The Medial Temporal Lobe Supports Mnemonic Discrimination For Event Duration

Nathan M. Muncy[1] and C. Brock Kirwan[1,2*]

[1] Department of Psychology, Brigham Young University, Provo, Utah, USA and [2] Neuroscience Center, Brigham Young University, Provo, Utah, USA

* Corresponding author

E-mail: kirwan@byu.edu (CBK)

Abstract

Time has an integral role in episodic memory and previous work has implicated the medial temporal lobe in both representing time and discriminating between similar information. Here we developed a novel paradigm to test mnemonic discrimination for temporal duration, as previous work has largely focused on order or maintaining information over time. Thirty-five healthy, young adults completed a continuous-recognition, temporal discrimination task in which participants were tasked with detecting a change in stimulus duration on the order of 0.5 seconds. Whole-brain high-resolution fMRI data were acquired. Behavioral results indicate that participants were successful at detecting whether or not the stimulus duration changed. Further, fMRI analyses revealed that the left entorhinal and perirhinal cortices were differentially involved in encoding and retrieval, respectively. These findings support the notion of the entorhinal cortex being involved in the encoding of temporal context information as well as the perirhinal cortex representing the conjunction of item and context during retrieval.

1 INTRODUCTION

Temporal information is critical for episodic memory. For example, the memory of a college lecture contains both when the lecture occurred as well as the length of the lecture, in addition to the visual, spatial, and auditory properties. Temporal information is unique in the sense that the temporal properties do not directly map to any receptor in the way that other sensory modalities do. Rather, time is a "hidden dimension" (Howard et al., 2014); the information is inferred through intermediate neural representations rather than actual interactions with the environment. Recent work suggests that it is precisely due to such intermediate representations that disparate information is able to be associated (Howard et al., 2014; Howard & Eichenbaum, 2013; MacDonald et al., 2011). For example, differing stimulus modalities in the example above (visual presentations, auditory explanations) arrive at the central nervous system with discrete but meaningful temporal associations which are then integrated into a neural representation of time, thereby allowing for the disparate information to be associated into a unique and unitized (Clewett & Davachi, 2017) memory representation.

The hippocampus receives multi-modal input from various cortical regions, including the visual stream as well as parietal, prefrontal, and temporal cortices (Aggleton, 2012; Baldassano et al., 2016; Cabeza et al., 2008; Eichenbaum et al., 2012; Mayes et al., 2007; Qin et al., 2016; Rockland & Van Hoesen, 1999; W. Suzuki & Naya, 2014; Thierry et al., 2000). As such, the hippocampus is ideally situated to form associations among disparate sensory modalities, stitching them together into a single representation that will subsequently be retrievable (Backus et al., 2016; DuBrow & Davachi, 2014; Howard & Eichenbaum, 2013; Thavabalasingam et al., 2018). Recent work has demonstrated that the hippocampus also generates a representation of time: work by Pastalkova et al. (2008) demonstrated that the hippocampus contained a self-

organized internal mechanism by which temporal information was maintained. Further, more recent modelling (Howard & Eichenbaum, 2013) has demonstrated that the hippocampus is capable of producing scale-invariant representations of time. It is through these representations that the recovery of contextual temporal information in episodic memory is possible, thereby allowing for the "backward jump in time" (Howard & Eichenbaum, 2013). MacDonald et al. (2011) has also shown that certain ensembles of hippocampal neurons, termed "time cells", had peak activity at different and sequential periods, effectively serving to "bridge the delay period" and maintain information through a representation of time. Further subsequent work by Howard et al. (2014) argued that varying time scales may also be represented by differing neural ensembles coding for different time constants. Such time constants are then thought to be combined with unimodal input from various cortical regions, thereby forming "holistic representation that captures the relationships between stimuli separated by time and space" (Howard et al., 2014, p. 4703; Staresina & Davachi, 2009). As such, not only does the hippocampus serve to stitch together multiple information modalities in time, it also constructs the temporal foundation upon which such associations are formed.

Given the intimate relationship between time and information in episodic memory, it follows that the hippocampus would be sensitive to event duration at different time scales. In addition to the varying scales formed via neural ensembles (Howard et al., 2014), the hippocampus has been shown to be sensitive to time scales both on the order of seconds (Barnett et al., 2014; Thavabalasingam et al., 2018) as well as on the order of minutes (Montchal et al., 2019). Given that pattern separation processes have been detected within hippocampal circuitry (Gilbert et al., 1998, 2001; Gilbert & Kesner, 2006; Hunsaker & Kesner, 2013), that pattern separation processes are information agnostic (Huffman & Stark, 2014; Yassa & Stark, 2011),

and hippocampal sensitivity to temporal information, we would expect the hippocampus to be capable of discriminating between similar but different temporal properties within episodic memory. Many have studied temporal pattern separation or mnemonic discrimination (Gilbert et al., 2001; Hunsaker & Kesner, 2013; Kesner et al., 2002; Montchal et al., 2019), but these paradigms have largely tested the sensitivity of hippocampal processes to order of stimuli. While the order of events is important for episodic representations, event duration is also critical. Importantly, while order contains temporal components, order itself is not inherently temporal, given that "[o]rdinal information can be extracted from a temporal representation, but the converse is not true" (Howard & Eichenbaum, 2013, p. 1212). This idea was addressed by Montchal et al. (2019) when discussing the importance of considering the relationship of sequence and duration, concluding "[i]t is likely that both types of information are important for making temporal judgments" (p. 287). However, the literature on the ability of human subjects to discriminate duration differences at short (1-2 second) time scales is sparse. Further, although implicated by previous studies, there are no demonstrations that the human hippocampus performs pattern separation for event duration. We therefore designed a set of experiments to (1) determine whether participants can distinguish between highly similar temporal durations and (2) implicate the important neural regions associated with detecting changes in temporal information. In the first experiment we hypothesized that participants would be (a) sensitive to changes in temporal duration on the order of 0.5 seconds, (b) more sensitive when fewer stimuli separate the first presentation from the Target or Lure, and (c) more sensitive to increases than decreases in stimulus duration. In the second experiment, we hypothesized that (d) the medial temporal regions, and in particular the CA1, would be involved in successful Lure detection, given that this region is largely implicated by extant research (Azab et al., 2014; Gilbert et al.,

2001; Howard et al., 2014; Kitamura et al., 2014; Montchal et al., 2019; Schapiro et al., 2016; Thavabalasingam et al., 2018); we expected an increased BOLD response in the CA1 that corresponded with successful Lure detection relative to an error. Further, we expected that (e) a gradient would exist in which the anterior hippocampus (head) would show greater sensitivity to temporal information (DuBrow & Davachi, 2014; Montchal et al., 2019) than more posterior regions of the hippocampus.

2 METHODS – Behavioral Experiment 1

2.1 Participants

Forty healthy, young-adult participants were recruited from the university student population. This number was determined via a priori G*Power (Bruin, n.d.) calculations, where the test family = F tests, statistical test = ANOVA: repeated measures, within factors, Effect size = 0.25, Power = 0.95, Number of groups = 1, Number of measurements = 4, Correlation = 0.5, and Nonsphericity correction = 1; such input yielded a required sample size of 36. The inclusion criteria consisted of speaking English as a native language and having normal or corrected-to-normal vision. Exclusion criteria consisted of a history of psychologic disorder or brain injury, and color blindness. The university's Institutional Review Board approved the research, and all participants gave written informed consent prior to participation. Participants were compensated for their time via course credit.

