Brain correlates of memory reconsolidation: A role for the TPJ

Katharine C. N. S. Simon, Rebecca L Gómez, Lynn Nadel and Paige E. Scalf[2]
[1]Department of Psychology, The University of Arizona
[2]Department of Psychology, Durham University

Address Correspondence to:
Katharine C. N. S. Simon

Department of Psychology
1503 E University Blvd.
P.O. Box 210068
Tucson, AZ 85721
Tel: (520) 626-0278
knsmith@email.arizona.edu

Abstract

In this paper, we investigate the process by which new experiences reactivate and potentially update old memories. Such memory reconsolidation appears dependent on the extent to which current experience deviates from what is predicted by the reactivated memory (i.e. prediction error). If prediction error is low, the reactivated memory is likely to be updated with new information. If it is high, however, a new, separate, memory is more likely to be formed. The temporal parietal junction TPJ has been shown across a broad range of content areas (attention, social cognition, decision making and episodic memory) to be sensitive to the degree to which current information violates the observer's expectations -- in other words, prediction error. In the current paper, we investigate whether the level of TPJ activation during encoding predicts if the encoded information will be used to form a new memory or update a previous memory. We find that high TPJ activation predicts new memory formation. In a secondary analysis, we examine whether reactivation strength -- which we assume leads to a strong memory-based prediction -- mediates the likelihood that a given individual will use new information to form a new memory rather than update a previous memory. Individuals who strongly reactivate previous memories are less likely to update them than individuals who weakly reactivate them. We interpret this outcome as indicating that strong predictions lead to high prediction error, which favors new memory formation rather than updating of a previous memory.

Introduction

That long-term memories can be altered by subsequent experience is now well established in work with both animal models and humans (Hupbach, Hardt, Gomez, & Nadel, 2007; Nadel, Hupbach, Gomez, & Newman-Smith, 2012; Nader, Schafe, LeDoux, 2000; Walker, Brakefield, Hobson, & Stickgold, 2003). When a current experience evokes a memory from a related circumstance in the past, aspects of the current experience can be integrated into, and thereby alter, the older, reactivated, memory. Alternatively, current experience can form the basis of an entirely separate memory, leaving the older memory intact.

When people encounter truly novel information; that is, information about which they have neither experience nor expectations, they form a new and distinct memory trace (Barto, Mirolli, & Baldassarre, 2013; Fernandez, Boccia, & Pedreira, 2016). Most situations, however, are not entirely novel, hence they give rise to some expectations as an experience unfolds. In these cases, apparently, the difference between the predicted and the actual experience is assessed (Exton-McGuinness, Lee, & Reichelt, 2015). The degree of difference can determine whether information about the new situation is integrated into an old memory or kept separate in a new memory trace. We believe that when the degree of violation is small, the system reacts by integrating new information into the old memory. Alternatively, when the degree of violation is large, a new memory is constructed instead, and the old memory is left unchanged. Research supporting this idea was reported by Sevenster, Beckers, & Kindt (2013) who demonstrated that pharmacologically

mediated fear-response mitigation is dependent upon the reactivation condition being different from the original conditioning; the agent itself is not sufficient to reduce a fear response. Furthermore, such reduction requires that expectations about the conditioned stimulus be violated multiple times (Sevenster, Beckers, & Kindt, 2012; Sevenster, Beckers, & Kindt 2014). Another study initiated expectation violation by altering the timing interval between previously learned conditional and unconditional stimulus pairs (tone and foot shock). They found that the novel timing, which clearly violated expectations, resulted in reconsolidation. Without such a violation, reconsolidation did not occur (Diaz-Mataix, Martinez, Schafe, LeDoux, & Doyère, 2013). Together, these studies demonstrate that some violation of expectation (prediction) is a condition necessary to support memory reconsolidation.

What neural mechanisms underlie the evaluation of whether prediction error is high enough to merit the formation of a new memory? Although this question has not been addressed within the memory reconsolidation literature, there are clues available from previous research in the domains of attention, social neuroscience, decision making and episodic memory. Findings from each of these literatures suggest that the temporal parietal junction (TPJ; a part of the ventral posterior parietal lobe), plays a central role in determining the degree to which current circumstances deviate from expectation. Within the attention literature, the TPJ has been shown to be sensitive to trial history effects, such that it is active if the correct response to a given stimulus class on a current trial is different than the correct response to the same stimulus on the immediately preceding trial (Scalf, Ahn, Beck & Lleras 2014). The TPJ also plays a critical role in the conscious

detection of subtle, moment to moment stimulus change (Micheli, Kaping, Westendorff, Valiante, & Womelsdorf, 2015). Within the social neuroscience literature, the TPJ has been shown to be active when the actions taken by another individual do not match those predicted either by the individual's stated intention (Behrens, Hunt, & Rushworth, 2009) or by the individual's previous actions (Hampton, Bossaerts & O'Doherty, 2008). More limited data from the reward/decision making literature suggest that TPJ activation is high when a contextually important, relatively infrequent event occurs (Kahnt & Tobler, 2013), even when there is no direct social or emotional content to the decision. For our purposes, the most convincing piece of evidence comes from an episodic memory paradigm, in which participants were cued about the likelihood of a target word being "old" or "new". The TPJ was sensitive not to the memory status of the target word, but to whether the memory cue was valid or invalid (O'Connor, Han & Dobbin, 2010). What all of these results have in common is the finding that when current circumstances are different than those predicted by previous information, the TPJ is engaged. This may be the "evaluative" role of the TPJ suggested by Han & Marois, (2014); for a plausible "box and arrow" model of how TPJ might interact with other brain regions in evaluating prediction error, see Seghier, (2013).

