion involves reactivating a previously stored pattern of firing based on a noisy or degraded input (i.e. a part can recall the whole). Pattern completion requires retrieving previously stored information and comparing it with current inputs. Pattern completion emphasizes the similarity/overlap of two given inputs whereas pattern separation emphasizes each input's unique characteristics.

Hippocampal Circuitry Supports Pattern Separation

Pattern separation in the hippocampus is proposed to be a function of the dentate gyrus whereas pattern completion is proposed to be a function of the CA1 region (Norman and O'Reilly, 2003). The circuitry of the hippocampus is such that inputs coming from the entorhinal cortex first feed into the hippocampus via the perforant path into the dentate gyrus region. The dentate gyrus then projects to the CA3 region via mossy fibers. CA3 then projects to CA1 via Schaffer collaterals, and CA1 projects out of the hippocampus and back into the entorhinal cortex via the subiculum. This loop through the hippocampus has two special features that allow for pattern separation and pattern completion to occur:

The auto-associative properties of CA3 back projections facilitate pattern separation in the hippocampus (Amaral and Witter, 1989; Treves and Rolls, 1994). As inputs activate a sparse representation in the dentate gyrus, that representation activates cells in CA3. CA3 back projections reactivate a portion of those same synapses, strengthening them. Therefore, subsequent presentations of the same inputs activate a modified response in CA3 due to previously strengthened synapses. In this way, the dentate gyrus-to-CA3 mossy fibers can pattern

separate a similar lure from a previously seen stimulus as the representation of the previously seem stimulus has potentiated synapses whereas the representation of the similar lure does not.

The comparator properties of the CA1 facilitate pattern completion in the hippocampus (Vinogradova, 2001; Duncan et al., 2011). The CA1 receives direct projections from the entorhinal cortex as well as projections from the CA3 region. As these signals from the CA3 regions also originated in the entorhinal cortex, the CA1 is receiving two copies of the same information, one processed and one unprocessed. In this way, the CA1 is able to compare the inputs from the entorhinal cortex (i.e. the unprocessed representation of the current inputs) with the inputs from the CA3 region (i.e. the processed representation that will be modified if the input has been previously seen). This match-mismatch detection allows the CA1 to pattern complete if there is a match between the inputs received from the entorhinal cortex and the inputs received from the CA3 region.

Because of sparse representations in the dentate gyrus subregion, the hippocampus is especially biased toward pattern separation (Treves and Rolls, 1994). However, this does not mean that the hippocampus does not pattern complete or that other areas of the cortex do not pattern separate (Rotshtein et al., 2005; Eichenbaum et al., 2007). The distinction between pattern separation in the hippocampus and in the cortex is that to generate the same change in output the hippocampus requires a smaller change in input whereas the cortex requires a larger change in input (McClelland et al., 1995; O'Reilly and Rudy, 2001; Norman and O'Reilly, 2003).

Evidence for Pattern Separation in Rodents

Electrophysiology in rodents suggests that pattern separation occurs in the hippocampus (Lee and Kesner, 2004; Leutgeb et al., 2004; Leutgeb et al., 2005; Wills et al., 2005; Leutgeb et

al., 2007; Leutgeb and Leutgeb, 2007; Kesner, 2009). Lee and colleagues used a Hebb-Williams maze to test spatial memory in rats with electrolytic lesions to perforant path inputs into CA3 or neurotoxic lesions to the dentate gyrus. The dentate gyrus lesions were meant to disrupt pattern separation (an encoding process) by blocking input to CA3. The CA3 lesions were meant to disrupt pattern completion (a retrieval process) by blocking inputs to CA1. Electrolytic lesion PPCA3 rats had deficits in retrieval whereas neurotoxic lesion DG rats had deficits in encoding. S. Leutgeb and colleagues placed rats in novel rooms with common spatial elements and measured the cell ensembles that were activated. They found that in CA3 distinct populations were activated despite the common spatial elements. In CA1 the cell populations overlapped, i.e. portions of the cell population were activated by more than one stimulus, with increased overlap for increased similarity of spatial elements. In a separate study, J. Leutgeb and colleagues (2005) again measured cell populations in CA3 and CA1 but used for spatial cues rooms morphed in quantifiable steps. They found that CA3 activation depended significantly both on the direction of morphing and the amount of prior testing. Later, J. Leutgeb and colleagues (2007) again used morphed rooms and measured activity in the dentate gyrus and CA3 region. They found that when the environment was changed new cell populations were recruited in CA3 but not in the dentate gyrus, which supports the idea that new cell populations can be recruited during pattern separation. Based on these and prior results, they concluded that pattern separation operates by a dual mechanisms such that either changes in the dentate gyrus coincidence patterns, i.e. the correlation of the firing of dentate gyrus cells, or the recruitment of new cell populations in CA3 can signal pattern separation. The results from all three studies are consistent with computational models of pattern separation, which predict that unique, sparse representations in CA3 are able to

distinguish similar inputs by orthogonalizing the memory representation whereas representations are more overlapping in CA1.

Immediate-early gene studies in rodents confirm electrophysiology results suggesting that pattern separation occurs in the hippocampus (Vazdarjanova and Guzowski, 2004; Kubik et al., 2007). Vazdarjanova and Guzowki used Arc/H1a catFISH to look at cell populations activated by two experiences separated by 30 minutes. When rats were twice exposed to the same environment the cell populations activated had a similarly high degree of overlap in both CA3 and CA1. When the two environments had similar but not identical spatial cues, there was decreased overlap compared to twice exposure to the same environment. However, the overlap in CA3 was greater than in CA1. When rats were exposed to two distinct environments the cell populations activated had a low degree of overlap, with the overlap lower in CA3 than CA1. The authors concluded that highly similar environments bias the CA3 towards pattern completion, thus the representations in CA3 had a high degree of overlap. However, when the two environments were sufficiently different, CA3 was biased towards pattern separation and thus the representations in CA3 had a low degree of overlap. Thus CA3 has a discontinuous response whereas CA1 has a graded response, consistent with predictions of pattern separation and pattern completion. They also found that the context representation was much smaller in CA3 (18%) than in CA1 (35%). These results are also consistent with computational models that predict a sparse representation in CA3 activating a larger representation in CA1.

Evidence for Pattern Separation in Humans

Evidence of pattern separation from rodent studies suggests that pattern separation could also occur in humans. Differences exist between the rodent and human hippocampus that

necessitate investigations specifically in humans. However, only three such investigations have been completed. Because single-cell recordings and immediate-early gene studies are not feasible in human research, all three prior studies have used functional MRI (fMRI) to investigate pattern separation activity in the hippocampus. fMRI measures the ratio of oxygenated to deoxygenated hemoglobin, which is correlated with neuronal activity. As brain regions become activated their metabolic demands increase, causing first an increase in deoxygenated hemoglobin as the cells use oxygen and then a decrease in deoxygenated hemoglobin as blood vessels dilate and more blood rushes to the area. This is known as the Blood Oxygen Level Dependent (BOLD) Effect.

Kirwan and Stark investigated pattern separation by showing participants pictures of common objects or faces in an intentional memory paradigm while collecting high-resolution functional MRI (fMRI) data (Kirwan and Stark, 2007). In this continuous recognition task participants were asked to make an explicit memory judgment and to classify each image seen as "new" (novel stimuli), "old" (exact repeats), or "similar" (lure objects that was either an object similar to the original or a different picture of the same face). Although results were not consistent across the left and right hippocampus, they concluded that the hippocampus plays a role in pattern separation because hippocampal activity distinguished between correctly identified true repeats, correctly rejected similar lures, and false alarms to similar lures.

In another study from the same group, Bakker and colleagues investigated pattern separation by showing participants pictures of common objects in an incidental memory paradigm while collecting high-resolution fMRI data (Bakker et al., 2008). In this task there was no overt memory judgment and participants merely looked at a series of images, some of which subsequently repeated or were followed by similar lures. To ensure that participants were

attending to the items, they were asked to respond if the item was predominantly an indoor or an outdoor item. Bakker et al. concluded that in an incidental memory task the CA1 region supports pattern completion whereas the CA3/DG regions supports pattern separation.