2.2 Temporal Discrimination Task

Task description. Each block followed a continuous-recognition paradigm in which a continuous stream of trials was presented (Figure 1). Each trial consisted of a fixation cross (a black cross on a white background) for 0.5s, the stimulus (a colored image of an everyday object) for a variable duration (see below), a colored masking image to combat iconic memory

presented for 0.5s, and a response screen displayed for 2.5s. If the stimulus was novel (a Foil or the first presentation of either the Target or Lure), one of three potential response screens was presented at random, prompting the participant to indicate a judgment about a visual property of the object via a button response. These response options were a) whether the object was Smooth, Rough, or Sharp, b) whether the object was made of Metal, Plastic, or Other, and c) whether the item's weight was Heavy, Medium, or Light. Each response option was presented an equal number of times. The aim of these response options was to maintain engagement in the task as the perception of time is related to attention (Coull et al., 2004; Radua et al., 2014). If the stimulus had been presented before, (i.e., a Target or Lure), the response screen prompted the participant to decide whether the stimulus was presented for either a Longer, Same Time, or Shorter duration than the first presentation of the same stimulus. Targets were trials where the same stimulus was presented with the same duration as the initial presentation. Lures were trials where the same stimulus was presented but for a different duration: 1.5s if the first counterpart was presented for 1s, and vice versa if the first was presented for 1.5s. In total, the earliest a second presentation could occur, assuming Lag = 4 (see below) and all intermediate durations = 1s, was 17.2 seconds, and the latest was 57.6 seconds (Lag = 12, Duration = 1.5s). Note that while it is possible that the second presentation could occur within a timeframe governed by working memory, it was expected that the cognitive demand elicited by the first-presentation response prompts would overwhelm the processes such that second-presentation responses are reflective of episodic memory processes. Prior to the first block, the participant was instructed in the task via a video with explicit instructions as well as a practice period, and no feedback on performance was given during the task. Stimuli were presented in PsychoPy (v2.0, n.d.).

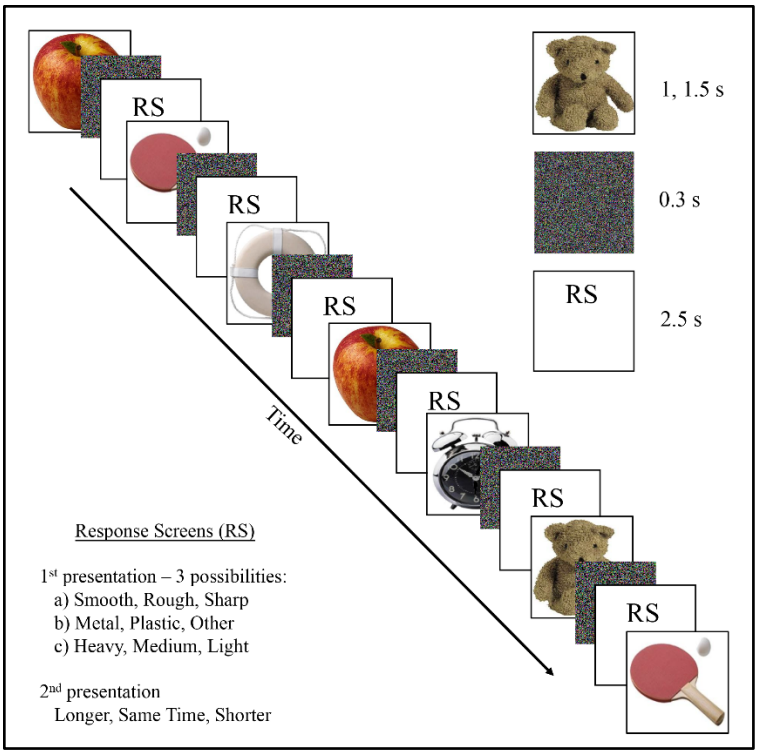

Figure 1. Temporal discrimination paradigm. A trial started with a fixation cross (0.5s, not shown) and then a stimulus was presented for either 1 or 1.5s. Following the stimulus, a colored mask was presented for 0.3s, and then a response screen (RS) was presented for 2.5s. Four RS were possible: for first presentations one of three memory prompts for visual properties were presented, and for second presentations a memory prompt for stimulus duration was presented. Targets and Lures (second presentations) followed their first presentation counterpart by either 4 or 12 trials. Targets had the same duration as the first presentations, whereas Lures were presented for 1.5s if the first counterpart was presented for 1s, and vice versa if the first was presented for 1.5s.

Stimuli, duration, and lag. Stimuli for the task consisted of randomly sampling 324 images from the 570 stimuli used in the Mnemonic Similarity Task (Stark et al., 2019) stimuli sets C-E, type “a”, for each participant. The 324 stimuli were then assigned as either Target (120), Lure (120), or Foil (84) trials. Target and Foil trials were presented for either 1 or 1.5 seconds (if the first presentation of the Target had a duration of 1 second, then the second presentation also had a duration of 1 second). Lures were first presented for 1 or 1.5 seconds and then the duration of the second presentation was adjusted by 0.5s, where if the first presentation had a duration of 1s then the second presentation had a duration of 1.5s, and vice versa; in this way all stimuli (Target, Lure, Foil) were presented for either 1 or 1.5s but Lure trials either

increased or decreased by 0.5s. Targets and Lures repeated after either 4 or 12 stimuli (Lag = 4, 12). With 324 stimuli, 240 of which repeated once, the total number of trials was 564. Duration and Lag were counterbalanced such that (a) an equal number of stimuli were presented for both durations of 1 and 1.5s (282 each), (b) an equal number of Targets were presented for both durations (60 1s, 60 1.5s), (c) an equal number of Lures increased and decreased in stimulus duration (60 increase, 60 decrease), (d) an equal number of Foils were presented for both durations (42 each), and (e) an equal number of Targets and Lures repeated at Lag = 4 or 12 (60 Lag = 4, 60 Lag = 12). Further, each Lag (e.g., 4) had an equal number of trial durations for Targets (30 1s, 30 1.5s) and Lures (30 increase, 30 decrease). The stimuli were presented in 6 blocks of 94 trials, where each block was counterbalanced for stimulus type (Target, Lure, Foil), duration, and lag. Stimuli were presented in a pseudorandom order with the constraints of Lag and number of trials. Each block contained 20 Targets (5 for each combination of Lag and Duration), 20 Lures (5 for each combination of Lag and In/Decrease), and 14 Foils (7 of each Duration).