TPJ activity is also known to occur during the performance of memory tasks, but its role in these tasks has been unclear. Although some have suggested that this activation reflects "attention to memory" (Cabeza, Ciaramelli, Olsen, & Moscovitch, 2008), we suspect that it may instead reflect the TPJ's role in successful memory formation. Previous research shows that the TPJ is activated during successful semantic and perceptual

encoding (Daselaar, Prince, & Cabeza, 2004), and is an integral part of the autobiographical memory network (Svoboda, McKinnon, & Levine, 2006). Multi-voxel pattern analysis of TPJ content during encoding positively predicts retrieval success (Lee, Chun and Kuhl, 2016). Together, these results suggest to us that the TPJ plays a role in successful generation of new memories (see Shimamura, 2011).

In order to study the role of prediction error and whether TPJ plays an evaluative role in memory reconsolidation, we created a modified computer version of the Hupbach, Hardt, Gomez, & Nadel (2007) paradigm where participants learn information that is later reactivated in the presence of new information. Some of the new material becomes incorporated into the existing memory, leading to a reconsolidated original memory trace. For this modified paradigm, participants learned Set 1, twenty objects paired with their typically associated sounds. For example, participants saw a train and heard a train whistle. 48 hours later, we reactivated participants' memory of the Set 1 objects by playing some of the learned sounds. In our previous work, reactivation of an older memory depended on reinstating the actual physical context (Hupbach et al., 2007). Here we used the object-sounds as contextual reminders within the learning episode, allowing us to run the second portion of the study in an MRI scanner. All participants then learned a second, new set of twenty objects. Forty-eight hours later, we assessed participants' Set 1 and 2 memories to determine whether or not they had been altered. Our previous work identified that reactivating the Set 1 memory prior to learning the Set 2 objects resulted in the alteration of Set 1. Objects from Set 2 became attributed to the first learning episode,

"intruding" into the memory of Set 1. If participants were not reminded of Set 1 prior to learning Set 2, no such alteration occurred (Hupbach et al., 2007).

Our paradigm allowed us to observe the brain activity specific to the second experiment day, namely, new Set 2 object encoding and old Set 1 memory reactivation. We looked for differences in the neural activity observed during the encoding of Set 2 objects that were subsequently added to the first set as compared to those that were segregated and maintained in a separate Set 2 memory. Because previous work indicates the TPJ activates when expectations are violated, we anticipated that the TPJ would be more active to items that were encoded into a new memory (prediction violation) than to items that were added to the old memory (prediction confirmation). We also investigated patterns of neural activity during Set 1 reactivation, because the quality of memory reactivation should determine the quality of predictions derived from it.

Materials and Methods

Participants

We recruited a total of 14 students (7 female) from the University of Arizona to participate in this study, as approved by the Institutional Review Board of Arizona. All but one of the participants were right-handed, had normal or corrected-to-normal visual acuity, and had no past or current psychological or medical disorders. Prior to participation, we administered oral and written consent. We paid participants for their time. We eliminated three participants due to movement artifact or falling asleep during the scanning session. The final analysis includes data from 11 participants.

Stimuli

The experimental stimuli consisted of 60 common objects and the sounds typically associated with them (see Table 1).

Set 1	Set 2	Novel Objects
Apple	Ball	Ambulance
Airplane	Bell	Balloon
Alarm clock	Blow Dryer	Bicycle
Arrow	Camera	Calculator
Car	Cork	Cellphone
Coins	Doorbell	Chimes
Cymbals	Drill	Crayon
Door	Flute	Dice
Drum	Golf club	Eraser
Fan	Hairspray	Gong
Frying Pan	Hammer	Key
Hands	Phone	Noisemaker
Leaf Blower	Shoe	Nutcracker
Matchstick	Soda	Pot
Saw	Train	Scissors
Smoke Detector	Typewriter	Spring
Sprinkler	Vacuum	Stapler
Teakettle	Whip	Tissues
Toilet	Whistle	Toothbrush
Zipper	Window	Washing Machine

Table 1. Sets of objects presented on Day 1, Day 2, and Novel Objects in the recognition test.

Pictures of all objects were presented in 2-D, in the center of a computer screen on a white background. Participants also performed two 'distractor tasks', in which they counted varying numbers of grey birds on a light blue background or watched a short clip of a nature video of United States National Parks.

Procedure

Using a computer-driven object-learning paradigm modified from Hupbach, Gomez, Hardt, and Nadel (2007), participants participated in 3 sessions each separated by 48 hours. Stimuli at each session were presented using EPrime 2.0 software on Windows XP (Psychological Tools, Pittsburgh, PA).