In a recent fMRI experiment, Lacy and colleagues investigated pattern separation using an incidental memory task much like Bakker et al (Lacy et al., 2011). Here the researchers attempted to have tighter control over stimulus similarity by using lures that were either low similarity or high similarity. Their conclusions were similar to Bakker et al., in that the CA1 region supports pattern completion whereas the CA3/DG regions supports pattern separation in an incidental memory task with lures of high or low similarity.

Proposed Research

Previous research (Kirwan and Stark, 2007; Bakker et al., 2008) has used semantically related targets and lures to investigate hippocampal responses to mnemonic interference, but target-lure similarity was not explicitly controlled. One prior study (Lacy et al., 2011) attempted to have more control over stimulus similarity by using two groups of lures, one with high overlap and one with low overlap. Here, we attempted to control the degree of target-lure similarity by using stimuli that consisted of the same objects photographed from different angles. This allowed us to quantify the response function of the hippocampus by inducing pattern separation with parametrically rotated stimuli. We proposed model patterns of activity for both pattern separation and pattern completion (Figure 1).

Pattern separation was defined as a power function with decreasing slope, based on modeling predictions that a sharp distinction in activity exists between old and similar stimuli (i.e. a marked difference in activity between the repeat and small rotation conditions is

observed). Pattern completion was defined as either a linear function or a power function with increasing slope, based on predictions that a gradual distinction in activity exists between old and similar stimuli (i.e. change in activity is graded and proportional to the change in stimuli, as in a linear function; or, activity for the small rotation conditions is similar to the repeat condition but a marked difference is seen in activity for large rotation conditions, as in a power function with increasing slope). We hypothesized that our model functions for pattern separation and pattern completion would fit activity in the hippocampus for rotated and repeat stimuli, respectively.

Previous studies (Bakker et al., 2008; Lacy et al., 2011) have used an incidental task design to investigate encoding and retrieval in the hippocampus without the confound of an overt memory decision, and have shown activity consistent with pattern separation. One prior study (Kirwan and Stark, 2007) has used an intentional design to study pattern separation in the hippocampus, and results were not consistent across stimulus type for different subregions of the hippocampus, possibly due to an effect of task demand. We proposed both an incidental and an intentional version of the task to investigate the role of task demands in modulating pattern separation in the hippocampus. This allowed us to directly compare activity within a region in both incidental and intentional encoding to better clarify what role intentional encoding has on pattern separation in the hippocampus. We hypothesized that intentional encoding would sharpen the distinction between true repeats and small rotations, thereby facilitating pattern separation.

Previous studies have looked at the distinction in activity between the hippocampus and surrounding MTL cortices during pattern separation (Kirwan and Stark, 2007; Bakker et al., 2008). We included this comparison in our study to clarify what distinctions exist between hippocampal and MTL function in pattern separation and how intentional encoding affects the hippocampus versus the surrounding cortices. Computational models predict the inputs necessary

for pattern separation (Norman and O'Reilly, 2003), but no work has been done to investigate these models in humans. We investigated the visual inputs coming into the hippocampus and how top-down processes modulating the effects of task demands affect these visual inputs. We hypothesized that top-down processing would affect task demands by sharpening the inputs coming into the hippocampus, thereby facilitating pattern separation.

MATERIALS & METHODS

Participants

Thirty right-handed volunteers (15 in the intentional condition: eight females, mean age 23.1 years, range 18-27 years; 15 in the incidental condition: seven females, mean age 23.9 years, range 18-29 years) gave written, informed consent before participation.

Materials

Stimuli consisted of images acquired from the Amsterdam Library of Images database (Geusebroek et al., 2005). The database contained photographs of 1,000 single, small objects. Each object was photographed 72 times by rotating the object at 5° intervals. Five hundred ninety-two objects were randomly selected from the database for presentation in the continuous recognition task (see below). Objects were presented in color in the center of the screen against a white background. Response options were presented across the bottom of the screen in black letters.

Procedure: Intentional Condition

At the time of scanning, participants were shown a series of 792 images of objects in four blocks of 198 images, one at a time for 2.5 seconds, and asked to identify each object as "new" (novel stimuli), "old" (exact repetitions), or "rotated" (previously seen objects shown from a different angle; see Figure 2). Pilot testing indicated that rotations of 15°, 25°, 35°, and 55° were optimal for obtaining an appropriate range of performance. Each block of 198 trials included 10 objects that were repeated, 40 objects that were subsequently rotated (10 per angle of rotation), and 98 objects that were not repeated. Object orientation for the initial representation was

randomly selected from the 72 possible orientations in order to prevent answer bias for the subsequent rotated trials. Images that were subsequently repeated were treated as the 0° in the first presentation, regardless of initial object orientation. Repeat images were shown after a mean lag of 20.9 trials (range, 11-51). Rotated images were shown after a mean lag of 19.8 trials (range, 10-41). The direction of rotation (clockwise or counter-clockwise) was randomly selected. The same images were used for all participants but were pseudo-randomized and were repeated only within the block. Block order was randomized across participants. Round or cylindrical stimuli were not included as old or rotated objects due to their symmetry but were included as new objects. Participants responded using an MR-compatible button box with buttons corresponding to the response options. Participants were instructed to respond while the image was still present on the screen.

Procedure: Incidental Condition

The same stimuli and stimulus presentation order were used in the incidental condition as in the intentional condition. At the time of scanning, participants were shown a series of images and asked to identify the objects as "toy" or "not toy". Participants were told to consider an object a toy if they could imagine a child playing with it. The participants' classifications were not used in the analysis but these instructions were given to encourage participants to attend to the stimuli.

fMRI Imaging

Imaging was performed on a 3T Siemens scanner at the Imaging and Neurosciences Center at the University of Utah. Functional images were acquired using a gradient-echo, echo-

planar, T2*-weighted pulse sequence (TR = 2,500 ms; 198 TRs/run; TE = 30 ms; flip angle 75°; matrix size = 64-64; field of view 22cm). The first four TRs acquired were discarded to allow for T1 equilibration. Forty-two oblique coronal slices (slice thickness = 3.3mm) were acquired parallel with the corpus callosum and covering the whole brain.

Structural MRI images were acquired using a T1-weighted MP-RAGE sequence (165×220 mm field of view; flip angle 12°; TE 2.58 ms; 128 slices; 1mm slice thickness; matrix size 144×192; voxel size 1.46×1.45×1mm).

fMRI Data Analysis

fMRI data were analyzed using the AFNI suite of programs (Cox, 1996). Functional data were coregistered in three dimensions to the whole-brain anatomical data, slice-time corrected, and coregistered to reduce effects of head motion. Large motion events, defined as TRs in which there was >0.3° of rotation or 0.6 mm of translation in any direction, were excluded from the deconvolution analysis by censoring the excluded time points (mean of 0.4 events per participant). We also excluded the TR immediately before and after the motion-contaminated TR.

Seven behavioral vectors were created that coded each study trial according to type (new, first, repeat, rotated 15°, rotated 25°, rotated 35°, rotated 55°). Trials in which there was no response or multiple responses were modeled but then excluded from additional analysis (intentional mean, 20.4 per participant; incidental mean, 32.8 trials per participant). The behavioral vectors and six vectors that coded for motion (three for translations and three for rotations) were used in the deconvolution analysis of the fMRI time series data in which a canonical hemodynamic response was convolved with the behavioral vectors. The resultant fit

coefficients (β coefficients) represent activity versus baseline in each voxel for a given time point and each of the trial types. Note that the stimuli in the response category "new" were further subdivided into first and new, where firsts had a subsequent second presentation and new were never repeated. Baseline consisted of new stimuli that were never repeated. The following fMRI contrasts of interest were all made within active task conditions and not relative to baseline.