2.3 Statistical Analyses

As there were two possibilities to incorrectly identify Targets and Lures in this experiment, an adjusted signal-detection naming convention was adopted (Table 1). A correct identification of Targets was termed "Hit-Same" (Hit_{Sa}) and incorrect identification was called either "Miss-Long" ($Miss_L$) or "Miss-Short" ($Miss_S$) according to whether the participant indicated if the Target duration increased or decreased with respect to the first presentation. For Lures which decreased in duration (first presentation = 1.5s, second = 1s), correctly identifying the stimulus was termed "Correct Rejection-Short" (CR_S), and incorrectly identifying the stimulus was termed either "False Alarm-Long" or "False Alarm-Same" (FA_L, FA_{Sa}), according

to whether the participant indicated that the Lure was presented for a longer or same duration as the first presentation, respectively. For Lures which increase in duration (first = 1s, second = 1.5s), correct identification was called "Correct Rejection-Long" (CR_L). Incorrect identification of the increasing Lure was termed either FA_{Sa} or "False Alarm-Short" (FA_S). Note that while some response types received the same classification, such as "Hit_{Sa}" resulting from correctly identifying a Target of either 1 or 1.5s, individual classifications were maintained separate during analyses.

Table 1

	Response		
Stimulus	Longer	Same Time	Shorter
Target (1s)	$Miss_L$	Hit_{Sa}	$Miss_S$
Target (1.5s)	$Miss_L$	Hit_{Sa}	$Miss_S$
Lure, Decrease (1s)	FA_L	FA_{Sa}	CR_S
Lure, Increase (1.5s)	CR_L	FA_{Sa}	FA_S

Response behavior classifications. Stimuli were presented for either 1 or 1.5s. Second presentations were either Targets or Lures, where a Lure stimulus duration differed from the first presentation by 0.5s. "Lure, decrease (1s)" corresponds to "Target (1.5s)", and "Lure, increase (1.5s)" corresponds to "Target (1s)". Participants responded whether the second presentation was presented for Longer (L), Same Time (Sa), or Shorter (S) than the first presentation.

A separate d' calculation was conducted for the 1-second and 1.5 second Target durations in order to identify the response criteria, according to the adjusted formulas

$$d'_{1.5s} = z(pHit) - z(pFA) \qquad \text{Equation 3}$$

where

$$pHit = \frac{(Hit_{Sa} + Miss_L)}{\#\ 1.5s\ Targets} \quad \text{and} \quad pFA = \frac{(FA_L + FA_{Sa})}{\#\ 1s\ Lures}$$

and

$$d'_{1s} = z(pHit) - z(pFA) \qquad \text{Equation 4}$$

where

$$pHit = \frac{(Hit_{Sa} + Miss_S)}{\#\ 1s\ Targets} \quad \text{and} \quad pFA = \frac{(FA_S + FA_{Sa})}{\#\ 1.5s\ Lures}$$

Note that while Hit_{Sa} and FA_{Sa} appear in both formulas, these response bins are kept separate in response to their respective stimulus duration.

D-prime scores were then used as the dependent variable to investigate whether or not a Lag, Duration, or interaction effect exists using a two-factor within-subject ANOVA utilizing a Greenhouse-Geisser correction for any violations of sphericity, and d' scores were individually tested against zero using the Student's t to determine if participant behavior differed from chance. A d' score significantly different from 0 would indicate that participants are sensitive to changes of stimulus duration on the order of 0.5 seconds (as in hypothesis [a]). A test of whether the d' for stimuli of Lag=4 that is significantly greater than the d' associated with Lag=12 tested hypothesis (b), and finally, a test of whether d' scores are greater for decreases in duration relative to increases tested hypothesis (c). The FDR method for correcting for multiple comparisons was used, when applicable.

3 RESULTS – Behavioral Experiment 1

Four participants were excluded due to computer malfunction, leaving a total n=36. Outliers were detected according to the 1.5 × IQR method; replacing outlier values with the median value had no effect on the significance of test statistics and so all statistics reported reflect the datasets where outliers were included. A two-factor within-subject ANOVA failed to detect any effect of Duration, Lag, or interaction thereof on d' scores (all p-values > 0.05), while one sample t-testing revealed that $d'_{1.5s}$ and d'_{1s} scores differed significantly from zero ($t(34) = 14.07$, $p_{FDR} < .001$, 95% CI [1.13, 1.52]; $t(34) = 13.83$, $p_{FDR} < .001$, 95% CI [1.21, 1.63],

respectively). Further, these d' scores did not differ from each other according to paired t-testing ($p_{FDR} > .05$; Figure 2, Experiment 1). Together, the evidence suggests that participant performance differs significantly from chance and that participants are equally sensitive regardless of whether the Lure increases, decreases, or appears after Lag 4 or 12.

