UC Merced

Proceedings of the Annual Meeting of the Cognitive Science Society

Title

Integration of Event Experiences to Build Relational Memory in the Human Brain

Permalink

https://escholarship.org/uc/item/0qp670z1

Journal

Proceedings of the Annual Meeting of the Cognitive Science Society, 44(44)

Authors

Leshinskaya, Anna
Nguyen, Mitchell A
Ranganath, Charan

Publication Date

2022

Peer reviewed

Integration of event experiences to build relational memory in the human brain

Anna Leshinskaya
(anna.leshinskaya@gmail.com)
Center for Neuroscience, University of California, Davis
1544 Newton Ct, Davis CA, 95618

Mitchell A. Nguyen (mitngu@ucdavis.edu)
Center for Neuroscience, University of California, Davis
1544 Newton Ct, Davis CA, 95618

Charan Ranganath (cranganath@ucdavis.edu)
Center for Neuroscience, University of California, Davis
1544 Newton Ct, Davis CA, 95618

Abstract

How are experiences of events used to update knowledge of predictive relations in semantic memory? We examined the roles of anterior-lateral entorhinal cortex (alEC), important for encoding recently experienced temporal relations, and middle temporal gyrus (MTG), involved in familiar event concepts. Participants underwent fMRI during exposure to novel event sequences and a memory probe phase (Session 1) and the same process a week later (Session 2). Across distinct sequences, predictive relations among similar events could either be Consistent, or the roles of the events could swap (Inconsistent). We examined the effect of Consistency on the strength of relational memory content. Areas that integrate across diverse experiences should be aided in the Consistent condition. We found that alEC performed this integrative role in Session 1, and at Session 2, similar effects were also observed in MTG. We suggest that these areas both contribute to building relational knowledge from experience.

Keywords: fMRI, semantic memory, learning, medial temporal lobe, temporal relations, event cognition

Introduction

The typical structure of relations among events is an important component of semantic memory (Carey, 2009; Gentner, 1983; Jones & Love, 2007; Markman & Gentner, 1993; Markman & Stilwell, 2001; Miller & Johnson-Laird, 1976; Pinker, 1989; Rehder & Ross, 2001)—for example, the causal structure captured in the concept *throw* or the sequential order of events at a restaurant. We likely use experiential observation of specific events to update this general knowledge. Yet exactly how encoding of experiences serves to update semantic memory of relations remains poorly understood.

Complementary Learning Systems (CLS) theory (McClelland, McNaughton, & O'Reilly, 1995; Norman & O'Reilly, 2003) proposes that two distinct systems are involved in updating memory systems from experience. An episodic system rapidly encodes recent individual experiences while a semantic system gradually comes to represent stable properties aggregated across experiences

Information integration is essential for building up semantic representations because it allows for their generality. For example, we are able to recognize the same event structure across restaurants that differ in taste, décor, and location, just as we can recognize that *throwing* may

describe events with similar causal outcomes but involving any of a variety of entities. To build general knowledge of *throwing* and *restaurants* we must therefore aggregate this common structure across diverse situations.

There is consensus that the episodic system depends on the hippocampus (HC) and likely the adjacent entorhinal cortex (EC). HC in particular is known to rapidly bind together elements (eg., time and place) within specific experiences (Eichenbaum, 2004; Eichenbaum & Cohen, 2001; Mishkin, 1997; O'Reilly & Rudy, 2001; Ranganath, 2010; Sutherland & Rudy, 1989). The role of HC and EC is often time-limited, such that lesions here can spare information learned days or weeks ago, particularly when that information is non-autobiographical or integrative (P. W. Frankland & Bontempi, 2005; Hodges & McCarthy, 1995; Lesburguères et al., 2011; Levy, Bayley, & Squire, 2004; Tse et al., 2007; Wang, Teixeira, Wheeler, & Frankland, 2009; Winocur, Moscovitch, & Bontempi, 2010).

The process of integration across individual experiences is also thought to be supported by HC along with ventro-medial prefrontal cortex (vmPFC; Bunsey & Eichenbaum, 1996; Preston & Eichenbaum, 2013; Schlichting & Preston, 2015). In associative inference paradigms, often used to study integration, participants are taught two separately presented stimulus pairs that share a common item, e.g., A-B and B-C. The extent to which participants link A with C is reliant on an intact HC in rodents (Bunsey & Eichenbaum, 1996; Dusek & Eichenbaum, 1997) and is correlated with HC engagement during learning in humans (Barron et al., 2020; Kuhl, Shah, Dubrow, & Wagner, 2010; Schlichting & Preston, 2016; Shohamy & Wagner, 2008; Wimmer & Shohamy, 2012; Zeithamova, Dominick, & Preston, 2012; Zeithamova & Preston, 2010). Similar effects are reported in vmPFC, particularly at remote timepoints (Barron et al., 2020; Long, Lee, & Kuhl, 2016; van Kesteren et al., 2013; van Kesteren, Fernández, Norris, & Hermans, 2010; van Kesteren, Rijpkema, Ruiter, & Fernández, 2010).

However, it is not clear if and how these integrated representations influence semantic memory areas, as studied with well-learned familiar concepts. Of particular relevance here, the middle temporal gyrus (MTG) and surrounding lateral temporal cortex are particularly involved in the relationally rich concepts of events, tools, and actions (Bedny, Caramazza, Grossman, Pascual-Leone, & Saxe,

2008; Bedny, Caramazza, Pascual-Leone, & Saxe, 2011; Bedny, Dravida, & Saxe, 2013; Bottini et al., 2020; Kable, Kan, Wilson, Thompson-Schill, & Chatterjee, 2005; Tarhan, Watson, & Buxbaum, 2016; Tranel, Kemmerer, Adolphs, Damasio, & Damasio, 2003) and encode temporal, thematic, causal, and syntactic relations (S. M. Frankland & Greene, 2015, 2020; Hernandez, Fairhall, Lenci, Baroni, & Caramazza, 2014; Kalénine & Buxbaum, 2016; Kalénine et al., 2009; Leshinskaya, Bajaj, & Thompson-Schill, 2021; Leshinskaya, Wurm, & Caramazza, 2020; Wu, Waller, & Chatterjee, 2007; Wurm & Caramazza, 2019, 2021). Thus, relational aspects of conceptual knowledge are particularly reliant on MTG. However, how novel experience and memory integration processes might affect MTG is unclear.