At Session 1 (encoding), held in the psychology department, we taught participants Set 1, which consisted of 20 common objects paired with their typically associated sounds. For example, participants viewed a picture of a drum while simultaneously hearing the sound of drumming. Set 1 objects were each presented in "learning blocks". During a given learning block, two randomly generated pairs of Set 1 objects (e.g. drum and matchstick) appeared on the computer screen. The participant chose which object s/he would like to see and hear first (e.g. the drum). The object then appeared in isolation with an associated sound for 5 seconds (e.g. participants saw the drum and heard drumming). The object pair would then return to the screen at which time the subject chose the alternate object to see and hear in isolation (e.g. the matchstick and the sound of a match lighting). Three blocks of learning occurred. Within each block, each Set 1 object was presented once and only once. New pairings of Set 1 objects were used (e.g. coins and sprinkler) across blocks. Across each of the three learning blocks, the pairings were ran-

domized without replacement (see Figure 1 for an example sequence). To minimize mental rehearsal between the learning blocks, participants engaged in the distractor task, consisting of a series of slides in which they were to count the birds on the screen. At the end of the learning session, we administered a one-time recall test to assess participants' memory of Set 1, 'please recall as many of the objects as you can'. At the end of each session, we instructed participants not to speak, write, or ruminate about the study procedure or objects.

Participants returned 48 hours later for Session 2, the scanning portion of the study, held at the University Medical Center. We attempted to reactivate Set 1 memory at the beginning of each scanning session. We gave participants visual instructions to "Please listen to the following sounds". Participants listened to 10 sounds from the Set 1 object-sound associations. These sounds were presented once through headphones (Resonance Technologies) in a 28-second period with intervals of 1 second of silence occurring between each sound. Sound order was randomized across participants.

The Set 2 learning phase began immediately after the sound reactivation phase (see Figure 1 for learning schematic). We taught participants 20 objects from Set 2 (see Table 1). Objects in Sets 1 and 2 were distinct, with no physical or conceptual overlap, however they could overlap in category, e.g. airplane, car, and train are all vehicles. Set 2 objects occurred in each of 3 fMRI runs; each Set 2 object appeared once and only once, in a random order, during each run. Within a run, objects occurred in isolation for 5 seconds followed by a 10 second inter-stimulus interval (see Figure 1 for an example learning sequence). In between fMRI runs, we presented participants a nature movie of United

States National Parks to minimize mental rehearsal. After scanning, we administered a one-time recall test to assess participants' memory of Set 2. As after Set 1 learning session, we again instructed participants to not to speak, write, or ruminate about the study procedure or objects.

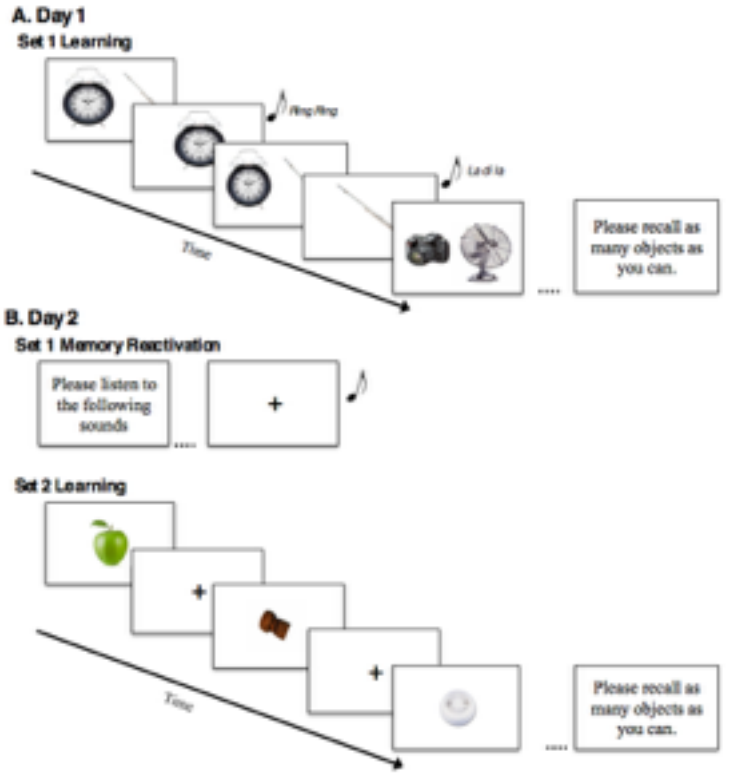

Figure 1. Learning schematic for Day 1 and Day 2. A. On Day 1, subjects learned twenty Set 1 objects. B. On Day 2, subjects were initially presented with sounds from Set 1 to reactivate the old memory. They were then presented with twenty new Set 2 objects.

At Session 3, 48-hours later, participants returned to the location used during the learning of Set 1 (a particular room in the Psychology building). Participants took a recognition test, comprised of the Set 1 and Set 2 objects along with 20 objects not seen

in the previous sessions. Objects were randomly presented on the computer screen without accompanying sounds, with directions to identify whether the object was learned on Day 1, Day 2, or had never been seen before. After the recognition test, participants filled out a debriefing questionnaire to determine whether they followed instructions to refrain from speaking, writing, or ruminating about the procedure or objects.