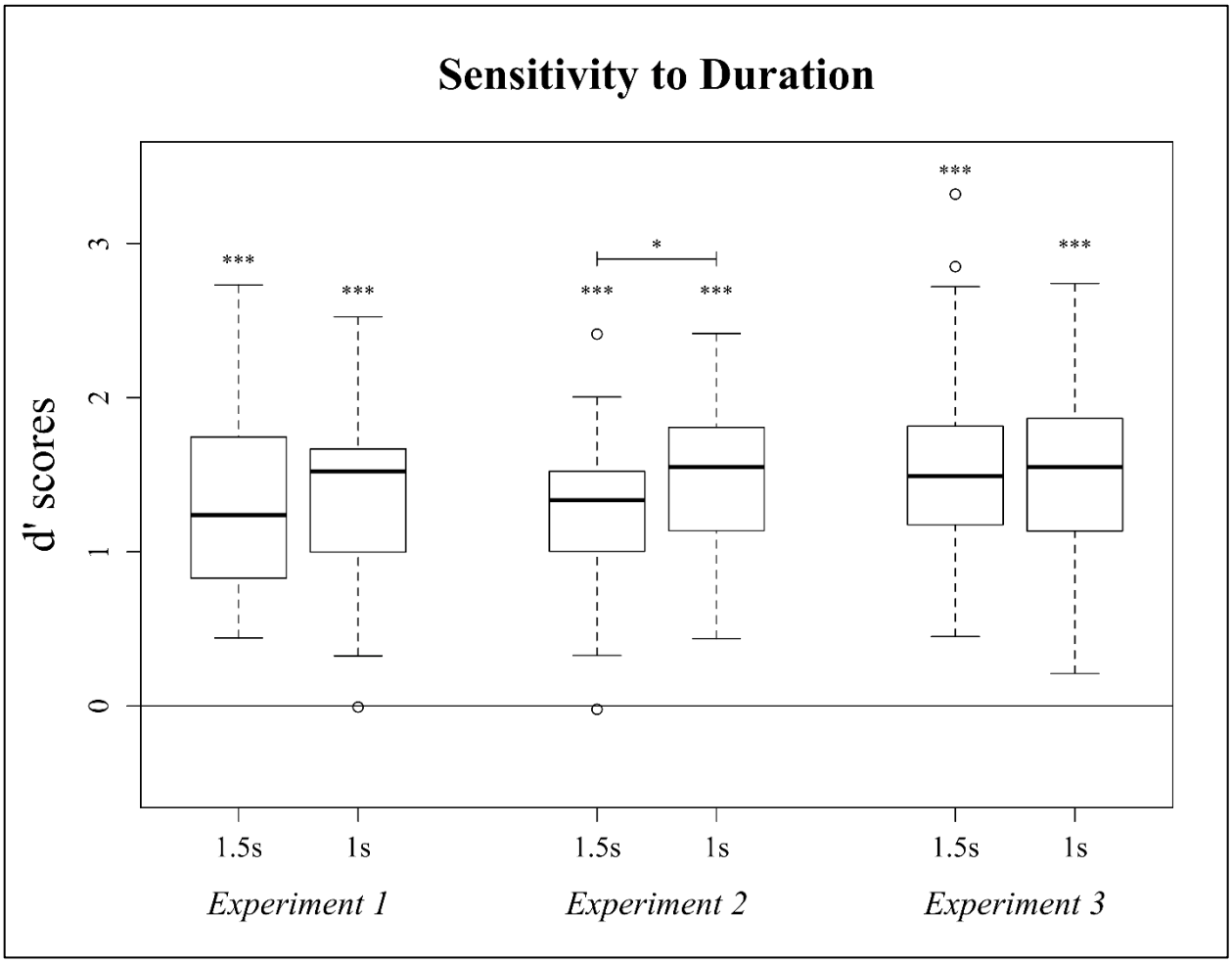

Figure 2. Boxplot of d' scores. 1.5s = 1.5 second Target, 1 second Lure; 1s = 1 second Target, 1.5 second Lure. *** = p < .001, * = p < .05.

4 METHODS – Behavioral Experiment 2

As no effect of duration, lag, or interaction thereof was detected in the previous analyses, and given that the experiment lasted for approximately 45 minutes, we elected to reduce the experiment length: the number of trials in each category was reduced by exactly one-half,

yielding 60 Targets, 60 Lures, and 42 Foils. The resulting experiment was still counterbalanced for duration and lag as well as Target and Lure types but no longer powered to investigate interactive effects of duration and lag, and had a duration of approximately 25 minutes. In order to make sure that such a reduction would not affect the outcome, 34 more participants (16 Female, Age = 20.1±1.7) were recruited to participate in the shortened version of the experiment. Participants gave written informed consent prior to participation. All methodologies and analyses conducted, save the reduction of trial items, remain identical to those reported above.

5 RESULTS – Behavioral Experiment 2

In the reduced experiment replacing outlier values with the group median again had no effect on test statistics and so all statistics reported include outliers. One-sample t-testing on the $d'_{1.5s}$ and d'_{1s} scores demonstrated that participants performed above chance ($t(33) = 14.85$, $p_{FDR} < .001$, 95% CI [1.08, 1.43]; $t(33) = 16.44$, $p_{FDR} < .001$, 95% CI [1.27, 1.64], respectively), but this time we detected that participants were more sensitive in d'_{1s} than $d'_{1.5s}$ according to paired t-testing ($t(33) = -2.22$, $p_{FDR} < .05$, 95% CI [-0.37, -0.02]; Figure 2, Experiment 2).

6 METHODS – fMRI Experiment

6.1 Participants

Forty healthy, young-adult participants were recruited from the Brigham Young University student population in order to replicate the procedures of Temporal information is critical for episodic memory. For example, the memory of a college lecture contains both when the lecture occurred as well as the length of the lecture, in addition to the visual, spatial, and auditory properties. Temporal information is unique in the sense that the temporal properties do not directly map to any receptor in the way that other sensory modalities do. Rather, time is a

235 “hidden dimension” (Howard et al., 2014); the information is inferred through intermediate
236 neural representations rather than actual interactions with the environment. Recent work suggests
237 that it is precisely due to such intermediate representations that disparate information is able to
238 be associated (Howard et al., 2014; Howard & Eichenbaum, 2013; MacDonald et al., 2011). For
239 example, differing stimulus modalities in the example above (visual presentations, auditory
240 explanations) arrive at the central nervous system with discrete but meaningful temporal
241 associations which are then integrated into a neural representation of time, thereby allowing for
242 the disparate information to be associated into a unique and unitized (Clewett & Davachi, 2017)
243 memory representation.

244 The hippocampus receives multi-modal input from various cortical regions, including the
245 visual stream as well as parietal, prefrontal, and temporal cortices (Aggleton, 2012; Baldassano
246 et al., 2016; Cabeza et al., 2008; Eichenbaum et al., 2012; Mayes et al., 2007; Qin et al., 2016;
247 Rockland & Van Hoesen, 1999; W. Suzuki & Naya, 2014; Thierry et al., 2000). As such, the
248 hippocampus is ideally situated to form associations among disparate sensory modalities,
249 stitching them together into a single representation that will subsequently be retrievable (Backus
250 et al., 2016; DuBrow & Davachi, 2014; Howard & Eichenbaum, 2013; Thavabalasingam et al.,
251 2018). Recent work has demonstrated that the hippocampus also generates a representation of
252 time: work by Pastalkova et al. (2008) demonstrated that the hippocampus contained a self-
253 organized internal mechanism by which temporal information was maintained. Further, more
254 recent modelling (Howard & Eichenbaum, 2013) has demonstrated that the hippocampus is
255 capable of producing scale-invariant representations of time. It is through these representations
256 that the recovery of contextual temporal information in episodic memory is possible, thereby
257 allowing for the “backward jump in time” (Howard & Eichenbaum, 2013). MacDonald et al.

258 (2011) has also shown that certain ensembles of hippocampal neurons, termed “time cells”, had
259 peak activity at different and sequential periods, effectively serving to “bridge the delay period”
260 and maintain information through a representation of time. Further subsequent work by Howard
261 et al. (2014) argued that varying time scales may also be represented by differing neural
262 ensembles coding for different time constants. Such time constants are then thought to be
263 combined with unimodal input from various cortical regions, thereby forming “holistic
264 representation that captures the relationships between stimuli separated by time and space”
265 (Howard et al., 2014, p. 4703; Staresina & Davachi, 2009). As such, not only does the
266 hippocampus serve to stitch together multiple information modalities in time, it also constructs
267 the temporal foundation upon which such associations are formed.

268 Given the intimate relationship between time and information in episodic memory, it
269 follows that the hippocampus would be sensitive to event duration at different time scales. In
270 addition to the varying scales formed via neural ensembles (Howard et al., 2014), the
271 hippocampus has been shown to be sensitive to time scales both on the order of seconds (Barnett
272 et al., 2014; Thavabalasingam et al., 2018) as well as on the order of minutes (Montchal et al.,
273 2019). Given that pattern separation processes have been detected within hippocampal circuitry
274 (Gilbert et al., 1998, 2001; Gilbert & Kesner, 2006; Hunsaker & Kesner, 2013), that pattern
275 separation processes are information agnostic (Huffman & Stark, 2014; Yassa & Stark, 2011),
276 and hippocampal sensitivity to temporal information, we would expect the hippocampus to be
277 capable of discriminating between similar but different temporal properties within episodic
278 memory. Many have studied temporal pattern separation or mnemonic discrimination (Gilbert et
279 al., 2001; Hunsaker & Kesner, 2013; Kesner et al., 2002; Montchal et al., 2019), but these
280 paradigms have largely tested the sensitivity of hippocampal processes to order of stimuli. While