One possibility is that the encoding and integration of new experiences, as previously studied, are not a mechanism for updating semantic areas like MTG. Alternatively, these processes have been missed due to ROI pre-selection and methodological factors.

For example, memory integration and learning studies often use stimuli that are difficult to interpret, such as abstract symbols or static images that are sequentially flashed on the screen, making it unclear if associations among them are meaningful or how they should be understood. Moreover, specializations among semantic areas likely mean that they are influenced by different aspects of learning. MTG is likely specialized for representing especially relationally complex information about events or actions. Indeed, our prior work has shown that novel, relational complex information designed to be semantically interpretable as about novel objects influenced memory representations in various parts of MTG (Leshinskaya & Thompson-Schill, 2019, 2020).

Here, we used functional magnetic resonance imaging (fMRI) to understand how newly learned relations are encoded and integrated in HC, EC, and MTG across two timepoints a week apart. We used stimuli similar to our prior work: animations interpretable as being about temporal or causal relations among novel objects and events. Participants learned predictive relations among pairs of events (A&B) by watching longer sequences (Figure 1). We measured relational memory strength for each A-B pair by assessing the extent to which the multivoxel neural response during recall was more correlated between events A and B than unrelated pairs (Figure 2), a measure termed associative coding (Erickson & Desimone, 1999; Hindy, Ng, & Turk-Browne, 2016; Leshinskaya & Thompson-Schill, 2020; Miyashita, 1993; Sakai & Miyashita, 1991; Schapiro, Kustner, & Turk-Browne, 2012). There were six distinct sequences, each shown with a different participating object, creating distinct contexts. Across these sequence contexts, the events shown were partly overlapping, but the relations among them could vary (Inconsistent condition) or stay the same (Consistent condition). Areas that integrate across contexts should benefit in the Consistent condition, such that associative coding should be strengthened, relative to the Inconsistent condition. We measured these effects at two timepoints a week apart to

understand how the roles of different areas change as a function of exposure and time.

Methods

Participants

30 participants were recruited from the University of California, Davis community and provided written informed consent. Procedures were approved by the UC Davis Institutional Review Board. Twenty-four participants (18 female, 6 male; mean age 24 years) were included in analyses: four were excluded for excessive head motion and two did not complete both sessions. All were neurologically healthy, right-handed, and eligible for fMRI.

Stimuli & Procedure

We taught participants pairs of predictive relations by presenting them within sequences of animated events that contained underlying regularities, which they were instructed to learn explicitly. In each sequence, an Event A strongly predicted an Event B, whereas Events C-F were unpredictable (Figure 1). During fMRI, a Learning phase presented this information by presenting the 150-event long sequences of the events A-F. The sequential appearance of events was governed by a transition matrix that specified the probability of any event appearing given the occurrence of any other (Figure 1A). Participants' task was to identify the predictable event, called "the effect", which they selected in a forced-choice question at the end of the run. The Learning phase was followed immediately by a Probe phase, used to measure memory representations (Figure 2A). Events no longer followed the predictive structure of the Learning phase; they instead appeared in counterbalanced order, such that each event followed every other an equal number of times (exactly 7), and also now appeared discontinuously: each event was replaced with a fixation cross for 1.7 s (Figure 2A). This design allowed us to estimate the neural response to each event when shown outside its typical predictive context.

Participants learned about six different sequences, with mostly overlapping events so that we could manipulate relational consistency among them (Figure 1B). The sequences were distinguished by a unique object present in all of that sequence's events. The sequences differed in the ways the particular stimuli were assigned each Event A-F. Sequences 1-3 were Consistent in their relational structure, while Sequences 4-6 were Inconsistent (Figure 2B).

In the Consistent sequences, each used a distinct object-based event as Event A (e.g., tilting, color changing, and rippling). Event B was always the same event in each (e.g., bubbles), as were events C (e.g., leaves) and D; the other events varied. The relational structure among events was thus kept consistent in that events which served the predictable vs unpredictable role stayed the same.

In the Inconsistent sequences, Events A varied exactly as in the Consistent sequences (e.g., were again tilting, color changing, rippling). However, the stimuli serving the roles of
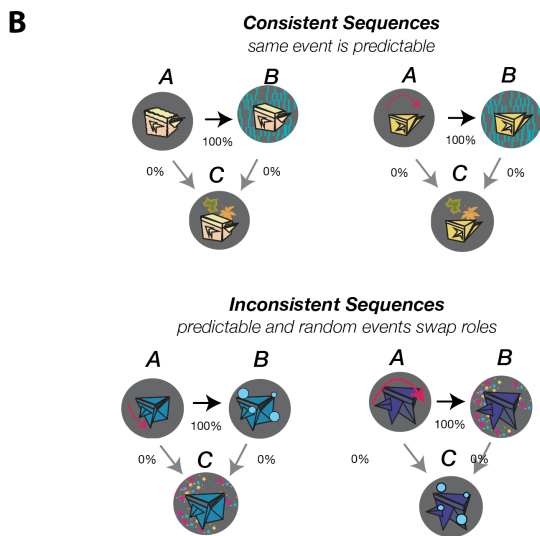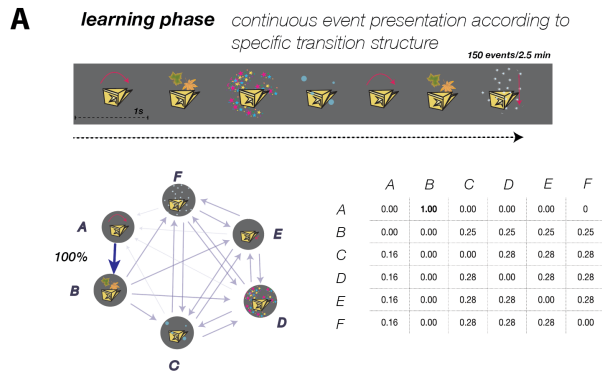

Figure 1. **A.** Learning Phase, example of one sequence, with transition structure depicted below. Event A was followed by Event B 100% of the time while other transitions were less predictable. All events are animated; pink arrows indicate movement direction. **B.** Consistency Manipulation: Consistent sequences used similar events for Events B and C. Among Inconsistent sequences, Events B and C flipped. Each sequence was cued with a unique object.