Data Acquisition and Analysis

We acquired the fMRI data using a 3.0T Sigma whole-body scanner (Sigma Echo Speed; General Electric, Milwaukee, WI) with a four-channel phased array head coil. We used a single-shot spiral in-out pulse sequence (TR = 2, TE = 25ms, flip angle = 90^{o}, 64x64 matrix, thickness = 5mm, gap =1mm, FOV = 120 x 120) to obtain functional images consisting of 30 ascending coronal slices. We collected 160 repetitions for the scan that included reactivation and learning run 1 and 154 repetitions for the scans that contained learning blocks 2 and 3. We administered two additional scans, a T2 weighted structural scan in plane with EPI images and an SPGR (1mm isotrophic) to assist in registering the EPI images to anatomical space.

We analyzed the functional data using FMRIB (Oxford University Centre for Functional MRI of the Brain) Software Library (FSL). Images were reconstructed offline, underwent brain extraction, were registered to standard space, had spatial smoothing (8mm), high pass filtering (sigma = 50 seconds), and low-pass filtering (sigma =2 seconds). Data were also prewhitened to eliminate effects of serial autocorrelation.

Set 2 objects that were correctly identified during Session 3 testing were termed "correct recall" (CR). Set 2 objects incorrectly attributed to Set 1 were termed intrusions, and served as markers that indicated set 1 memory updating.

Encoding Analysis. Functional data from the eight participants who showed any level of memory updating (at least one or more Set 2 objects recognized as Set 1) were used to look for differences in right and left TPJ activation for objects that were subsequently

correctly recognized compared to those that were subsequently misattributed to Set 1. Three subjects did not show any Set 1 memory modification (Set 2 objects recognized as Set 1), thus were not included in this analysis. Because we were specifically investigating whether the TPJ plays a role in adjudicating whether or not new memories are formed, we examined signal from the right and left posterior TPJ as defined by anatomical masks developed by Igelström, Webb, & Graziano (2015) (see Figure 2). We focused on the posterior TPJ because this region has previously been shown to be especially sensitive to changes in context that occur across multiple modalities (Downar etal., 2000). Because hippocampal (Hc) activation is ubiquitous in fMRI investigations of memory, we also examined activation in the right and left Hc (see Figure 3).

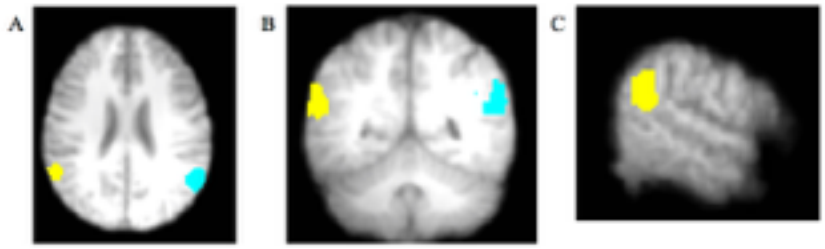

Figure 2. Right and left TPJ (Y = -50, Z=10, X= 48) as defined by anatomical masks developed by Igelström, Webb, & Graziano (2015).

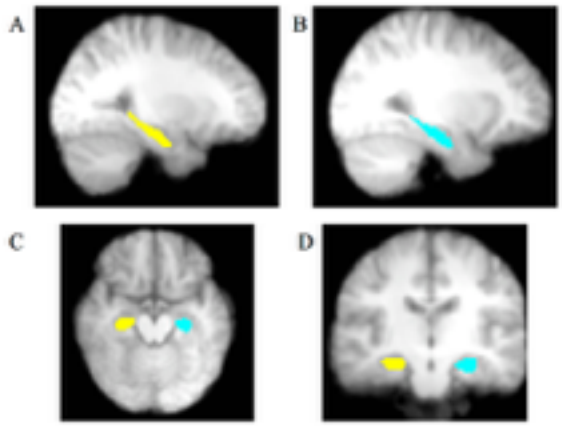

Figure 3. Right and left hippocampus masks. A. Sagittal view of right hippocampus mask (X = 29) B. Sagittal view of left hippocampus mask (X = -27) C. Axial view of right and left hippocampus (X = -35) D. Coronal view of right and left hippocampus (Y = -1)

As we were interested in the difference between "correct recall" and "intrusion" activation, but did not have the same number of trials for the two conditions, we did not subject encoding data to voxelwise GLM analysis. This type of analysis might well have found a difference in activation between the two conditions that was driven by differences in the power of the two regressors. Instead, we performed standard selective averaging on trials of each type. We extracted the data corrected for signal drift, motion, spatial nonhomogeneities and serial autocorrelation from each ROI in each subject. We spatially averaged each signal across each ROI. We identified the start time of each trial and extracted the fourteen seconds of data following it (recall that trial onset asynchrony was 15 seconds). We identified each trial as Correct Recognition or Intrusion and z-transformed transformed the BOLD signal data across trial types.