281 the order of events is important for episodic representations, event duration is also critical.
282 Importantly, while order contains temporal components, order itself is not inherently temporal,
283 given that "[o]rdinal information can be extracted from a temporal representation, but the
284 converse is not true" (Howard & Eichenbaum, 2013, p. 1212). This idea was addressed by
285 Montchal et al. (2019) when discussing the importance of considering the relationship of
286 sequence and duration, concluding "[i]t is likely that both types of information are important for
287 making temporal judgments" (p. 287). However, the literature on the ability of human subjects to
288 discriminate duration differences at short (1-2 second) time scales is sparse. Further, although
289 implicated by previous studies, there are no demonstrations that the human hippocampus
290 performs pattern separation for event duration. We therefore designed a set of experiments to (1)
291 determine whether participants can distinguish between highly similar temporal durations and (2)
292 implicate the important neural regions associated with detecting changes in temporal
293 information. In the first experiment we hypothesized that participants would be (a) sensitive to
294 changes in temporal duration on the order of 0.5 seconds, (b) more sensitive when fewer stimuli
295 separate the first presentation from the Target or Lure, and (c) more sensitive to increases than
296 decreases in stimulus duration. In the second experiment, we hypothesized that (d) the medial
297 temporal regions, and in particular the CA1, would be involved in successful Lure detection,
298 given that this region is largely implicated by extant research (Azab et al., 2014; Gilbert et al.,
299 2001; Howard et al., 2014; Kitamura et al., 2014; Montchal et al., 2019; Schapiro et al., 2016;
300 Thavabalasingam et al., 2018); we expected an increased BOLD response in the CA1 that
301 corresponded with successful Lure detection relative to an error. Further, we expected that (e) a
302 gradient would exist in which the anterior hippocampus (head) would show greater sensitivity to

temporal information (DuBrow & Davachi, 2014; Montchal et al., 2019) than more posterior regions of the hippocampus.

2 METHODS – 4 (the shortened experiment) and investigate any potential neural correlates of discrimination for temporal duration. All participants were naïve to the task. In addition to the inclusion and exclusion criteria defined above, exclusion criteria also consisted of incompatibilities with the magnet or head coil, colorblindness and left-handedness, and the capability to remain still for an hour. The university's Institutional Review Board approved the research, and all participants gave written informed consent prior to participation. Participants were compensated for their time via course credit, money ($20 USD), or a 3d-printed quarter-scale model of their brain.

6.2 Temporal Discrimination Task and Statistics

The task was identical to that in section 4. Correspondingly, analyses of behavioral data were conducted in an identical fashion to section 4.

6.3 MRI Acquisition

Functional and structural data were collected on a Siemens Tim Trio 3T MRI scanner at the Brigham Young University MRI Research Facility, using a 32-channel head coil. T1-weighted, T2-weighted, and T2*-weighted scans were collected from each participant. The T1-weighted structural scan was acquired using a magnetization-prepared rapid acquisition with gradient echo (MP-RAGE) sequence, according to the following parameters: TR = 1900 ms, TE = 2.26 ms, flip angle = 9°, FoV = 218 × 250, voxel size = 0.97 × 0.97 × 1 mm, slices = 176 interleaved. A high-resolution T2-weighted scan was used to image hippocampal subfields according to the following parameters: TR = 8020 ms, TE = 80 ms, flip angle = 150°, FoV = 150 × 150 mm, voxel size = 0.4 × 0.4 × 2 mm, slices = 30 interleaved; the T2 data were acquired

326 perpendicular to the long axis of the hippocampus. High-resolution multi-band echo-planar scans
327 were collected from each participant according to the following parameters: Multi-band factor =
328 4, TR = 2200 ms, TE = 45.2 ms, flip angle = 90°, acquisition matrix = 100 × 100 mm, voxel size
329 = 1.8 mm3, slices = 72 interleaved; the first 11 TRs were discarded to allow for T1 equilibration.
330 Finally, a reverse blip echo-planar scan was collected using the same parameters as the previous
331 protocol save that direction of acquisition was opposite (P>>A) and only 10 volumes were
332 collected.

333 **6.4 MRI Data Pre-Processing**

334 All pre-processing was conducted using the software packages dcm2niix (Li et al., 2016),
335 Analysis of Functional NeuroImages (AFNI; Cox, 1996), convert 3D (c3d; Yushkevich et al.,
336 2006) and Automatic Segmentation of Hippocampal Subfields (ASHS; Yushkevich et al., 2015).
337 AFNI and Mango (Lancaster et al., 2012) were used for visualizations.

338 T2*-weighted DICOMs were converted into NIfTI files. Field distortion was then
339 corrected by incorporating information from the reverse blip scan. Briefly, the median input of
340 all voxels from concatenated blip and experiment functional scans were individually calculated
341 and then the nonlinear transformation between the blip and experimental files were calculated
342 thereby producing warping and reverse warping vectors. These reverse warping files were then
343 used to "unwarp" the experimental files thereby recovering some signal in regions of high signal
344 distortion. The experimental volume with the minimum of voxel outliers was then extracted to
345 use as a volume registration base. To move data into template (MNI 152) space, the calculations
346 of (a) rigidly aligning the structural to the registration base (using an lpc+ZZ cost function), the
347 (b) non-linear warp of the structural file in original space to template space, and (c) the volume
348 registration (rigid transformation) of each volume to the registration base were concatenated and

applied to the functional data in native space such that all volumes were aligned with the template utilizing a diffeomorphic transformation via a single interpolation. A binary extension mask corresponding to regions within the domain with sufficient minimum signal was constructed; data within this region were scaled by the mean signal.

Single-subject regression used a generalized-least-squares fit utilizing a nonlinear residual maximum likelihood estimate to determine the best fitting autoregressive-moving-average model, where the timeseries corresponding to an eroded white matter mask was utilized as a nuisance regressor. Centered motion regressors for six degrees of freedom were included, and volumes that were (a) outliers in terms of total volume signal (>10% of the voxels in the volume had outlier signal) and (b) either preceded or were involved in a motion event (>0.3° rotation) were censored. Regressors for the various behaviors (described below) were modelled with a duration modulated block function. Two single-subject regressions were conducted, where the BOLD signal associated with behavioral responses was modelled using a boxcar convolution with the canonical hemodynamic response. First, test trials (when participants made their response) were modeled for correct and incorrect responses to Targets (Hits and Misses, respectively) and Lures (Correct Rejections and False Alarms, respectively); only the time between the start of the response screen and participant response was modelled. Second, responses to encoding the stimuli (when the stimulus was onscreen) were modeled for subsequent behavioral responses; the entire stimulus duration was modelled. Finally, participants that had more than 10% of their total volumes censored would have been excluded from all subsequent group-level analyses but no participant reach this criterion.