Events B were different in each, exchanging roles with Events C or D. For example, in Sequence 4, Event B could be stars, while Events C and D were bubbles and leaves. In Sequence 5, Event B would be leaves while events C and D are stars and bubbles, etc. Each sequence was shown in a separate run with a Learning and Probe phase. Within conditions, sequences were shown consecutively in order but the order of the two conditions was counterbalanced across subjects. In either order, Sequence 1 was never 'consistent' with anything prior and was thus considered Inconsistent for most analyses.

The entire procedure was repeated over two sessions, one week apart, to understand how associative coding changes across exposure and time in our regions of interest (HC, EC, and MTG). Thus, in Session 2, both learning and probe

phases were repeated with identical materials, providing more exposure and a delay relative to Session 1. This means
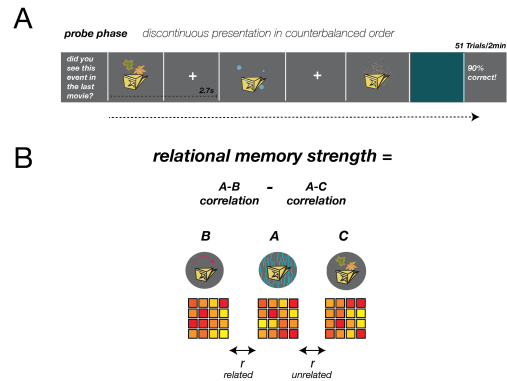

Figure 2. **A.** Probe phase example. Participants had to decide if they had seen each event in the prior sequence, but event order was randomized. **B.** Relational memory strength was measured as the difference between the correlation between Event A & B vs Event A & C (and A & D, not shown).

all sequences had additional familiarity, but Inconsistent sequences continued to conflict with each other locally.

Session 2 was also followed with additional forced-choice questions: participants selected between two snippets of event pairs drawn from one of the six sequences, comparing A-B vs A-C, A-B vs A-D. The correct choice depended on recalling which relations appeared with object. Here, Sequence 1 was grouped with the Consistent sequences since at this point, participants had been exposed to all of them.

fMRI Acquisition

MRI data were acquired using a Siemens Skyra 3T scanner at UC Davis using a 32-channel coil. Anatomical volumes were acquired with a T1- weighted MPRAGE sequence with 1×1×1 mm voxel resolution, 256 mm field of view, time to repetition (TR) = 1.90 s, and time to echo (TE) = 3.06 ms. Functional data were acquired with a multiband echo-planar imaging (EPI) blood oxygen level-dependent (BOLD) sequence using 64 interleaved slices with a multiband acceleration factor of 2, 3×3×3mm in-plane voxel resolution, 64×64 mm matrix size, TR = 1250s, TE = 24 ms, and flip angle=76 ∘. Slices were aligned to -36 degrees from ACPC. Static fieldmap estimation were performed by collecting 4 volumes in the reverse encoding direction as the main scans.

Analyses

Preprocessing was performed with the fMRIPrep package with standard defaults and freesurfer and AFNI packages. Functional data were registered to anatomical scans, slice-time corrected and corrected for distortion using a field map. Functional data were smoothed with a 4 mm full-width half-maximum gaussian kernel. Linear models were used to estimate coefficients on fMRI timeseries. Regressors of no-interest included 6 motion and rotation realignment

parameters and their first order derivatives; voxels flagged as signal outliers during preprocessing were excluded. Regressors of interest were created for each type of event seen during the Learning phase and Probe phase separately. Learning phase data were binned by time in order to examine changes during this phase: trials of each event type were assigned to a bin based on their order of appearance, such that bin 1 for event C included the first three appearances of event C, bin 2 the next three, and so on, for a total of 5 bins per event. As events A and B were perfectly colinear during the Learning phase, they formed the same regressor.

During learning, we computed a measure of 'surprise' as a contrast between the unpredictable events (C and D) minus the predictable pair AB, at each time bin. The slope of this measure across time bins were used as a measure of learning-related changes in an areas.

During the Probe phase, we measured relational memory strength using associative coding, a multivariate measure comparing voxelwise correlations among pairs of events. For each condition, the *t*-value of the coefficients from linear modeling was extracted in the voxels of a given ROI for each regressor. This vector of values was then correlated pairwise between specific pairs of conditions, here A & B, A & C, and A & D. The correlation between A & B minus the other two pairs indicated relational memory strength for A-B (stimuli used for events B, C and D were perfectly counterbalanced). Analyses were performed within each run, then averaged.

ROI Definition

HC was defined using automatic segmentations, then split using morphological criteria: the head was labeled as anterior (aHC) and the body and tail were labeled posterior (pHC). EC was hand-traced, with alEC and pmEC delineated using tracing criteria guided by previous validation studies (Maass, Berron, Libby, Ranganath, & Düzel, 2015). Our preregistration indicated that whole EC would also be considered but that the functional differences between these were important, with alEC more likely to be relevant here given past findings (Bellmund, Deuker, & Doeller, 2019); as this difference was very salient we continued with the split region. For MTG and other cortical areas, we used the Glasser atlas (Glasser et al., 2016) aligned to individual anatomical surfaces to create individual ROIs. Our pre-registration indicated two anatomical areas for MTG, right TE1p and TE1m, but pilot data (not reported) indicated TE1p to be particularly important for the present analyses. We selected right-lateralized ROIs based on prior work (Leshinskaya & Thompson-Schill, 2020).

Results

Probe Phase Associative Coding

During the Probe Phase, we measured the strength of associative coding in each ROI in each run by correlating the multivoxel response to Event A with that of Event B and testing whether it was stronger than the correlation between that of Event A and Event C or D (Figure 2B). We then tested

whether associative coding varied between consistency conditions (Consistent vs Inconsistent) to understand the extent to which this area integrated relational information
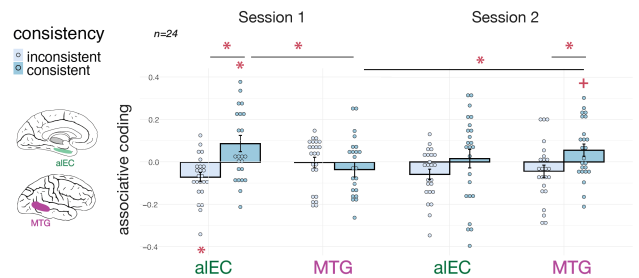

Figure 3. Associative coding (relational memory strength during the Probe phase) in alEC and MTG in Session 1 and Session 2 as a function of Consistency.

across sequences and between sessions (1 vs 2) to understand how it varied as a function of exposure and time. We expect semantic memory areas to be more involved in Session 2.