Initial spatial normalization was accomplished using each participant's structural MRI scan to transform the data to the atlas of Talairach and Tournoux (1988). Further spatial normalization was carried out using the Advanced Normalization Tools (ANTs; Avants et al., 2008; Klein et al., 2009; Yassa et al., 2010; Lacy et al., 2011) which uses diffeomorphic mapping to calculate a transformation from an individual participant to a model based on the grayscale structural MRI scan. Statistical maps also were transformed to Talairach space and then resampled to $3mm^3$ and smoothed using a Gaussian filter (5 mm full-width at half maximum) before being aligned to the template with ANTs.

After individual deconvolution analysis, individual participant parameter estimate maps were entered into group-level analyses and thresholded at a voxelwise p value of < 0.03. A cluster correction technique was used to correct for multiple comparisons, and Monte Carlo simulations (AFNI's ClustSim program) were used to determine how large a cluster of voxels was needed to be statistically meaningful ($p < 0.05$) (Forman et al., 1995; Xiong et al., 1995) for the entire brain (minimum cluster extent of 55 voxels).

RESULTS

Behavioral Performance

Figure 3 shows the mean number of trials for each condition according to the behavioral response for the intentional version of the task. Percent correct was calculated as the proportion of trials for which participants correctly identified the object (i.e. the number of times the participant identified an old object as "old" divided by the total number of old stimuli). Participants were highly accurate at identifying novel and repeat stimuli (89%, 87%, and 75% for the new, first, and repeat presentations, respectively). Accuracy for correctly identifying second-presentation stimuli was positively correlated with increasing the angle of rotation (22%, 35%, 50%, and 56% for stimuli rotated 15°, 25°, 35°, and 55°, respectively; $r = 0.63$; $p < 0.0001$). If pattern separation is described as correctly discriminating similar objects, pattern separation accuracy increased as the angle of rotation increased (i.e. as the objects became less similar).

fMRI Analyses

Our primary purpose was to examine the response function of the medial temporal lobe (MTL) to parametric manipulations of stimulus similarity. In order to define memory sensitive regions, we first looked for areas that showed an old/new effect by performing a voxel-wise t-test comparing the repeat condition (old stimuli) and the baseline condition (new stimuli that were never repeated). This contrast revealed two regions of interest (ROIs) in the MTL that exhibited an old/new effect (i.e. new>old). For this analysis, functional ROIs were defined by setting a voxel-wise threshold at $p = 0.03$ and a spatial extent threshold of a minimum ROI volume of 1485 mm^3 (55 voxels) with a connectivity radius of 3.1 mm (overall $p < 0.05$). The ROIs were then masked to exclude non-MTL voxels and to segregate the large functional MTL ROIs into their respective anatomical components using the MTL anatomical model from the cross-

participant alignment procedure. Figure 4C shows the four ROIs in the MTL revealed by masking: one in the left hippocampus body and tail, one in the right hippocampus body and tail, one in the left parahippocampal cortex, and one in the right parahippocampal cortex (see Table 1).

We next looked specifically within the MTL ROIs to define the response function to parametric manipulations of stimulus similarity. Figure 4A,B shows the mean activity within each of the ROIs for the trials rotated 0° (repeats), 15°, 25°, 35°, and 55°. We looked at activity in these regions across stimulus type for evidence of either pattern separation or pattern completion. Prior to our investigations, we proposed model curves for pattern separation and pattern completion (Figure 1). Pattern separation was defined as a power function with decreasing slope, based on computational predictions that a sharp distinction in activity exists between old and similar stimuli (i.e. between repeat and small rotation images). Pattern completion was defined as either a linear function or a power function with increasing slope, based on computational predictions that a more gradual distinction in activity exists between old and similar stimuli. Accordingly, we fit a linear and a power function to the activity for trials with rotations of 0° (repeats), 15°, 25°, 35°, and 55° (see Table 2). For this and subsequent analyses, areas were defined as performing pattern separation if the best-fit curve was a power function with decreasing slope (i.e. a marked difference in activity between the repeat and small rotation conditions was observed). Areas were defined as performing pattern completion if the best-fit curve was either linear (i.e. activity changed proportional to the change in angle of rotation) or a power function with increasing slope (i.e. activity for the small rotation conditions was similar to the repeat condition but a marked difference was observed in activity of large rotation conditions.) The best fit was defined as having the highest adjusted r^2. Graphs of the

activity were generated in MATLAB (Mathworks, Natick, MA) and were fit with either a linear or a power function using MATLAB's curve-fitting tool.

We fit separate curves to both the intentional and the incidental data in the two hippocamapal ROIs (see Table 2). In the incidental condition, the left hippocampus was better fit with a power function with decreasing slope (adj. $r^2 = 0.62$ and 0.27 for the power and linear fits, respectively). The right hippocampus was better fit with a linear function (adj. $r^2 = 0.33$ and 0.12 for the linear and power fits, respectively). In the intentional condition, the left hippocampus was better fit with a power function with increasing slope (adj. $r^2 = 0.84$ and 0.69 for the power and linear fits, respectively). The right hippocampus was better fit with a power function with decreasing slope (adj. $r^2 = 0.93$ and 0.75 for the power and linear fits, respectively). These data support the predictions of computational models of hippocampal function in that the response function in the hippocampus is consistent with pattern separation as determined by task demands.

Additionally, within the parahippocampal cortex ROIs (Figure 4C) we fit a linear and a power function to the activity from both the intentional and incidental task conditions (see Table 2). In the incidental condition, the left parahippocampal cortex was better fit with a power function with decreasing slope (adj. $r^2 = 0.57$ and -0.09 for the power and linear fits, respectively). The right parahippocampal cortex was better fit with a power function with decreasing slope (adj. $r^2 = 0.75$ and 0.09 for the power and linear fits, respectively). In the intentional condition, the left parahippocampal cortex was better fit with a power function with increasing slope (adj. $r^2 = 0.29$ and 0.16 for the power and linear fits, respectively). The right parahippocampal cortex was better fit with a power function with decreasing slope (adj. $r^2 = 0.92$ and 0.28 for the power and linear fits, respectively). Thus, our data support a role of the

parahippocampal cortex in signaling the hippocampus in pattern separation as determined by task demands.

Lastly we investigated the top-down processes modulating the effects of task demands via the inputs into the hippocampus. We first looked for areas that showed differential activation in the two task conditions by performing a voxel-wise t-test comparing the intentional and the incidental encoding conditions. Due to widespread activation, for this analysis functional ROIs were defined by setting a voxel-wise threshold at $p = 0.03$ and a spatial extent threshold of a minimum ROI volume of 2970 mm^3 (110 voxels) with a connectivity radius of 3.1 mm (overall $p < 0.0001$). Figure 5C shows the four ROIs revealed in this contrast where activity was greater for the intentional condition than the incidental condition: one in the left ventral visual stream, one in the right ventral visual stream, one in the left MTL and one in the right MTL (see Table 1). Figure 5A,B shows the mean activity within each of the ROIs for the trials with objects rotated 0° (repeats), 15°, 25°, 35°, and 55°. To classify this activity as consistent with either pattern separation or pattern completion, we fit a linear and a power function to the activity of all four ROIs in both the incidental and intentional conditions (see Table 3). In the incidental condition, neither the left nor the right ventral streams nor the left MTL was well fit by either function (all adj. $r^2 < 0$). The right MTL was better fit by a power function with decreasing slope (adj. $r^2 =$ 0.30 and 0.05 for the power and linear fits, respectively). Note that in each of these ROIs the data point at 35° rotation is significantly lower than the data point at both the 25° and 55° rotations. This point at 35° does not predict the fit well, resulting in negative adjusted r^2 values for the left and right ventral streams and left MTL. In the intentional condition, the left ventral stream is well fit by a linear function (adj. $r^2 = 0.98$ and 0.95 for the linear and power fits, respectively) whereas the right ventral stream is well fit by a power function with decreasing slope (adj. $r^2 =$

0.69 and 0.38 for the power and linear fits, respectively). The left MTL was better fit by a power function with increasing slope (adj. $r^2 = 0.42$ and 0.09 for the power and linear fits, respectively). The right MTL was better fit by a power function with decreasing slope (adj. $r^2 = 0.28$ and 0.12 for the power and linear fits, respectively). This pattern (of flat responses in the ventral visual stream and power responses in the MTL) is consistent with a role of top-down processing modulating ventral stream activity that subsequently feeds into the hippocampus.