Reactivation Analysis. All reactivation data were submitted to GLM analysis using FEAT (FMRI Expert Analysis Tool) v 5.98 [FSL 4.1.9; (Smith et al., 2004; Woolrich et al., 2001)]. Our hypothesis that the TPJ mediates memory reconsolidation based on the level of prediction error assumes that Set 1 reactivation is sufficient to create such a "prediction". Our reactivation procedure involved a passive listening task. To assess the extent to which Set 1 memory was reactivated, we examined the relationship between sensory activation, hippocampal activation and intrusion rate. Our initial analysis subjected the 28 seconds of scanning during Set 1 reactivation to GLM using a single regressor -

- “sound on”. This was a block analysis; the 10 seconds prior to and after reactivation served as our baseline condition. We convolved this regressor with a double-gamma model of the HRF (Phase 0s).

The statistical maps from the reactivation analysis were registered into the participant’s individual anatomical space and into standard space using FMRIB's Linear Image Registration Tool (FLIRT; Jenkinson et al., 2002).

Data from all eleven participants’ reactivation period were subjected to higher level group analysis. The statistical maps for the parameter estimate of interest were fed into separate ordinary least-squares group analyses by *FMRIB's Local Analysis of Mixed Effects* (FLAME). We identified clusters in the right and left auditory cortex, right and left visual cortex and right and left Hc whose activation exceeded the statistical threshold of Z=3.1. We found such cluster in the right and left auditory (K= 1067, X=50, Y=-22, Z=10; K=750, X=-56, Y=-26, Z=10) and visual cortices (K=124, X=16, Y=-86, Z=-2; K=126, X=-14, Y=-86, Z=-16). No such clusters existed in the right or left or left Hc. **Note that we do not necessarily consider these to be meaningful activations in and of themselves.** Our interest in these clusters lies in the extent to which their activation predicts behavioral intrusion rates, as we discuss in the following section.

Results

Behavioral Data

Objects could be identified as belonging to Set 1, Set 2, or as newly presented (see Figure 4 for group means or Figure 5 for individual object identification). Thus, objects could be identified correctly or could be misidentified and misattributed to an incor-

rect list. All participants showed high correct recognition of the Set 1 objects (M = 92%, SD = 9.31%). We call Set 2 objects identified as belonging to Set 1 "intrusions" and Set 1 objects identified as belonging to Set 2 "source errors" (Hupbach et al., 2007). Consistent with Hupbach et al. (2007, 2009), participants showed unidirectional effects, often misattributing objects from Set 2 to Set 1 (M = 22.27%, SD = 20.17%) while misattributing very few objects from Set 1 to Set 2 (M = 5.45%, SD = 8.79%), $t(10) = 2.454$, $p = .03$. However, participants showed varied rates of intrusions, ranging from 0 to 55% (see Figure 5), allowing us to investigate the relationship between reactivation activation and subsequent memory modification. Participants almost perfectly identified novel objects as newly presented (M = 99.09%, SD = .61%; see supplemental data Figure 1).

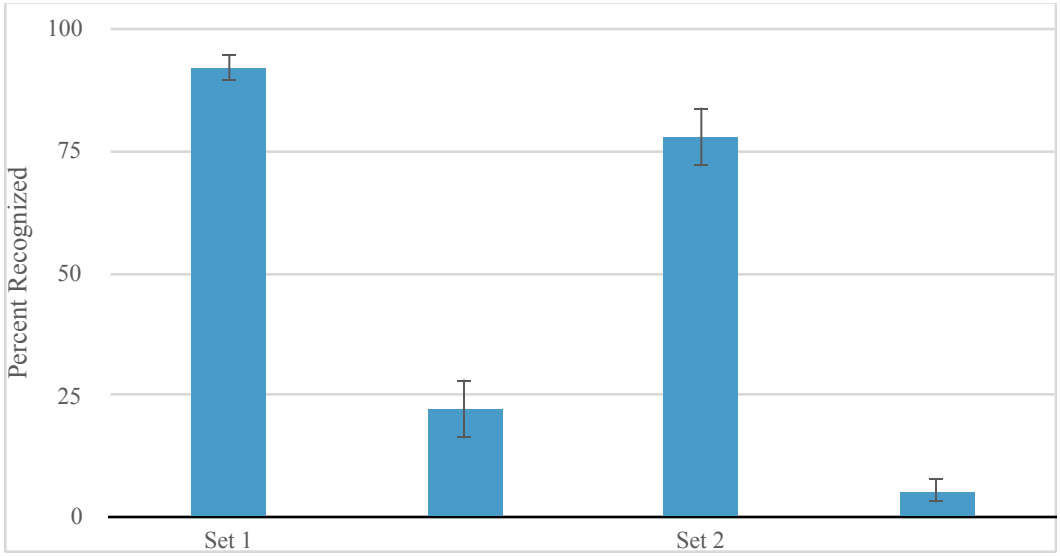

Figure 4. Mean percentage of all eleven participants' recognition data of Set 1 and Set 2 learned on Day 1 and Day 2 respectively. The day objects were learned could be correctly or incorrectly identified (intrusions or source errors). Error bars represent standard errors of means.