For *a priori* analyses, behavioral parameter estimates (β-coefficients) were extracted from anterior and posterior hippocampal regions of interests (ROIs) from each deconvolution

372 utilizing masks that were previously generated in template space. Briefly, ASHS was used to
373 segment the medial temporal regions of high-resolution T2-weighted scans for a number of
374 participants. Joint Label Fusion (H. Wang et al., 2013) then utilized this set of segmentations to
375 generate template hippocampal subfield priors. For this experiment, template MTL masks were
376 split along the anterior-posterior axis at X=-20, the CA2, CA3, and DG masks were combined,
377 and then masks were resampled into functional dimensions. Any voxels labeled by more than
378 one mask were excluded, thereby producing anterior and posterior, right and left Subiculum,
379 CA1, and CA2-3-DG masks. A two-factor within-subject MANOVA was then used to
380 investigate the role of hippocampal structures in the modeled behaviors, where factor A was the
381 ROI, factor B the behavioral responses, and the parameter estimate was the dependent variable.
382 ROIs in the left hemisphere were treated as independent from the right, and a separate analysis
383 was conducted on the anterior and posterior masks for both the encoding and response estimates.
384 The FDR method was used to correct for multiple comparisons.

385 For exploratory analyses, an intersection mask was constructed, which indicated where
386 meaningful signal exists for both T1- and T2*-weighted scans across all participants, and
387 multiplied with a gray matter mask that had been generated in template space, thereby producing
388 an intersection-gray-matter mask that was used to constrain the number of voxels on which
389 analyses were conducted. Further, a small volume mask was generated in a similar fashion but
390 only using masks associated with the gray matter of bilateral hippocampi, entorhinal cortex,
391 perirhinal cortex, and parahippocampal cortex. Noise was modelled by calculating the
392 autocorrelation function of single-subject regression residuals from voxels which lay within the
393 generated masks, and these parameter estimates were then used in Monte Carlo simulations to
394 generate multiple-comparison correction criteria. A multivariate model was used to investigate

any regions that show differential signal associated with the various behaviors modelled where the behaviors were modeled as within-subject factors. Clusters which showed differential activity were then used to extract mean parameter estimates in order to report the (a) difference in parameter estimates and (b) statistics. All scripts used for running these experiments and analyzing the data are available at https://github.com/nmuncy/MST_Temporal.

7 RESULTS – fMRI Experiment

7.1 Behavioral Results

From the 40 participants recruited, five were excluded from analyses due to equipment problems and incompatibilities (n=3), responding with the wrong button presses (n=1), and "excessive eye watering" during the task which was reported to be "very distracting" and resulted in at-chance performance (n=1). The group size reported below is therefore n=35, 19 female, age=22.9±2.7.

As above, statistics were conducted both with and without outliers. Replacing outlier values with median values had no effect on test statistics and so all analyses below include outliers. Performance was very similar to the above experiments (Figure 2, Experiment 3). Participants d' scores differed significantly from 0 according to one-sample t-testing for both increases and decreases in duration ($t(34)=13.9$, $p_{FDR}<.001$, 95% CI [1.35, 1.81]; $t(34)=16.4$, $p_{FDR}<.001$, 95% CI [1.32, 1.69], respectively). In addition, and similarly to the results of experiment 1 but not experiment 2, no difference was detected between sensitivity to changes in increases versus decreases according to two-sample t-testing ($t(34)=0.65$, $p_{FDR}=.52$, 95% CI [-.16, .31]).

7.2 FMRI Results - Encoding

As no effect of Lag, Duration, or an interaction thereof was detected in behavioral performance (Section 3) and participants performed equally well regardless of increasing or decreasing the Lure duration (Section 7.1), responses were collapsed across Lag and Duration, and further, types of Misses, Correct Rejections, and False Alarms (Table 1) were collapsed as well. Collapsing resulted in 28 Hits, 31 Misses, 31 Correct Rejections, and 23 False Alarms, on average.

The effect of encoding on task performance was assessed by investigating the BOLD response to stimulus presentation that preceded a task response (Hit, CR, etc.). For the *a priori* ROIs, no effect was determined via a two-factor within-subject MANOVA for either ROI, Behavior, or an interaction thereof (all p-values > .05 once correcting for sphericity via the Greenhouse-Geisser method) for both the anterior and posterior regions of the hippocampus.

An exploratory whole-brain analysis also failed to detect any clusters which showed differential signal during trials preceding task responses (Trials preceding Hit, FA, CR, Miss) when using the thresholding criteria of cluster size k = 20, NN = 1, two-sided comparison, p < .001, FWE = .05. A small-volume correction, using masks corresponding to the MTL (hippocampus, entorhinal, and parahippocampal cortex) did, however, reveal two clusters with differential activity using the thresholding criteria of k = 6, NN = 1, two-sided comparison, p < .001, FWE = .05. Neuroanatomic classification of the clusters for these and subsequent analyses were determined by the criteria established by Frankó et al. (2014). The left entorhinal cortex was more active during encoding trials preceding a Hit versus a Miss (LEC, Figure 3 Left, Table 2) while the right hippocampus was more active during encoding trials preceding a FA than a CR (RHC, Figure 3 Middle, Table 2).