A second set of ROIs was revealed by the intentional-incidental contrast that largely consisted of default network regions. Activity in these regions appeared to be related to inattention in the (less engaging) incidental task and was not modulated by stimulus type (i.e. first, repeat, rotated). The coordinates of these ROIs are listed in Table 1 for archival purposes.

DISCUSSION

Participants were shown a series of images in either an incidental or intentional encoding paradigm during fMRI scanning. In the intentional paradigm, participants were asked to identify each object as "new" (novel stimuli), "old" (exact repeats), or "rotated" (previously seen objects shown from a different angle). In the incidental paradigm, participants were asked to perform a semantic classification of the objects ("toy" or "not toy"). We performed two analyses of the data, investigating pattern separation according to both stimulus similarity (parametric rotations of stimuli) and task demands (intentional or incidental encoding).

Pattern Separation Processes in the Hippocampus

Our principal investigation in this study was to define the hippocampal pattern separation response function. We first examined the behavioral data of the intentional paradigm to confirm that participants were behaviorally pattern separating (Bakker et al., 2008). Participants successfully identified old objects (75.3% correctly identified). Whereas participants had a difficult time correctly identifying objects rotated 15° (21.7%) their success more than doubled for objects rotated 55° (56.3%), indicating that behavioral pattern separation was positively correlated with decreasing stimulus similarity.

We looked at activity within the hippocampus to define the pattern separation response function. Computational models predict that pattern separation demonstrates an old/new effect (new>old) (Norman and O'Reilly, 2003). Single-cell recordings from human hippocampus confirm these predictions (Viskontas et al., 2006). Previous investigations (Bakker et al., 2008; Lacy et al., 2011) have used this effect as a mask to isolate areas performing pattern separation.

Here, two MTL ROIs were revealed in the old/new contrast, and a subsequent anatomical mask divided these ROIs into hippocampus and parahippocampal cortex.

Consistent with previous investigations showing hippocampal pattern separation in an incident memory task (Bakker et al., 2008; Lacy et al., 2011), we observed pattern separation in both the left and right hippocampus. By parametrically rotating the stimuli we further quantified the exact function of pattern separation, such that both high-similarity stimuli (i.e., objects rotated 15°) and low-similarity stimuli (i.e., objects rotated 55°) were treated like novel stimuli. Consistent with our predictions, activity in the hippocampus fit the pattern separation curve modeled in Figure 1. Task demands determined the laterality of the pattern separation.

In the incidental condition, pattern separation was observed in the left hippocampus. The activity curve was well fit by a power function with decreasing slope ($r^2 = 0.62$). In contrast, activity in the right hippocampus was better fit by a pattern completion linear function ($r^2 = 0.33$). In this condition, participants classified objects as "toy" or "not a toy", and thus used semantic information to make this judgment (i.e., task demands emphasized object identity more than object orientation). Left hippocampal activation is associated with verbal memory (Powell et al., 2007; Pereira et al., 2010). Left temporal lobectomy patients have impaired learning, recall, and recognition of prose passages (Milner, 1958; Frisk and Milner, 1990), word lists (Dennis et al., 1988; Baxendale, 1997), and object names (Incisa della Rocchetta and Milner, 1993). In normal controls, prior investigations using semantic classification of either animacy (i.e., "living" or "non-living") (Otten et al., 2001; Otten and Rugg, 2001; Fliessbach et al., 2010) or concreteness (i.e., "concrete" or "abstract") (Baker et al., 2001), have led to stronger activation of the left hippocampus than non-semantic discriminations. When performing classifications, participants use prior semantic knowledge about the identify of the object to

abstract its grouping under task constraints (Fliessbach et al., 2010). It is likely that the left lateralized pattern separation in the incidental task results from semantic inputs that more strongly activate the left hippocampus.

In the intentional condition, pattern separation was observed in the right hippocampus, as the activity curve was well fit by a power function with decreasing slope ($r^2 = 0.93$). In contrast, activity in the left hippocampus was well fit by a pattern completion power function with increasing slope ($r^2 = 0.84$). In this condition, participants identified objects as "new", "old", or "rotated", and thus used spatial information to make this judgment (i.e., task demands emphasized object orientation more than object identity). Right hippocampal activation is associated with navigational skills (Maguire et al., 1997; Iaria et al., 2008) and spatial memory (Kohler et al., 2005; Aradillas et al., 2011). Right temporal lobectomy patients have impaired spatial memory (Feigenbaum et al., 1996; Morris et al., 1996; Abrahams et al., 1997; Bohbot et al., 1998), topographical memory (Spiers et al., 2001), and memory dependent on the geometric relationship between spatial cues and environmental reference (Finke et al., 2011). Viewpoint dependence in spatial memory relies on mental rotation (compared to representations that are viewpoint independent), as evidenced through response latencies for shifted-view images compared to control images (King et al., 2002). We see the same response latency for all rotated conditions compared to first presentation images (see Table 4), consistent with the interpretation that participants were mentally rotating objects prior to responding. We also see response latency for the repeat images, possibly because participants were also mentally rotating the repeat images to confirm their decision of "old". It is likely that the right lateralized pattern separation seen in the intentional task results from spatial inputs that more strongly activate the right hippocampus.

Pattern separation of semantic information occurred in the left hippocampus in a semantic classification task and pattern separation of spatial information occurred in the right hippocampus in a mental rotation task. We conclude that pattern separation is the default operation of the hippocampus, as driven by the information most relevant to the task (Yassa and Stark, 2011). As the hippocampus receives a sufficient level of input (increased semantic input in the incidental task and increased spatial input in the intentional task), it easily pattern separates. We hypothesized that the incidental task would allow isolation of hippocampal activity without the influence of top-down processes, whereas the intentional task would demonstrate the effects of task demands on pattern separation (Kirwan and Stark, 2007; Bakker et al., 2008). However, we see that left-lateralized pattern separation in our incidental task is influenced by semantic memory, and thus is also affected by top-down processes. Curves fit to the intentional data have better fits ($r^2 = 0.84$ and 0.93 for the left and right hippocampus, respectively) than those fit to the incidental data ($r^2 = 0.62$ and 0.33 for the left and right hippocampus, respectively), indicating that intentional memory encoding strongly biases the hippocampus towards pattern separation, but pattern separation still occurs in an incidental task.

Top-down Processing Modulates Pattern Separation in the Ventral Stream

We examined activity in the ventral stream inputs into the hippocampus looking for an effect of task demand. If task demands drive pattern separation in the hippocampus, this effect likely originates in the ventral stream inputs, and not just in the hippocampus proper. Ventral stream activity mirrored hippocampal activity: pattern separation-like curves were seen in the left hippocampus for incidental encoding and in the right hippocampus for intentional encoding; pattern completion-like curves were seen in the left hippocampus for intentional encoding and in

the right hippocampus for incidental encoding. In contrast to activity in the hippocampus, activity in the ventral stream was not well fit by power or linear functions (see Tables 2 and 3). This indicates that while top-down processes bias the ventral stream towards pattern separation, the hippocampus amplifies the signal received into true pattern separation. Our results are consistent with prior research showing that top-down processing modifies inputs as they are received in the visual cortex (Coutinho et al., 2010). Consistent with hippocampal activity, ventral stream activity was better fit by curves in the intentional condition compared to the incidental condition. Consistent with previous results (Reber et al., 1998), we observed decreased activation in the ventral stream during incidental encoding compared to intentional encoding.

We see that the default operation of the hippocampus is pattern separation as driven by information pertinent to the task. Top-down processes driven by task demands modulate inputs into the hippocampus as early as the ventral visual stream. Unique memory representations result from pattern-separation-like activity in the ventral stream that is subsequently amplified in the hippocampus.