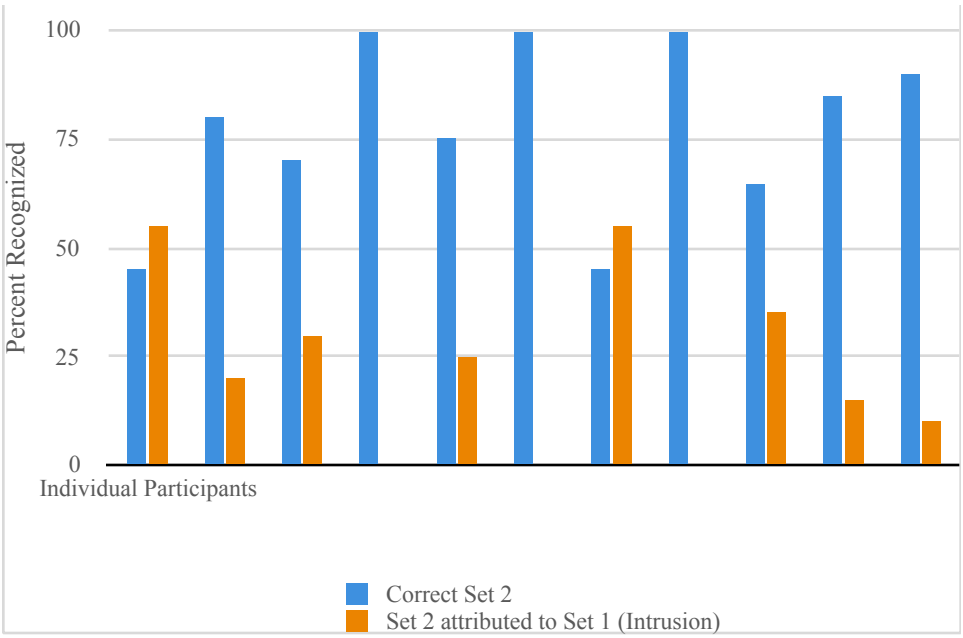

Figure 5. Individual participant object recognition data for Set 2. Objects could be correctly recognized or attributed to Set 1 (Intrusions).

Functional Data

Set 2 Encoding Analysis. We were interested in differences in BOLD signal to CR and I trials. The single gamma model of the HRF follows a quadratic function; a difference in activation between the two conditions should manifest in the ability of a quadratic function to account for their variance across time. We therefore analyzed the data extracted from each ROI for a tendency to follow a quadratic function. We found a significant quadratic trend in the left Hc ($F(1,7)=6.46$, $p =.039$) and a marginally significant quadratic trend in the right Hc ($F(1,7)= 4.54$, $p =.071$) (see Panels A and B in Figure 6). This indicates that the Hc was active during both Correct Recognition and Intrusion trials. Neither left ($p = .175$) nor right ($p = .557$) TPJ showed a significant quadratic trend across trial types. Consistent with our prediction that TPJ is sensitive to prediction error, however,

we found a significant interaction in the right TPJ as a function of trial type (Correct Recognition vs. Intrusion), $F(1,7)= 5.258$, $p =.046$ (see Panel C in Figure 6). Right TPJ activation followed a quadratic trend during trials that were correctly recalled as part of a new memory (violating the predictions made by the set 1 memory), but did not follow such a trend during trials that were added to the set 1 memory (intrusions).

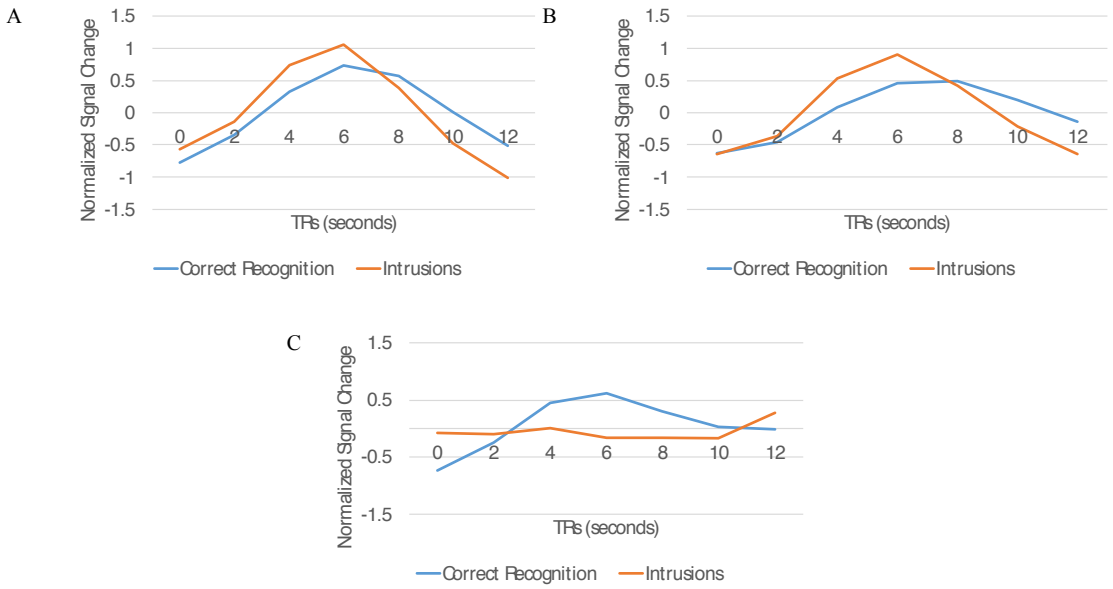

Figure 6. Encoding activation for Correct Recognition and Intrusions in A. Left hip-pocampus B. Right hippocampus C. Right TPJ.