Hippocampus HC was split into anterior (aHC) and posterior (pHC) subregions. We saw no evidence of associative coding in either ROI in any condition, nor any effects of condition.

Anterior-Lateral Entorhinal Cortex A Session by Consistency ANOVA in alEC showed a main effect of Consistency, $F(23,1) = 8.999$, $MSE = 0.323$, $p = .006$, with no effect of Session (Figure 3). Within Session 1, there was an effect of Consistency, $M = 0.158$, $t(23) = 3.214$, $p = .004$, such that Consistent sequences exhibited significant associative coding, $M = 0.088$, $t(23) = 2.349$, $p = .028$, while Inconsistent sequences exhibited significant *negative* associative coding (i.e., differentiation), $M = -0.071$, $t(23) = -3.306$, $p = .003$. Within Session 2, there was no effect of Consistency. Consistent sequences did not show effects but there was significant differentiation in Inconsistent sequences, $M = -0.059$, $t(23) = -2.463$, $p = .022$. There were no interactions with Session, however.

Middle Temporal Gyrus In MTG, a Consistency by Session ANOVA showed a Consistency by Session interaction, $F(23,1) = 6.589$, $MSE = 0.106$, $p = .017$ (Figure 3). In Session 1, there was no effect of Consistency and no evidence of associative coding in any condition. In Session 2, a Consistency effect emerged, $t(23) = 2.99$, $p = .007$. Associative coding was marginal in the Consistent sequences, $M = 0.055$, $t(23) = 1.970$, $p = 0.061$, but not significant in the Inconsistent ones, $M = -.044$, $p > .13$. Correspondingly, there was stronger associative coding in Session 2 than Session 1 within Consistent sequences, $t(23) = -2.491$, $p = .020$, but not within Inconsistent ones, $p > .25$.

We tested whether MTG showed a reliably different pattern than alEC using an ROI by Session by Consistency ANOVA, which revealed a main effect of Consistency, $F(23,1) = 7.388$, $MSE = .266$, $p = .012$, an ROI by Consistency interaction, $F(23,1) = 5.709$, $MSE = .083$, $p = .026$, and a 3-way interaction between ROI, Session, and Consistency $F(23,1) = 6.59$, $MSE = .141$, $p = .017$. Within

Session 1, there was an ROI by Consistency interaction, $F(23,1) = 14.39$, $MSE = .220$, $p < .001$, while in Session 2 there was a main effect of Consistency, $F(23,1) = 7.439$, $MSE = 0.180$, $p = .012$, and no interactions. This reveals that both ROIs were sensitive to Consistency in Session 2, but in Session 1, alEC was more sensitive than MTG. Follow-up *t*-test showed that associative coding was stronger in alEC than MTG among Consistent objects in Session 1, $t(23) = 2.488$, $p = .021$, and that the Consistency effect in Session 1 was stronger in alEC than MTG, $t(23) = 3.794$, $p < 0.001$. Overall, this indicates that MTG showed an effect of consistency primarily in Session 2, while alEC did so at both timepoints, and the 3-way interaction demonstrated that these patterns of effects were reliably different between the ROIs.

A correlation analysis failed to find a relationship between MTG and alEC associative coding strength within or across sessions.

Learning Phase

Exploratory analyses investigated how these ROIs responded during the Learning phase, while participants were exposed to the predictive information, to understand how the regions' responses during learning relates to their patterns of response during recall. We used "surprise" as an index of sensitivity to the predictive information, computed as the difference in response to unpredictable minus predictable events. We then measured how much the surprise index *changed* as a function of exposure, by computing the difference of surprise between first and last time point across the learning phase; this was used as proxy for learning rate. Change in surprise was then compared between Sessions and Consistency conditions.

Hippocampus   In aHC, a Session by Consistency ANOVA over change in surprise showed no effects. However, within Session 1, there was significant change in surprise in Consistent sequences, $M = -0.057$, $t(23) = -2.535$, $p = .019$, and marginally in Inconsistent sequences, $M = -0.040$, $t(23) = -2.01$, $p = .056$, with no difference between them. Surprise was negative overall in aHC, meaning there was a stronger response to predictable than unpredictable events, and it became more negative during each learning phase. In Session 2, there was no change in surprise or any differences, all $p > .20$. Thus, aHC showed reliable learning-related signatures in Session 1, but no effects of Session or Consistency. There were no effects in pHC.
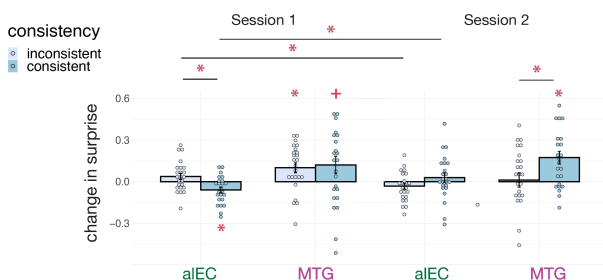

Figure 4. Effects during the Learning phase (change in surprise) in alEC and MTG as a function of Session and Consistency.

Anterior-Lateral Entorhinal Cortex   A Session by Consistency ANOVA for change in surprise revealed a Consistency by Session interaction, $F(23,1) = 12.100$, $MSE = 0.154$, $p = .002$ (Figure 4). In Session 1, Consistent sequences showed negative change in surprise, $M = -0.061$, $t(23) = -3.01$, $p = .006$, but Inconsistent sequences did not, $M = 0.037$, $p > .10$, leading to a significant difference, $t(23) = -3.215$, $p = 0.004$. In Session 2, there was no evidence of change in surprise in either condition, $p > .10$. Simple effects revealed that Consistent sequences showed more negative change in surprise in Session 1 than Session 2, $t(23) = 2.256$, $p = .034$, whereas Inconsistent sequences showed more change in surprise in Session 2 than in Session 1, $t(2\ 3) = 2.240$, $p = .035$, explaining the interaction. Thus, change in surprise in alEC was sensitive to Consistency and Session, with stronger effects in Consistent sequences in Session 1 than in in Session 2, but Inconsistent ones behaving in the opposite manner.