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FIGURE LEGENDS

Figure 1. Graph of hypothetical activity curves for pattern separation and pattern completion, as predicted by computational models. Predictions are that regions performing pattern separation have a sharp distinction in activity for true repeats versus small rotations (i.e. a power function with a decreasing slope) whereas regions performing pattern completion have a more gradual response to the parametric rotations (i.e. a linear function or power function with increasing slope). Curves above the diagonal (area in green) represent pattern separation. Curves below the diagonal and including the diagonal (area in purple) represent pattern completion.

Figure 2. Examples of stimuli presented in the intentional task. Upon first presentation all stimuli were classified as "new". Upon second presentation, stimuli were classified as "old" or "rotated" depending upon their orientation. Old stimuli were exact copies of the original image (i.e. rotated 0°). Rotated stimuli were rotated either 15°, 25°, 35°, or 55°. Note that stimuli in the experiment were presented in full color.

Figure 3. Behavioral performance during the intentional encoding paradigm. For each stimulus type ('New', 'First', 'Repeat', 'R-15°', 'R-25°', 'R-35°', 'R-55°), participant responding is graphed according to the chosen response of 'Old', 'New', or 'Rotated'. Response rates were taken out of the total number of trials of a given type (e.g., repeats) for which there was a behavioral response.

Figure 4. A-B: Activity during the incidental (red) and intentional (blue) encoding conditions in the left (Panel A) and right (Panel B) hippocampus and parahippocampal cortex. Brackets show ±SEM. Left Hippocampus: intentional, adj. $r^2 = 0.84$; incidental, adj. r = 0.62. Left Parahippocamal Cortex: intentional, adj. $r^2 = 0.26$; incidental, adj. r = 0.57. Right Hippocampus: intentional, adj. $r^2 = 0.93$; incidental, adj. r = 0.33. Right Parahippocampal Cortex: intentional, adj. $r^2 = 0.92$; incidental, adj. r = 0.75.
C: Coronal (top) and sagittal (bottom) slices display the hippocampal and parahippocampal cortex ROIs: Left Hippocampus (lime green); Left Parahippocampal Cortex (purple); Right Hippocampus (pink); Right Parahippocampal Cortex (teal).

Figure 5. A-B: Activity during the incidental (red) and intentional (blue) encoding conditions in the left (Panel A) and right (Panel B) ventral streams and MTL. Brackets show ±SEM. Left Ventral Stream: intentional, adj. $r^2 = 0.98$; incidental, adj. r = -0.30. Left Medial Temporal Lobe: intentional, adj. $r^2 = 0.42$; incidental, adj. r = -0.23. Right Ventral Stream: intentional, adj. $r^2 = 0.69$; incidental, adj. r = -0.30. Right Medial Temporal Lobe: intentional, adj. $r^2 = 0.28$; incidental, adj. r = 0.30.
C: Coronal (top) and sagittal (bottom) slices display the ventral stream and MTL ROIs: Left Ventral Stream (not pictured); Left MTL (red); Right Ventral Stream (Blue); Right MTL (yellow).