Reactivation Analysis. We hypothesized that new memory formation requires a certain level of "prediction error". Prediction error first requires a robust prediction. In a memory reconsolidation paradigm, the strength of the prediction can be directly tied to the strength of the memory reactivation. We therefore hypothesized that those participants who showed strong reactivation of Set 1 memory would manifest fewer intrusions of Set 2 items into Set 1 memory. Because our reactivation took the form of a passive listening

task, we used the strength of sensory activation as a proxy for memory reactivation. Because any activation of visual cortex during the reactivation period could reflect only visual imagery on the part of the participant (recall that the participant viewed a blank screen during this period), we were particularly interested in the relationship between visual cortex activation and intrusion rates. For each cortical region, we ran a Kendall tau-b correlation by ranking both the neural activation and the intrusion absolute number to determine the relationship between an individual's neural activation and intrusion rate. We found the ranked activity in the right and left occipital cortices negatively correlated with the ranked intrusion level (Right Occipital Cortex τ_b = -.472, p = .048, Left Occipital Cortex τ_b = -.519, p =*.032*) while neither ranked auditory region showed a significant relationship (Right Auditory Cortex τ_b = -.397 p = .097, Left Auditory Cortexis τ_b = -.359, p = .133) (see Figure 7). As such, greater visual region activation negatively predicted the likelihood of Set 1 object memory modification. Those who showed significantly greater activation in visual processing regions during the replay of sounds linked to Set 1 memory demonstrated more veridical memory at the Session 3 test.

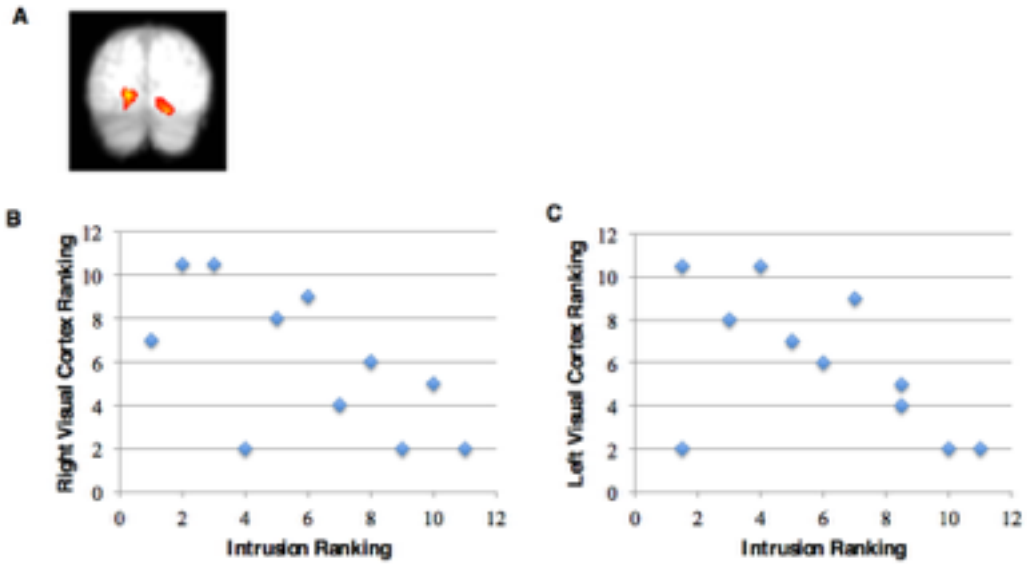

Figure 7. A. Right and left visual cortex activation during Set 1 reactivation (16, -86, 4). B. Ranked activation in the right visual cortex and ranked intrusions negatively correlated. C. Ranked activation in the left visual cortex and ranked intrusions negatively correlated.

Discussion

The present study investigated 1) the role of the TPJ in determining whether new experiences are kept distinct from older reactivated memories and 2) how neural activity during the reactivation of an old memory is linked to subsequent alteration of that memory.

Updating an old memory

Our model of memory reconsolidation gives a prominent role to prediction error; whether new experience modifies an old, reactivated, memory or serves as the basis for a new memory is strongly influenced by the degree to which that new experience violates the expectations, or predictions, generated by the old reactivated memory. When predic-

tion error is relatively high, an entirely new memory is formed, as the brain has 'decided' that these two "events", which differ considerably from one another, must be parts of separate events. When prediction error is relatively low, some or all of the content of the new experience might be integrated into the old reactivated memory – in this case the brain has 'decided' that the two events are sufficiently alike and perhaps part of the same larger event. This latter condition leads to memory updating and what we have called in our work "intrusions".