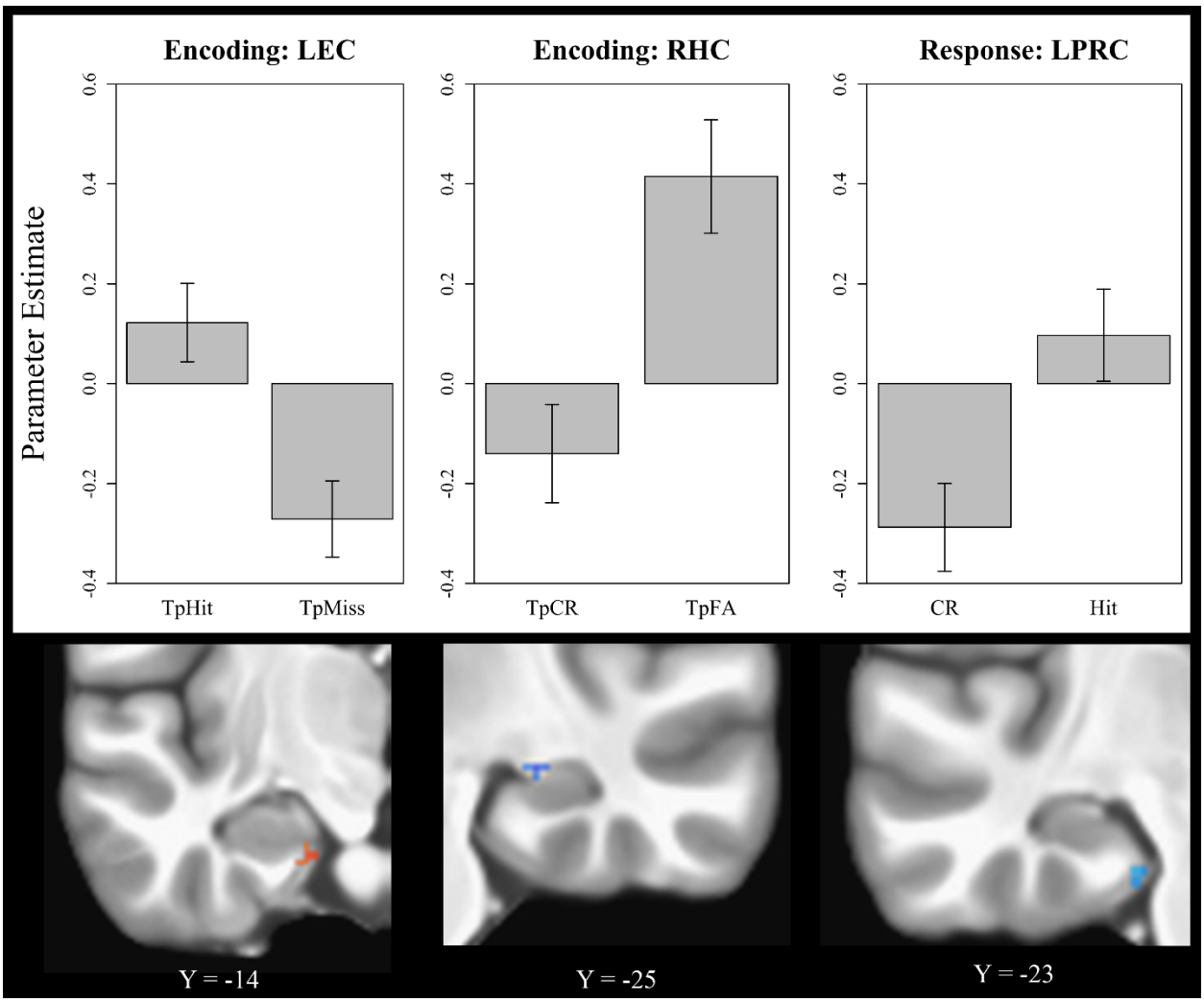

Figure 3. Regions engaged in duration detection. Left and Middle: left entorhinal cortex (LEC) and right hippocampus (RHC) are differentially engaged during encoding trials preceding task performance. Right: Left perirhinal cortex (LPRC) is differentially involved in Target detection. "Tp" = trial preceding a test response.

Table 2

Phase	Cluster	K	X	Y	Z	T(34)	Sig	LB	UB
Encoding	LEC	9	-16	-13	-25	4.13	***	.21	.62
	RHC	7	27	-25	-9	-4.55	***	-.81	-.31
Retrieval	LPRC	7	-18	-23	-25	-3.15	**	-.61	-.13

Cluster descriptions of small-volume corrected analyses. K = cluster size, X-Z = peak MNI coordinate. T(34) = paired t-test with 34 df, LB UB = lower and upper bound of 95% confidence interval. LEC = left entorhinal cortex, RHC = right hippocampus, LPRC = left perirhinal cortex. *** = $p < .001$, ** = $p < .01$.

7.3 FMRI Results – Retrieval

To investigate processes associated with task performance the HRF was modeled for the time in which participants responded to Target and Lure stimuli. *A priori* investigations into the subregions of the medial temporal lobe failed to detect a significant interaction between region and behavior in either portion of the hippocampus. Correspondingly, an exploratory whole-brain analysis using the same thresholding criteria as was reported above failed to detect any clusters that demonstrated differential activity for the various task behaviors. A small-volume correction, however, detected a cluster in the left perirhinal cortex that was differentially engaged in correct responses (LPRC, Figure 3 Right, Table 2). That is, this cluster was more active during the correct identification of Targets (Hits) than during the correct identification of Lures (CRs).

8 DISCUSSION

This set of experiments investigated whether mnemonic discrimination was possible for stimulus duration and identified functional neuroanatomic correlates thereof. The task (Figure 1) involved serially presenting images of everyday items in a continuous-recognition paradigm for either 1 or 1.5 seconds. Following the first presentation of a stimulus the participants performed an orienting task wherein they made decisions from memory about physical properties of the stimulus. If a stimulus repeated, it was either presented for the same duration (Targets) or for a difference of 0.5 seconds (Lures); in these cases, the participants were explicitly instructed to attend the presentation duration and subsequently tasked with deciding whether a change of stimulus duration occurred. Such a small change in stimulus duration was intentionally selected in order to elicit a sufficient number of Misses and FAs for functional BOLD analyses. The paradigm was conducted three times in naïve groups of participants, experiments 2 and 3 serving

to replicate the behavioral findings of experiment 1 and bringing the total number of participants that performed the task to n=69.

These experiments had several findings. First, behavioral evidence indicated that participants were successful at remembering and detecting changes of stimulus duration on the order of 0.5 seconds and that they were equally sensitive regardless of the direction of duration change (3 RESULTS – Behavioral Experiment 1). With respect to these behavioral findings, we reject the null of hypothesis (a), given that participants had d' scores which differed significantly from zero, but fail to reject the null of hypotheses (b) and (c); participants were equally sensitive at Lag 4 as at Lag 12 and were equally sensitive to increases and decreases in duration. These subsecond findings replicate those of Palombo et al. (2019), in which amnestic patients were tasked detecting whether test spinwheels spun for a different duration than study pinwheels. Palombo et al. (2019) noted, as we do here, that participants had strong d' scores and were sensitive to both increases and decreases in duration. Further, in the present experiment, no effect of lag was detected; equal performance at either lag suggests that the distracting task was sufficiently difficult to overwhelm working memory such that behavioral results here are reflective of episodic memory processes. Were this not the case, we would expect to see an interaction between d' scores and lag due to Lag 4 performance being governed more by short-term memory and Lag 12 by episodic. Corresponding with this line of reasoning, the Palombo et al. (2019) experiment, who tested participants within the domain of short-term memory, presented d' scores that where two standard deviations higher than those presented here. Finally, the behavioral evidence suggests that the detected effect is robust as the d' scores were stable across three different groups of participants.

Second, two clusters showed differential activation during the encoding of the stimuli which was predictive of subsequent test performance. A cluster in the right hippocampus (Figure 3, middle) was differentially engaged in encoding such that the cluster was more active preceding the incorrect detection of Lures (FA) compared to correct detection (CR). This pattern of activity is consistent with the deleterious effect that the default mode network has on subsequent test performance; we interpret this cluster as being indicative of participants failing to attend the training stimulus such that subsequent performance was adversely affected (H. Kim, 2011). It should be noted, though, that a second *a posteriori* whole-brain analysis did not identify any additional clusters to those detected in the small-volume correction. As such, the lack of additional default-mode findings weakens the interpretation of this hippocampal cluster.