FIGURES

Figure 1

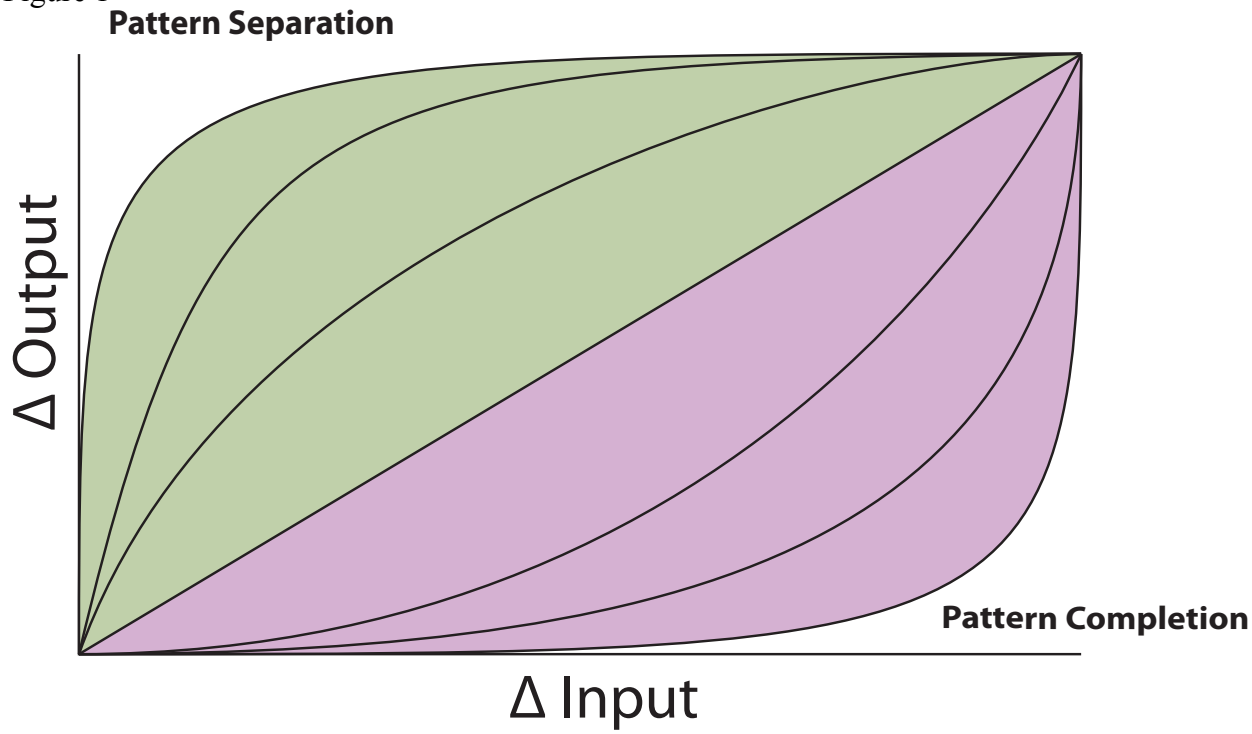

Figure 2

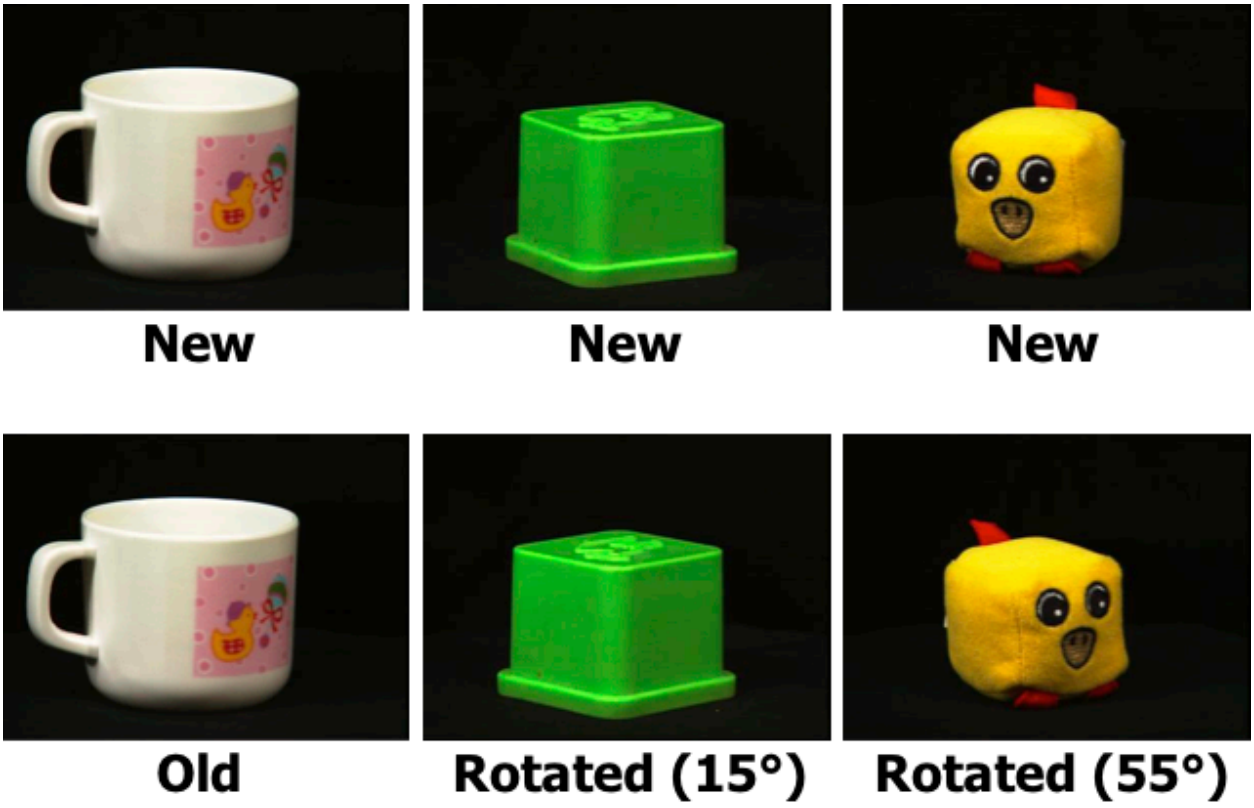

Figure 3

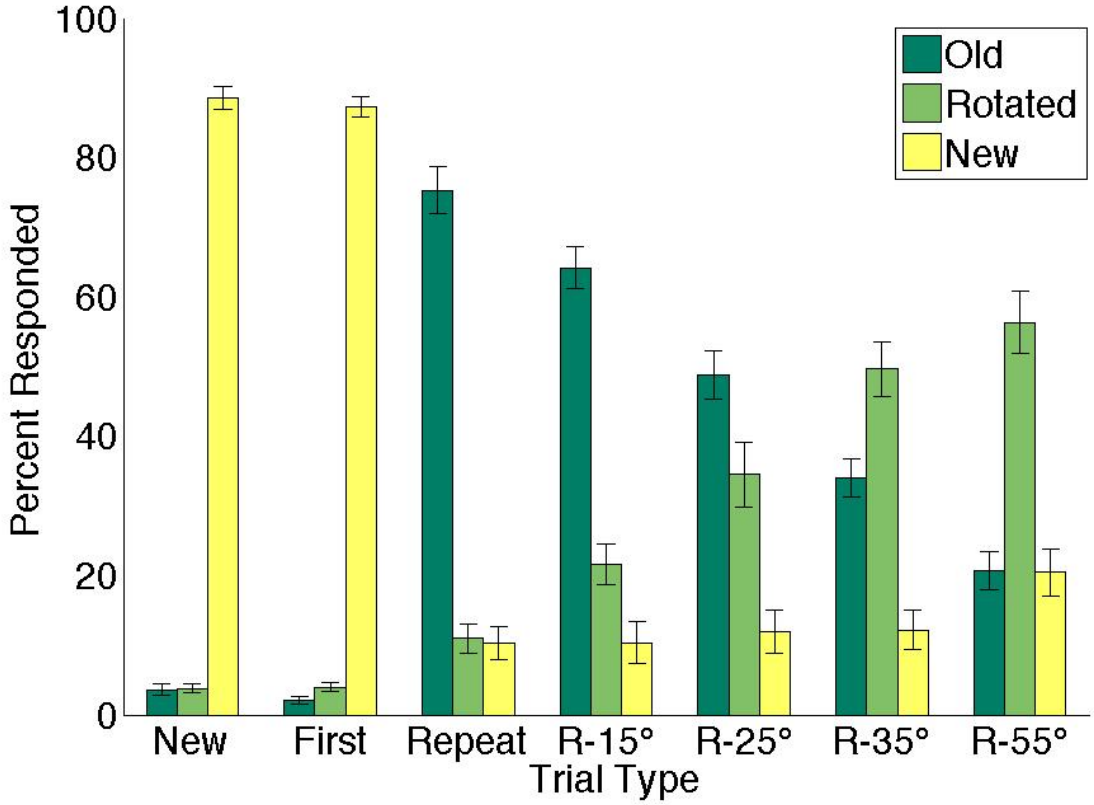

Figure 4

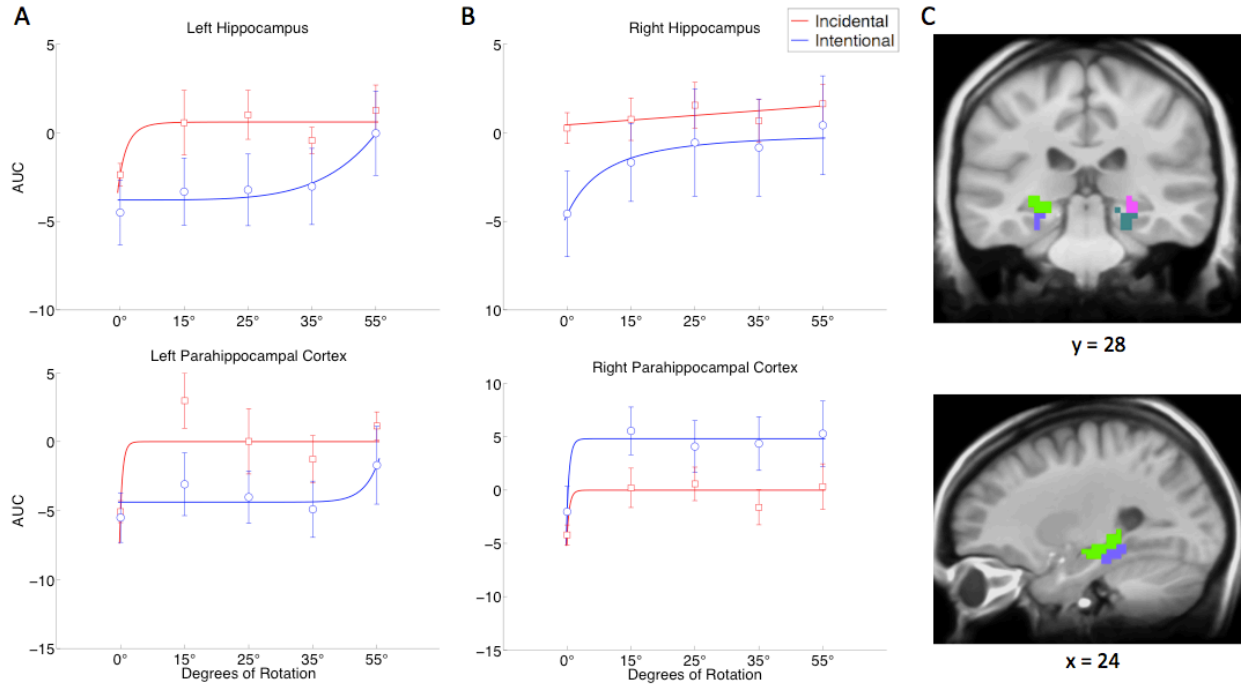

Figure 5

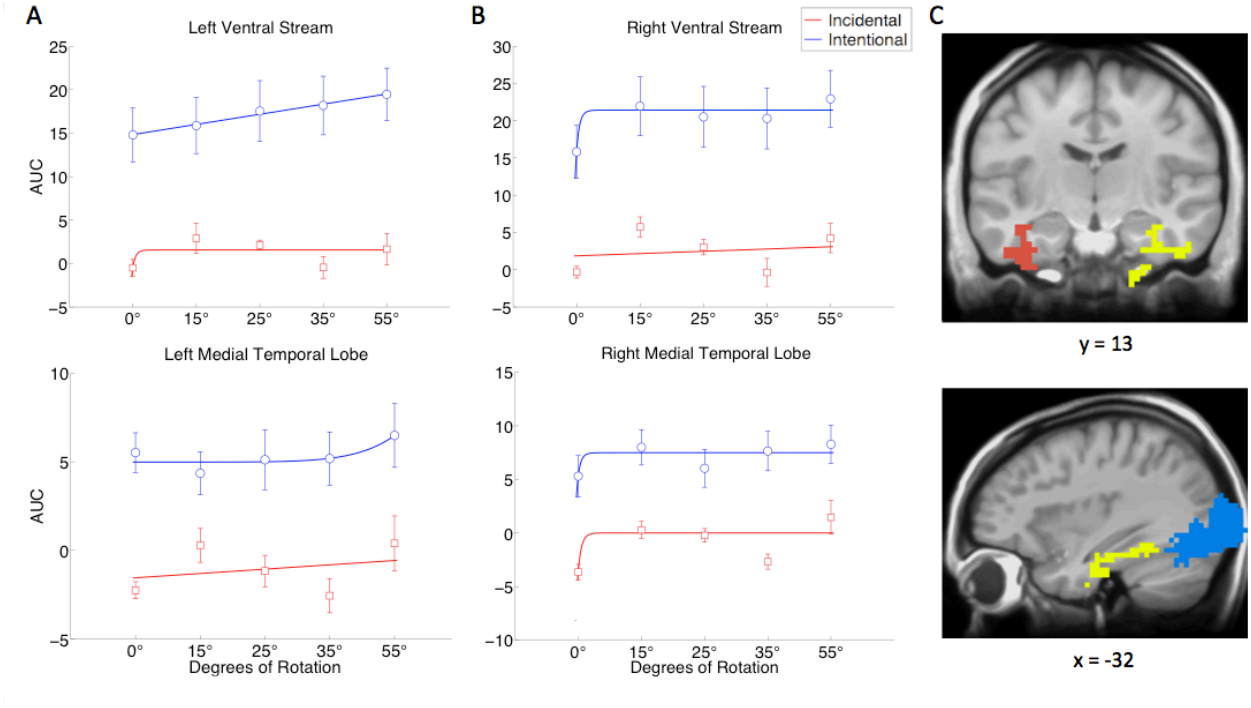
A
Left Ventral Stream
AUC
Left Medial Temporal Lobe
AUC
Degrees of Rotation
B
Right Ventral Stream
Incidental
Intentional
Right Medial Temporal Lobe
Degrees of Rotation
C
y = 13
x = -32

TABLE LEGENDS

Table 1 – Regions of Interest (ROIs) isolated in the Intentional v. Incidental and First v. Repeat t-test contrasts
L, Left; Ventral, Ventral Stream; R, Right; MTL, Medial Temporal Lobe; H, hippocampus; PHC, parahippocampal cortex; Mid, Midline; Par, Parietal Cortex; DLFr, Dorsolateral Frontal Cortex; VLFr, Ventrolateral Frontal Cortex; LTL, Lateral Temporal Lobe

Table 2 – Curves fit to the hippocampal and parahippocampal cortex ROIs
L, Left; H, hippocampus; R, right; PHC, parahippocampal cortex; Linear, linear fit; Power, power fit; Adj. r^2, adjusted r-squared value; r^2, r-squared value; RMSE, root mean squared error; SSE, sum of squares error; DFE, degrees of freedom error.

Table 3 – Curves fit to the ventral stream and MTL ROIs
L, Left; Ventral, Ventral Stream; R, Right; MTL, Medial Temporal Lobe; Linear, linear fit; Power, power fit; Adj. r^2, adjusted r-squared value; r^2, r-squared value; RMSE, root mean squared error; SSE, sum of squares error; DFE, degrees of freedom error.

Table 4 – Mean reaction time (RT) for intentional task
A t-test comparison between rotated conditions compared to first presentation stimuli revealed significant differences between all rotated conditions and first presentation stimuli. This response latency indicates mental rotation for rotated conditions. A significant response latency is also seen for repeat images, possibly because participants were mentally rotating the repeat images to confirm their decision of "old".

TABLES

Table 1

Contrast	Region	*x*	*y*	*z*	*μ*l
Intentional v. Incidental (t-test)	L Ventral	34	80	-2	33,831
	R Ventral	-28	88	0	24,786
	L MTL	37	12	-25	3,861
	R MTL	-29	26	-21	4,401
First v. Repeat (t-test)	L H	26	26	-6	1,566
	R H	-23	29	-4	270
	L PHC	23	32	-10	891
	R PHC	-21	33	-10	999
Intentional v. Incidental (t-test) Default Network	Mid, R Par, L DLFr, L VLFr, R VLFr	-13	12	22	199,503
	L Par, L LTL	54	47	16	22,896
	L DLFr	45	-15	4	12,256

Table 2

ROI	Condition	Fit Type	Model	adj. r^2	r^2	RMSE	SSE	DFE
L Hy	Incidental	Linear	f(x) = 0.6249x - 1.87	0.27	0.45	1.26	4.80	3
		Power	f(x) = -2.969 * x^(-7.304) + 0.6024	0.62	0.82	0.92	1.67	2
	Intentional	Linear	f(x) = 0.9237x - 5.596	0.69	0.77	0.92	2.54	3
		Power	f(x) = 0.0001894 * x^ (6.145) - 3.797	0.84	0.92	0.67	0.91	2