We used a 3-way ROI by Session by Consistency ANOVA on change in surprise to determine if alEC was more sensitive to Consistency than aHC. This revealed a 3-way interaction, $F(23,1) = 4.434$, $MSE = 0.049$, $p = .046$ and a two-way interaction between Session and Consistency, $F(23,1) = 6.685$, $MSE = 0.112$ $p = .017$. Simple effects revealed that across both ROIs, the effect of Consistency was overall larger (more negative) in Session 1 vs Session 2, $t(23) = -2.586$, $p = .017$. Moreover, the Consistency effect changed more between Session 1 and Session 2 in alEC than aHC, $t(23) = -2.106$, $p = .046$. However, Consistency effects were not greater in alEC than aHC.

Middle Temporal Gyrus   In MTG, a Session by Consistency ANOVA revealed a marginal main effect of Consistency, $F(23,1) = 3.887$, $MSE = 0.197$, $p = .061$ and no interactions (Figure 4). Within Session 1, Consistent sequences showed a marginal positive change in surprise, $M = 0.112$, $t(23) = 1.945$, $p = .064$, and a significant one in Inconsistent ones, $M = 0.100$, $t(23) = 2.900$, $p = .008$, but there was no difference between them, $p > .70$. Within Session 2, change in surprise was significantly positive within Consistent sequences, $M = 0.174$, $t(23) = 3.847$, $p < .001$, but not within Inconsistent ones, $M = 0.013$, $p > .80$, with a significant difference, $t(23) = 2.511$, $p = .020$.

Comparing MTG and alEC with a 3-way ROI by Session by Consistency ANOVA showed a main effect of ROI, $F(23,1) = 13.890$, $MSE = 0.559$, $p = .001$, an interaction between ROI and Consistency, $F(23,1) = 6.066$, $MSE = 0.140$, $p = .022$, and an interaction between Session and Consistency, $F(23,1) = 8.642$, $MSE = 0.272$, $p = .007$. Within Session 1, there was a main effect of ROI, $F(23,1) = 7.82$, $MSE = .354$, $p = .01$, reflecting that change in surprise was more positive in MTG than alEC, and a marginal ROI by Consistency interaction, $F(23,1) = 3.73$, $MSE = 0.0829$, $p = .066$, suggesting a stronger Consistency effect in alEC. In Session 2, there was a main effect of ROI, $F(23,1) = 10.08$, $MSE = 0.2138$, $p = .004$, and a main effect of Consistency, $F(23, 1) = 6.00$, $MSE = 0.301$, $p = .022$, indicating no difference between ROIs in the Consistency effect. Simple

effects indicated that Consistency had an overall stronger effect in Session 2 than Session 1, $t(23) = -2.940$, $p = .007$. In addition, Consistency effects were more positive in MTG than alEC overall, $t(23) = -2.463$, $p = .022$. Overall, this indicates that MTG showed positive change in surprise while alEC showed negative change, and that alEC may have had stronger Consistency effects than MTG in Session 1, but that the ROIs showed equal Consistency effects in Session 2.

In summary, learning-related changes during sequence exposure revealed a role for aHC but not pHC during learning. alEC showed a dramatic effect of Consistency, particularly at Session 1, whereas MTG showed Consistency effects more reliably at Session 2. Thus, these latter findings largely mirrored the effects seen in the Probe phase.

Correlations with Behavior

Questions at the end of Session 2 asked participants to recall the predictive relations (A-B vs A-C) in each sequence. Because predictive relations were highly conflicting among the sequences, these questions were expected to be difficult. On Inconsistent sequences, participants were not above chance (50%), $M = 46\%$, $p > .35$, but did weakly succeed on Consistent ones, $M = 0.556$, $t(23) = 2.106$, $p = .046$, with no significant difference between them. We capitalized on the variability in this behavior to look for correlations with neural signals. We found effects only in HC. Averaging across all sequences, accuracy correlated positively with associative coding in aHC Session 1, $r = 0.467$, $t(22) = 2.476$, $p = .021$ and negatively with change in surprise (since this increased negatively during learning) in posterior HC in Session 2, $r = -0.444$, $t(22) = -2.323$, $p = .029$.

Discussion

Integration is an important step in building semantic memory from experience. We investigated the role of several neural areas previously implicated in episodic and semantic memory in the process of building new, integrated relational representations. We measured neural relational memory strength for predictively related event pairs as a function of session (time and exposure) and their consistency with pairs shown in other sequence contexts. Sensitivity to consistency indicated an influence of previously seen relations and thus integrative representations.

In alEC, we saw positive relational memory signals of event pairs when they were consistent across contexts, but hampered (indeed, negative) ones when inconsistent. This effect was significant in Session 1, but not at Session 2, though it did not significantly decline. This suggests a role of alEC in rapidly integrating information across contexts and perhaps maintaining them, and positions alEC as a mediator between episodic and semantic memory.

MTG performed a similar role as alEC but only in Session 2, after a week delay and more exposure: here we saw strong effects of cross-sequence consistency and significant increases relative to Session 1. Thus, both alEC and MTG built integrative representations of experiences, but MTG did so subsequently to alEC.

We conclude that alEC and MTG both serve to integrate experience. It is unclear whether representations in these areas emerge independently, or if MTG builds on the representations in alEC. Having failed to see correlations between effects these areas here, we await further research.

HC did not show relational memory or integrated representations during recall, in contrast to some past work (Schapiro, Turk-Browne, Norman, & Botvinick, 2016; Tompary & Davachi, 2017). However, our paradigm created higher integration demand because individual event pairs were shown in separately presented contexts with distinguishing cues (the objects). If HC did not integrate across these contexts, it could not benefit from consistency, which could have led to weaker relational memory signals overall. A broader integrative role of alEC (vs HC) is consistent with prior work suggesting that EC serves a particularly integrative function and that memory integration might arises from recurrence between EC and HC, which are bidirectionally connected (Koster et al., 2018; Kumaran & McClelland, 2012)

However, in line with findings reviewed in the introduction, we did find learning-related changes in HC during exposure, and these learning signals (in pHC) and associative coding during recall (in aHC) predicted participants' later ability to recall which predictive event pairs went with which context. Thus, HC plays a behaviorally relevant role, perhaps in binding relational information to its context.