Previous work on the TPJ lead us to hypothesize that it might play a role in this process, perhaps by providing some critical input that helps the brain 'decide' whether new experience should give rise to a new memory or to the updating of an old memory. Our findings indicate that this is indeed the case; the TPJ is more active during the processing of information that will be used to form a new memory than it is during the processing of information that will instead be used to update an old memory.

Our main finding supports the claim that the right TPJ is part of the brain networks that confirm or disconfirm previous predictions (Hans & Marois, 2014; Seghier, Leff, Green, & Price, 2014; O'Connor et al., 2010). Within the memory literature, activity in the TPJ is often linked with the amount of detail represented in episodic memory. By indicating, evaluating, or even controlling, the level of episodic detail the TPJ could directly affect the computation of prediction error. Increased TPJ engagement, signaling increased detail evaluation, highlights any differences between the current and previous memory contexts (Exton-McGuinness, Lee, & Reichelt, 2015; Lee, 2009). This in turn increases prediction error, which should favor the formation of independent memory

traces, and little updating. And this is exactly what we see – as TPJ engagement goes up, intrusions go down.

Reactivation of the old memory

In order for high prediction error (and thus new memory formation) to occur, a relatively robust prediction must first be made. A more robust prediction should result in greater sensitivity to prediction error, which in turn should result in lower incidence of memory updating and greater incidence of new memory formation. In the case of a memory reconsolidation paradigm, the "prediction" is generated during reactivation. During our reactivation period, no visual stimulation occurred. Any activity in visual cortices during that period, then, must reflect retrieval of representations of the objects triggered by the matched sounds presented during our reactivation procedure. Using activity in visual cortex as a measure of reactivation strength, we found that those individuals showing greater extrastriate activation during memory reactivation generated fewer intrusions of Set 2 when tested for Set 1 memory. As we expected, greater reactivation was associated with a diminished likelihood of intrusions and memory alteration.

This finding seems at odds with an account of memory reconsolidation using a temporal context model (TCM) framework. This approach predicts that greater contextual reinstatement during old-memory reactivation should result in increased intrusion rates (Sederberg, Gershman, Polyn, & Norman, 2011). In contrast to TCM models, we see at least two things happening: (1) stronger reactivation of an old memory trace could strengthen and stabilize that trace, protecting it from modification by new experience;

and (2) as we argued above, the more faithfully a long-term episodic memory trace is re-activated, the less likely it is to match with current experience.

Conclusion

The present study examined brain activity associated with integrating or separating new encoding from old reactivated memories, with a focus on the role of the TPJ. The fate of specific memory items (objects in our learning paradigm) was related to the extent of TPJ activation, which we believe reflected the extent of detail in the brain's representation of current and past memories. We also found that increased activity levels in primary visual regions during reactivation—which we suppose signifies true reactivation and stronger retrieval— correlated with reduced memory updating. When these regions were less active and, we assume, memory reactivation was weaker, the likelihood that the reactivated memory would be modified and updated increased. Our study highlights some of the brain dynamics during memory reactivation, and possible updating, demonstrating an interplay between regions that mediate attention to the details of both past and current experiences.

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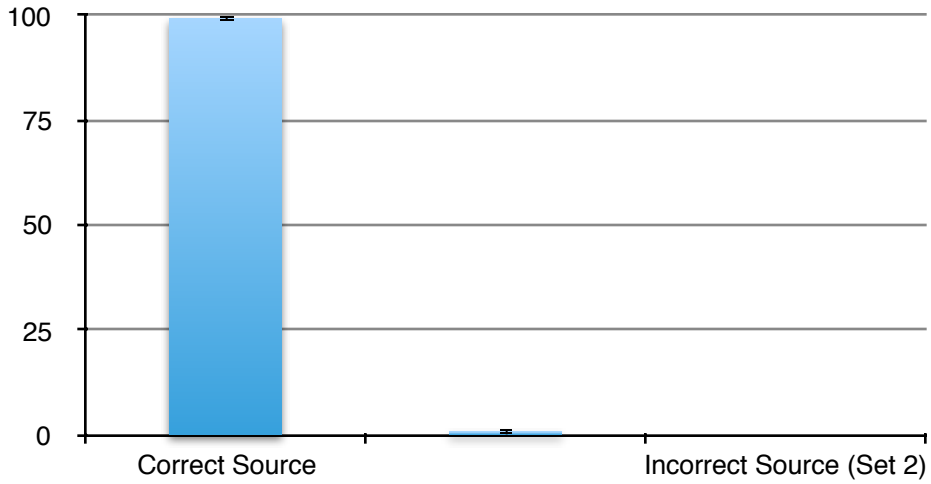
Supplemental Figures.



Supplementary Figure 1. Mean percentage of all eleven participants' recognition data of novel objects on Day 3. The objects could be identified as never seen before, Day 1, or Day 2. Error bars represent standard errors of means.