L Phy	Incidental	Linear	f(x) = 0.8183x - 2.898	-0.09	0.18	3.15	29.81	3
		Power	f(x) = -5.075 * x^(-23.96)	0.57	0.68	1.98	11.73	3
	Intentional	Linear	f(x) = 0.5788x - 5.584	0.16	0.37	1.38	5.71	3
		Power	f(x) = 1.488e-15 * x^(21.82) - 4.387	0.26	0.63	1.30	3.36	2
R Hy	Incidental	Linear	f(x) = 0.2658x + 0.1747	0.33	0.50	0.49	0.71	3
		Power	f(x) = -1.807 * x^(-0.5949) + 2.058	0.12	0.56	0.56	0.62	2
	Intentional	Linear	f(x) = 1.082x - 4.695	0.75	0.81	0.96	2.76	3
		Power	f(x) = -4.617 * x^(-1.687)	0.93	0.95	0.50	0.76	3
R Phy	Incidental	Linear	f(x) = 0.7257x - 3.111	0.09	0.32	1.93	11.16	3
		Power	f(x) = -4.204 * x^(-25.03)	0.75	0.81	1.02	3.11	3
	Intentional	Linear	f(x) = 1.347x - 0.5775	0.28	0.46	2.65	21.06	3
		Power	f(x) = -6.864 * x^(-24.11) + 4.835	0.92	0.96	0.87	1.51	2

Table 3

ROI	Condition	Fit Type	Model	adj. r^2	r^2	RMSE	SSE	DFE
L MTL	Incidental	Linear	f(x) = 0.244x - 1.787	-0.23	0.08	1.52	6.96	3
		Power	f(x) = -1.484 * x^(-24.02) - 0.7579	-0.53	0.23	1.70	5.79	2
	Intentional	Linear	f(x) = 0.2758x + 4.498	0.09	0.32	0.74	1.63	3
		Power	f(x) = 1.101e-06 * x^(8.775) + 4.98	0.42	0.71	0.59	0.70	2
L Ventral	Incidental	Linear	f(x) = 0.09061x + 0.8777	-0.32	0.01	1.78	9.47	3
		Power	f(x) = -2.047 * x^(-22.95) + 1.559	-0.30	0.35	1.76	6.20	2
	Intentional	Linear	f(x) = 1.166x + 13.67	0.98	0.99	0.25	0.18	3
		Power	f(x) = 14.47 * x^(0.1734)	0.95	0.97	0.40	0.47	3
R MTL	Incidental	Linear	f(x) = 0.726x - 3.141	0.05	0.29	2.07	12.89	3
		Power	f(x) = -3.65 * x^(-19.79)	0.30	0.48	1.78	9.48	3
	Intentional	Linear	f(x) = 0.5622x + 5.366	0.12	0.56	1.23	3.01	2
		Power	f(x) = -2.193 * x^(-21.76) + 7.491	0.28	0.46	1.11	3.70	3
R Ventral	Incidental	Linear	f(x) = .3052 + 1.556	-0.29	0.03	3.11	29.05	3
		Power	f(x) = -3.491 * x^(-24.6) + 3.17	-0.35	0.33	3.18	20.23	2
	Intentional	Linear	f(x) = 1.258x + 16.53	0.38	0.53	2.15	13.90	3
		Power	f(x) = -5.599 * x^(-21.48) + 21.42	0.69	0.84	1.52	4.64	2

Table 4

Condition	Mean RT	*p*-value
First	1019.7	-
0°	1340.0	4.4E-11
15°	1355.0	3.4E-10
25°	1354.9	2.9E-10
35°	1299.1	1.0E-08
55°	1285.1	7.2E-08

· S a r a h E l i s a b e t h M o t l e y ·

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EDUCATION

January 2011 – present	**Master's Candidate, Neuroscience** Brigham Young University, GPA 4.0 Laboratory of Dr. Brock Kirwan *'A Parametric Investigation of Pattern Separation Processes in the Medial Temporal Lobe'*
December 2010	**Bachelor of Science, Neuroscience, Minor in Italian** Brigham Young University, GPA 3.83, Cum Laude

PUBLICATIONS

October 2011	Under review, Journal of Neuroscience **Motley, SE** and Kirwan, CB. '*A Parametric Investigation of Pattern Separation Processes in the Medial Temporal Lobe*.'