Overall, our work connects the literature on memory integration with that of semantic memory. While the former has highlighted the role of HC and vmPFC, it has been less clear how memory integration processes might serve to update representations in areas highlighted in semantic memory research, like MTG. We targeted MTG on the basis of its role in semantic memory of actions and events as well as our prior work showing novel predictive representations about a week after learning (Leshinskaya & Thompson-Schill, 2020; Leshinskaya et al., 2020). If the integration of new experiences contributes to updating semantic representations, we predicted we should see such integrative signals here, at least after some delay. Our findings of integrated representations in MTG at Session 2 are consistent with this prediction. One caveat, however, is that while we have twice observed relational memory representations in *right* MTG, action and event concepts are often left-lateralized, perhaps due to their links with linguistic labels. We hope to test in future studies how the nature of stimulus materials affects the sites of new memory about them.

While we have begun to bridge learning and semantic memory, much more is required to empirically connect the outputs of new learning and sites for semantic memory. While we observed similar functional signatures in EC and MTG here, it remains unclear if these emerge independently or by an interactive process, a question we also hope to address in future work.

Acknowledgments

References

Barron, H. C., Reeve, H. M., Koolschijn, R. S., Perestenko, P. V., Shpektor, A., Nili, H., … Dupret, D. (2020). Neuronal computation underlying inferential reasoning in humans and mice. *Cell*, *183*, 228–243. https://doi.org/10.1016/j.cell.2020.08.035

Bedny, M., Caramazza, A., Grossman, E., Pascual-Leone, A., & Saxe, R. R. (2008). Concepts are more than percepts: the case of action verbs. *Journal of Neuroscience*, *28*(44), 11347–11353. https://doi.org/10.1523/JNEUROSCI.3039-08.2008

Bedny, M., Caramazza, A., Pascual-Leone, A., & Saxe, R. R. (2011). Typical neural representations of action verbs develop without vision. *Cerebral Cortex*, *22*(2), 286–293. https://doi.org/10.1093/cercor/bhr081

Bedny, M., Dravida, S., & Saxe, R. R. (2013). Shindigs, brunches, and rodeos: The neural basis of event words. *Cognitive, Affective & Behavioral Neuroscience*, *14*(3), 891–901. https://doi.org/10.3758/s13415-013-0217-z

Bellmund, J. L. S., Deuker, L., & Doeller, C. F. (2019). Mapping sequence structure in the human lateral entorhinal cortex. *ELife*, *8*, 1–20. https://doi.org/10.7554/eLife.45333

Bottini, R., Ferraro, S., Nigri, A., Cuccarini, V., Bruzzone, M. G., & Collignon, O. (2020). Brain regions involved in conceptual retrieval in sighted and blind people. *Journal of Cognitive Neuroscience*, *32*(6), 1009–1025. https://doi.org/10.1162/jocn_a_01538

Bunsey, M., & Eichenbaum, H. B. (1996). Conservation of hippocampal memory function in rats and humans. *Nature*, Vol. 379, pp. 255–257. https://doi.org/10.1038/379255a0

Carey, S. (2009). *Origin of Concepts*. Oxford: Oxford University Press.

Dusek, J. A., & Eichenbaum, H. B. (1997). The hippocampus and memory for orderly stimulus relations. *Proceedings of the National Academy of Sciences of the United States of America*, *94*(June), 7109–7114.

Eichenbaum, H. B. (2004). Hippocampus: Cognitive processes and neural representations that underlie declarative memory. *Neuron*, *44*(1), 109–120. https://doi.org/10.1016/j.neuron.2004.08.028

Eichenbaum, H. B., & Cohen, N. J. (2001). *From conditioning to conscious recollection: Memory systems of the brain*. Oxford: Oxford University Press.

Erickson, C., & Desimone, R. (1999). Responses of macaque perirhinal neurons during and after visual stimulus association learning. *The Journal of Neuroscience*, *19*(23), 10404–10416.

Frankland, P. W., & Bontempi, B. (2005). The organization of recent and remote memories. *Nature Reviews Neuroscience*, *6*(2), 119–130. https://doi.org/10.1038/nrn1607

Frankland, S. M., & Greene, J. D. (2015). An architecture for encoding sentence meaning in left mid-superior temporal cortex. *Proceedings of the National Academy of Sciences*, *112*(37), 11732–11737. https://doi.org/10.1073/pnas.1421236112

Frankland, S. M., & Greene, J. D. (2020). Two ways to build a thought: distinct forms of compositional semantic representation across brain regions. *Cerebral Cortex*, *30*(6), 3838–3855. https://doi.org/10.1093/cercor/bhaa001

Gentner, D. (1983). Structure mapping: A theoretical framework for analogy. *Cognitive Science*, *7*(2), 155–170. https://doi.org/10.1016/S0364-0213(83)80009-3

Glasser, M. F., Coalson, T. S., Robinson, E. C., Hacker, C. D., Harwell, J., Yacoub, E., … Van Essen, D. C. (2016). A multi-modal parcellation of human cerebral cortex. *Nature*, *536*(7615), 171–178. https://doi.org/10.1038/nature18933

Hernandez, M., Fairhall, S. L., Lenci, A., Baroni, M., & Caramazza, A. (2014). Predication drives verb cortical signatures. *Journal of Cognitive Neuroscience*, *26*(8), 1829–1839. https://doi.org/:10.1162/jocn_a_00598

Hindy, N. C., Ng, F. Y., & Turk-Browne, N. B. (2016). Linking pattern completion in the hippocampus to predictive coding in visual cortex. *Nature Neuroscience*, *19*(5), 665–667. https://doi.org/10.1038/nn.4284

Hodges, J. R., & McCarthy, R. A. (1995). Loss of remote memory: a cognitive neuropsychological perspective. *Current Opinion in Neurobiology*, *5*(2), 178–183. https://doi.org/10.1016/0959-4388(95)80024-7

Jones, M., & Love, B. C. (2007). Beyond common features: The role of roles in determining similarity. *Cognitive Psychology*, *55*(3), 196–231. https://doi.org/10.1016/j.cogpsych.2006.09.004

Kable, J. W., Kan, I. P., Wilson, A., Thompson-Schill, S. L., & Chatterjee, A. (2005). Conceptual representations of action in the lateral temporal cortex. *Journal of Cognitive Neuroscience*, *17*(12), 1855–1870. https://doi.org/10.1162/089892905775008625

Kalénine, S., & Buxbaum, L. J. (2016). Thematic knowledge, artifact concepts, and the left posterior temporal lobe: Where action and object semantics converge. *Cortex*, *82*, 164–178. https://doi.org/10.1016/j.cortex.2016.06.008

Kalénine, S., Peyrin, C., Pichat, C., Segebarth, C., Bonthoux, F., & Baciu, M. (2009). The sensory-motor specificity of taxonomic and thematic conceptual relations: a behavioral and fMRI study. *NeuroImage*, *44*(3), 1152–1162. https://doi.org/10.1016/j.neuroimage.2008.09.043

Koster, R., Chadwick, M. J., Chen, Y., Berron, D., Banino, A., Düzel, E., … Kumaran, D. (2018). Big-Loop

Recurrence within the hippocampal system supports integration of information across episodes. *Neuron*, *99*(6), 1342-1354.e6. https://doi.org/10.1016/j.neuron.2018.08.009

Kuhl, B. A., Shah, A. T., Dubrow, S., & Wagner, A. D. (2010). Resistance to forgetting associated with hippocampus-mediated reactivation during new learning. *Nature Neuroscience*, *13*(4), 501–506. https://doi.org/10.1038/nn.2498

Kumaran, D., & McClelland, J. L. (2012). Generalization through the recurrent interaction of episodic memories: A model of the hippocampal system. *Psychological Review*, *119*(3), 573–616. https://doi.org/10.1037/a0028681

Lesburguères, E., Gobbo, O. L., Alaux-Cantin, S., Hambucken, A., Trifilieff, P., & Bontempi, B. (2011). Early tagging of cortical networks is required for the formation of enduring associative memory. *Science*, *331*(6019), 924–928. https://doi.org/10.1126/science.1196164

Leshinskaya, A., Bajaj, M., & Thompson-Schill, S. L. (2021). Novel objects with causal schemas elicit selective responses in tool- and hand-selective lateral occipito-temporal cortex. *PsyArXiv*.

Leshinskaya, A., & Thompson-Schill, S. L. (2019). From the structure of experience to concepts of structure: how the concept "cause" applies to streams of events. *Journal of Experimental Psychology-General*, *148*(4), 619–643.

Leshinskaya, A., & Thompson-Schill, S. L. (2020). Transformation of event representations along middle temporal gyrus. *Cereb Cortex*, *30*(5), 3148–3166. https://doi.org/10.1167/19.10.91a

Leshinskaya, A., Wurm, M. F., & Caramazza, A. (2020). Concepts of actions and their objects. In D. Poeppel, G. Mangun, & M. S. Gazzaniga (Eds.), *The Cognitive Neurosciences* (pp. 757–765).

Levy, D., Bayley, P. J., & Squire, L. R. (2004). The anatomy of semantic knowledge: medial vs. lateral temporal lobe. *Proceedings of the National Academy of Sciences of the United States of America*, *101*(17), 6710–6715. https://doi.org/10.1073/pnas.0401679101

Long, N. M., Lee, H., & Kuhl, B. A. (2016). Hippocampal mismatch signals are modulated by the strength of neural predictions and their simi- larity to outcomes. *The Journal of Neuroscience*, *36*(50), 1850–16. https://doi.org/10.1523/JNEUROSCI.1850-16.2016

Maass, A., Berron, D., Libby, L. A., Ranganath, C., & Düzel, E. (2015). Functional subregions of the human entorhinal cortex. *ELife*, *4*(JUNE), 1–20. https://doi.org/10.7554/eLife.06426

Markman, A. B., & Gentner, D. (1993). Structural alignment during similarity comparisons. *Cognitive Psychology*, *25*(4), 431–467. https://doi.org/http://dx.doi.org/10.1006/cogp.1993.1011

Markman, A. B., & Stilwell, C. H. (2001). Role-governed categories. *Journal of Experimental & Theoretical Artificial Intelligence*, *13*(4), 329–358. https://doi.org/10.1080/09528130110100252

McClelland, J. L., McNaughton, B. L., & O'Reilly, R. C. (1995). Why there are complementary learning systems in the hippocampus and neo-cortex: Insights from the successes and failures of connectionists models of learning and memory. *Psychological Review.*, *102*(3), 419–457.

Miller, G. A., & Johnson-Laird, P. N. (1976). *Language and Perception*. Cambridge, MA: Harvard University Press.

Mishkin, M. (1997). Hierarchical organization of cognitive memory. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *352*(1360), 1461–1467. https://doi.org/10.1098/rstb.1997.0132

Miyashita, Y. (1993). Inferior temporal cortex: Where visual perception meets memory. *Annual Review of the Neurosciences*, *16*, 245–263.

Norman, K. A., & O'Reilly, R. C. (2003). Modeling hippocampal and neocortical contributions to recognition memory: A complementary-learning-systems approach. *Psychological Review*, *110*(4), 611–646. https://doi.org/10.1037/0033-295X.110.4.611

O'Reilly, R. C., & Rudy, J. W. (2001). Conjunctive representations in learning and memory: Principles of cortical and hippocampal function. *Psychological Review*, *108*(1), 83–95. https://doi.org/10.1037//0033-295X.

Pinker, S. (1989). *Learnability and Cognition: The acquisition of argument structure*. Cambridge, MA: MIT Press.