WORK EXPERIENCE

January 2010 – present	**Research Assistant, Brock Kirwan, PhD** *Rotated Objects Project* ·Designed behavioral experiment in E-Prime. ·Ran subjects in pilot testing at Brigham Young University (BYU). ·Ran subjects in fMRI experiment at the University of Utah. ·Analyzed behavioral and functional data using AFNI and MATLAB. ·Wrote and submitted publication to Journal of Neuroscience. *Red Green Project* ·Designed behavioral experiment in E-Prime. fMRI testing in preparation
January 2010 – present	**Subject Coordinator, Memory and Cognition Lab** ·Managed the subject database and lab email. ·Screened and scheduled subjects for participation in studies. ·Sent subject registration papers to the Imaging & Neurosciences Center.
January 2011 – present	**Undergraduate Research Mentor** ·Trained undergraduate students in EEG testing protocol, experiment design in E-Prime, and hippocampus tracing in AFNI.
Winter 2012	**Assistant Teacher, Roy Silcox, PhD** *PDBio 305 (Human Physiology)* ·Taught 4 of 18 chapters for the Life Sciences Teaching Practicum: Ch. 4.) Neuronal and Hormonal Communication, Ch. 5.) The Central

Nervous System, Ch. 6.) The Peripheral Nervous System, Part A, Ch. 7.) The Peripheral Nervous System, Part B

Fall 2011 — **Assistant Teacher, Roy Silcox, PhD**
PDBio 205 (Human Biology)
·Taught 2 of 25 class units for the Life Sciences Teaching Practicum: 1.) The Nervous System: Integration and Control, 2.) Sensory Mechanisms.
·Graded student term papers and related assignments.

Fall 2010 – Fall 2011 — **Teaching Assistant, Brock Kirwan, PhD**
Neuro 380 (Behavioral Neuroscience): Sep – Dec 2010, Sep – Dec 2011
Psych 381 (Behavioral Neurobiology): Jan – Apr 2010
·Graded student work: weekly quizzes, mid-term exams, final exams.

LAB SKILLS

January 2010 – present

fMRI data analysis
MATLAB · Proficient at statistical analysis, graph making, curve fitting
AFNI · Proficient at AC/PC and Talairach aligning, data processing, hippocampus tracings, deconvolution analyses, t-tests and ANOVAs

Experiment design
Psychtoolbox · Proficient at experiment designing using MATLAB
E-Prime · Proficient at experiment designing

EEG testing protocol
Net Station · Proficient at EEG testing protocol

MEETINGS, COURSES, AND INTERNSHIPS

November 2011 — **Society for Neuroscience Meeting**
·Presented poster for Rotated Objects Project.

July 2011 — **Biology of Memory Course, Cold Springs Harbor Laboratory**
·Selected as a participant after competitive application review.
One of 3 master's students, along with 15 PhD students and post-docs

January 2006 – March 2006 — **Internship, US Olympic Committee, 2006 Winter Olympics, Torino**
·Translated Italian, Torino Olympic Village and US Operations Center.

FELLOWSHIPS, SCHOLARSHIPS, AND AWARDS

January 2012, September 2011 — **Neuroscience Fellowship ($1,000)**
January 2011 — BYU Department of Physiology and Developmental Biology

January 2012, September 2011 — **Neuroscience Teaching Assistantship ($5,000)**
January 2011 — BYU Department of Physiology and Developmental Biology

September 2011 — **Student Travel Award ($600)**
BYU Department of Physiology and Developmental Biology
To present a poster at the 2011 SfN Annual Meeting (Washington, DC)

September 2011	**College of Life Sciences Scholarship ($500)** BYU College of Life Sciences
May 2011	**Neuroscience Research Assistantship ($5,000)** BYU Department of Physiology and Developmental Biology
June 2009	**Winter 2009 Semester Dean's List** BYU College of Family, Home, and Social Sciences
October 2007	**Abstract published, Proceedings of 2007 BIOT Symposium (Biotechnology and Bioinformatics)** K. Clement, **S. Motley**, D. McClellan. *BCL-2 Apoptosis Regulation*
September 2004	**National Merit Scholarship (4-year, full-tuition)** Brigham Young University

LEADERSHIP AND OUTREACH

January 2011 – present	**Neuro Student Association, BYU, Service Rep, Board Member** ·Saw the need to promote the neuroscience major. Conceived, oversaw on-campus events for Brain Awareness Week to promote neuroscience. ·Collaborated with other board members to plan events and raise funds.
January 2011 – December 2011	**Women in Science, BYU, Founding Club President** ·Chosen by faculty, students to be first President of Women in Science. ·Created club organization, committees. Wrote final draft of club charter. ·Directed events/guest speakers committee and presidency meetings. ·Directed monthly club meetings. Maintained club email. ·Developed recurring student-run microbiology microscope activity in local elementary schools to give children women in science role models. ·Arranged guest speakers, organized field trips to provide club members with adult women in science role models in various careers/stages of life. ·Conceived and organized An Evening Celebrating Women, the first campus-wide event involving all organizations promoting women. Event to be in March 2012 in conjunction with Women's History Month. ·Developed marketing strategy to increase club awareness. (2nd Semester Opening Social attendees: 77; 1st Semester Opening Social attendees: 41)
September 2006 – May 2007	**Women in Medicine, BYU, Service Chair, Board Member** ·Organized monthly volunteer opportunities for club members. ·Collaborated with other board members to plan events and raise funds.

SOCIETY MEMBERSHIPS

2011 – present	**Society for Neuroscience (SfN)**
2011 – present	**American Association for the Advancement of Science (AAAS)**

2010 – present	**Phi Kappa Phi Honour Society, inducted as a junior** Top 7.5% of university juniors, top 10% of university seniors
2005 – present	**Golden Key International Honour Society, inducted as a sophomore** Top 15% of university sophomores, juniors, and seniors

VOLUNTEER EXPERIENCE

Friday's Kids Respite	Non-profit providing respite for parents of kids with disabilities
June 2009 – present	**Volunteer Coordinator,** 2-3 times/month, 4 hours/shift ·Recruited volunteers through BYU's Center for Service & Learning. ·Oriented and supervised volunteers. Assigned volunteers to each child. ·Organized all activities. Cleaned up facilities after each shift.
January – June 2009	**Volunteer,** 4 times/month, 3.5 hours/shift
Provo Youth Mentoring	Mentoring program through BYU for Provo 6th Graders
June 2009 – May 2010	**Program Director** ·Organized weekly activities for the on-campus program at BYU. ·Placed volunteers with students in the on- and off- campus programs. ·Coordinated with community partners in Provo City Schools. ·Organized and ran board meetings. Managed the email account.
January – June 2009	**History Committee Chair, Board Member** ·Recorded mentoring events during the year. Wrote end-of-year report. **6th Grade Mentor, 1 hour/week** also October – December 2010, September 2006 – May 2007
The Church of Jesus Christ of Latter-day Saints July 2007 – December 2008	Utah Salt Lake City Temple Square Mission **Volunteer Church Representative**