Preston, A. R., & Eichenbaum, H. B. (2013). Interplay of hippocampus and prefrontal cortex in memory. *Current Biology*, *23*(17), R764–R773. https://doi.org/10.1016/j.cub.2013.05.041

Ranganath, C. (2010). A unified framework for the functional organization of the medial temporal lobes and the phenomenology of episodic memory. *Hippocampus*, *20*(11), 1263–1290. https://doi.org/10.1002/hipo.20852

Rehder, B., & Ross, B. H. (2001). Abstract coherent categories. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *27*(5), 1261–1275. https://doi.org/10.1037//0278-7393.27.5.1261

Sakai, K., & Miyashita, Y. (1991). Neural organization for the long-term memory of paired associates. *Nature*, *354*(6349), 152–155. https://doi.org/10.1038/354152a0

Schapiro, A. C., Kustner, L. V., & Turk-Browne, N. B. (2012). Shaping of object representations in the human medial temporal lobe based on temporal regularities. *Current Biology*, *22*(17), 1622–1627. https://doi.org/10.1016/j.cub.2012.06.056

Schapiro, A. C., Turk-Browne, N. B., Norman, K. A., & Botvinick, M. M. (2016). Statistical learning of

temporal community structure in the hippocampus. *Hippocampus*, *26*(1), 3–8. https://doi.org/10.1002/hipo.22523

Schlichting, M. L., & Preston, A. R. (2015). Memory integration: Neural mechanisms and implications for behavior. *Current Opinion in Behavioral Sciences*, *1*, 1–8. https://doi.org/10.1016/j.cobeha.2014.07.005

Schlichting, M. L., & Preston, A. R. (2016). Hippocampal–medial prefrontal circuit supports memory updating during learning and post-encoding rest. *Neurobiology of Learning and Memory*, *134*(Part A), 91–106. https://doi.org/10.1016/j.nlm.2015.11.005

Shohamy, D., & Wagner, A. D. (2008). Integrating Memories in the Human Brain: Hippocampal-Midbrain Encoding of Overlapping Events. *Neuron*, *60*(2), 378–389. https://doi.org/10.1016/j.neuron.2008.09.023

Sutherland, R. J., & Rudy, J. W. (1989). Configural association theory: The role of the hippocampal formation in learning, memory, and amnesia. *Psychobiology*, *17*(2), 129–144. https://doi.org/10.3758/BF03337828

Tarhan, L. Y., Watson, C. E., & Buxbaum, L. J. (2016). Shared and distinct neuroanatomic regions critical for tool-related action production and recognition: Evidence from 131 left-hemisphere stroke patients. *Journal of Cognitive Neuroscience*, *27*(12), 2491–2511. https://doi.org/10.1162/jocn

Tompary, A., & Davachi, L. (2017). Consolidation promotes the emergence of representational overlap in the hippocampus and medial prefrontal cortex. *Neuron*, *96*(1), 228-241.e5. https://doi.org/10.1016/j.neuron.2017.09.005

Tranel, D., Kemmerer, D., Adolphs, R., Damasio, H., & Damasio, A. R. (2003). Neural correlates of conceptual knowledge for actions. *Cognitive Neuropsychology*, *20*(3), 409–432. https://doi.org/10.1080/02643290244000248

Tse, D., Langston, R. F., Kakeyama, M., Bethus, I., Spooner, P. A., Wood, E. R., … Morris, R. G. (2007). Schemas and memory consolidation. *Science*, *316*(5821), 76–82. https://doi.org/10.1126/science.1135935

van Kesteren, M. T. R., Beul, S. F., Takashima, A., Henson, R. N., Ruiter, D. J., & Fernández, G. (2013). Differential roles for medial prefrontal and medial temporal cortices in schema-dependent encoding: From congruent to incongruent. *Neuropsychologia*, *51*(12), 2352–2359. https://doi.org/10.1016/j.neuropsychologia.2013.05.027

van Kesteren, M. T. R., Fernández, G., Norris, D. G., & Hermans, E. J. (2010). Persistent schema-dependent hippocampal-neocortical connectivity during memory encoding and postencoding rest in humans. *Proceedings of the National Academy of Sciences of the United States of America*, *107*(16), 7550–7555. https://doi.org/10.1073/pnas.0914892107

van Kesteren, M. T. R., Rijpkema, M., Ruiter, D. J., & Fernández, G. (2010). Retrieval of associative information congruent with prior knowledge is related to increased medial prefrontal activity and connectivity. *Journal of Neuroscience*, *30*(47), 15888–15894. https://doi.org/10.1523/JNEUROSCI.2674-10.2010

Wang, S. H., Teixeira, C. M., Wheeler, A. L., & Frankland, P. W. (2009). The precision of remote context memories does not require the hippocampus. *Nature Neuroscience*, *12*(3), 253–255. https://doi.org/10.1038/nn.2263

Wimmer, G. E., & Shohamy, D. (2012). Preference by association: How memory mechanisms in the hippocampus bias decisions. *Science*, *338*(6104), 270–273. https://doi.org/10.1126/science.1223252

Winocur, G., Moscovitch, M., & Bontempi, B. (2010). Memory formation and long-term retention in humans and animals: Convergence towards a transformation account of hippocampal-neocortical interactions. *Neuropsychologia*, *48*(8), 2339–2356. https://doi.org/10.1016/j.neuropsychologia.2010.04.016

Wu, D. H., Waller, S., & Chatterjee, A. (2007). The functional neuroanatomy of thematic role and locative relational knowledge. *Journal of Cognitive Neuroscience*, *19*(9), 1542–1555. https://doi.org/10.1162/jocn.2007.19.9.1542

Wurm, M. F., & Caramazza, A. (2019). Distinct roles of temporal and frontoparietal cortex in representing actions across vision and language. *Nature Communications*, *10*(1). https://doi.org/10.1038/s41467-018-08084-y

Wurm, M. F., & Caramazza, A. (2021). Two "what" pathways for action and object recognition. *Trends in Cognitive Sciences*, *23*(2), 103–116. https://doi.org/10.1016/j.tics.2021.10.003

Zeithamova, D., Dominick, A. L., & Preston, A. R. (2012). Hippocampal and ventral medial prefrontal activation during retrieval-mediated learning supports novel inference. *Neuron*, *75*(1), 168–179. https://doi.org/10.1016/j.neuron.2012.05.010

Zeithamova, D., & Preston, A. R. (2010). Flexible memories: Differential roles for medial temporal lobe and prefrontal cortex in cross-episode binding. *Journal of Neuroscience*, *30*(44), 14676–14684. https://doi.org/10.1523/JNEUROSCI.3250-10.2010