Next, the left medial entorhinal cortex (mEC) demonstrated differential activity which predicted subsequent Target-trial performance, in that the cluster was more active preceding a Hit relative to preceding a Miss (Figure 3, left). This cluster appears to be critically involved in the encoding the temporal properties of the stimuli, as visual information remained identical between study and test, a finding that is consistent with the previous literature: numerous studies have detected cells with a selectivity for temporal information within the mEC. For instance, Kraus et al. (2015) demonstrated mEC grid cell activity which signaled for elapsed time in addition to distance traveled, showing an integration of time and distance, and Heys and Dombeck (2018) demonstrated both that while the mEC is sensitive to elapsed time, it can also remap its sensitivity according to contextual task demands (also, see Sugar & Moser, 2019). Robinson et al. (2017) showed that the mEC helps support the hippocampal CA1 representation of time, and further, Suh et al. (2011) demonstrated that the monosynaptic side of the perforant pathway, the connection between the mEC and CA1, is integral for temporal associations. This

517 hippocampal structure, the CA1, is downstream from the mEC and has been strongly implicated
518 in the temporal aspects of memory (Allen et al., 2016; Cai et al., 2016; Dimsdale-Zucker et al.,
519 2018; MacDonald et al., 2011; Mankin et al., 2012; Salz et al., 2016; Suh et al., 2011; Y. Wang
520 et al., 2015). Finally, inactivation of the mEC is also associated with disruptions in temporal
521 processing (Heys & Dombeck, 2018; Robinson et al., 2017; Sugar & Moser, 2019). As such, the
522 mEC is proposed to bind information of different modalities (i.e. item, spatial, temporal) as well
523 as providing a scaffold of spatiotemporal information to the hippocampus (Sugar & Moser,
524 2019).

525 Further, Maass et al. (2015) and Schröder et al. (2015) demonstrate that the mediolateral
526 divisions of the rodent entorhinal cortex do not translate to the human entorhinal cortex, but that
527 the human entorhinal cortex is functionally divided along an anterolateral-posteromedial axis
528 such that the human homologue of the rodent mEC is the posteromedial entorhinal cortex
529 (pmEC). Maass et al. (2015) shows the PHC is functionally coupled with the pmEC, implicating
530 this region in processing contextual information as opposed to item information which tends to
531 be sent from the PRC to the lateral anterior EC (Aminoff et al., 2007; Diana et al., 2013; Hsieh et
532 al., 2014; Jenkins & Ranganath, 2010; Naya et al., 2017; F. Wang & Diana, 2017). Critically, the
533 cluster detected in this experiment during the encoding phase of the experiment entirely
534 corresponds with the pmEC. Further still, Schröder et al. (2015) demonstrated that pmEC forms
535 part of the posterior-medial system, a system which carries spatial information. The rodent and
536 human literature in conjunction therefore implicate the pmEC in processing not just spatial but
537 contextual information which varies in a dimension (i.e. temporal information) according to task
538 demands, a notion that is reminiscent of Salz et al. (2016), who noted that temporal processing in

539 the hippocampus mirrors that of spatial. In the current experiment, then, the detected pmEC
540 cluster is believed to be processing the temporal context information associated with each item.
541 Third, a cluster within the left perirhinal cortex (PRC) was differentially engaged during
542 the test phase such that it was more active during Hits than Correct Rejections (Figure 3, right).
543 Similarly, recent work implicated the PRC in processing temporal information during the test
544 phase of an experiment: Montchal et al. (2019) had participants first view a television episode
545 and then tested participants by having them place still-frames from the episode on a timeline, a
546 task designed to test memory for temporal order. While the paper emphasized the roles of the
547 anterior-lateral EC and subregions of the HC, Montchal et al. (2019) nevertheless demonstrated
548 that the PRC was differentially engaged in high versus low accuracy for temporal information. In
549 a separate but related vein, the Binding of Item and Context theory (Diana et al., 2013) has
550 proposed a functional dissociation in the medial temporal lobe where the parahippocampus
551 processes contextual information, the PRC item information, and the hippocampus serving to
552 bind together item and context; the role of the PRC in such a model has recently been supported
553 (Diana et al., 2013; Hsieh et al., 2014; F. Wang & Diana, 2017). Together then, the PRC has
554 been implicated in processing both temporal and item information. Such a conjunction of item
555 and time is supported by F. Wang et al. (2017), who noted PRC activation associated with the
556 retrieval of contextual temporal information, perhaps due to the 'unitization' of the item and
557 context (Ford et al., 2010; Giovanello et al., 2006). More explicitly, work using single-unit
558 recordings in non-human primates demonstrated that PRC cells fired for both item and temporal
559 information (Naya et al., 2017). Thus, the PRC activation detected in this experiment is
560 consistent with the conjunction of item-temporal information processing, in which the PRC
561 differentially aides in the successful retrieval of item and temporal duration information. Indeed,

increased signal from this region is associated with Hits, i.e., correctly retrieving the duration information (as the visual information was identical), while suppressed signal is associated with a mismatch detection between the Lure duration and that of the original.

A number of limitations exist for this experiment. First, while only Targets (same duration) and Lures (different duration) were tested in this experiment, participants had three response options necessitating an adjustment to the d' calculations. This adjustment resulted in collapsing across some response types such that these adjusted-d' scores do not represent a bias-corrected deflection point but rather indicate sensitivity to whether a change occurred. Indeed, in calculating $d'_{1.5s}$ (when the Target was 1.5s and the Lure was 1s), *pHit* combined both responses that did not involve a "shorter" judgment for Targets, and *pFA* did the same. With such a calculation, a higher adjusted-d' score therefore indicates that a participant is less likely to respond "shorter" on longer Target trials and more likely to respond the same on Lure trials, a response pattern that is related to, but separate from, accuracy in judging stimulus duration in episodic memory. Second, and related, several response categories were collapsed across in the functional analyses: as no main effect of Lag or Duration was detected, the same responses from different stimulus types (such as $Hits_{a}$ for both a 1.5s and 1s Target for both Lags) were combined into the same bin. This method ensured a proper number of trials per behavioral bin existed such that the shape of the hemodynamic response function could reasonably be modeled, but it nevertheless may have contributed noise to the analyses. Indeed, if certain regions of tissue were involved in only detecting increases, decreases, or no change in stimulus duration then such a combination would likely have introduced unnecessary noise to any existing signal. As such, our functional findings do not illustrate signal associated with correctly identifying increases or decreases of duration in Targets and Lures, but rather demonstrate signal associated with

detecting temporal change between the study and test stimuli. Third, while the hippocampal subregion CA1 has been shown to be critically involved in temporal processing for memory tasks (Allen et al., 2016; Cai et al., 2016; Dimsdale-Zucker et al., 2018; MacDonald et al., 2011; Mankin et al., 2012; Montchal et al., 2019; Robinson et al., 2017; Salz et al., 2016; Y. Wang et al., 2015), our results did not replicate these findings. This is likely due to the fact that the rodent studies which have implicated the CA1 have largely involved requiring the rodent to maintain information over time (e.g., Kraus et al., 2015; Pastalkova et al., 2008), information which is not necessarily temporal and is commonly a previous decision. Our experiment instead involved the retrieval of temporal duration information, and likewise it is unsurprising that we detected signal associated with tissue in a different region. With respect to previous studies involving humans (Aminoff et al., 2007; Clewett & Davachi, 2017; Diana et al., 2013; El-Kalliny et al., 2019; Hsieh et al., 2014; Jenkins & Ranganath, 2010, 2016; Montchal et al., 2019; F. Wang & Diana, 2017), our results are similar in nature and any differences are likely due to the fact the we here tested for episodic memory of temporal duration rather than temporal order or sequence, or working memory for temporal duration (Palombo et al., 2019). As such, we partially reject hypothesis (d), as we did find differential activation in the MTL associated with the task, but not in the hypothesized region of CA1. Further, we reject hypothesis (e), as no differential signal was detected in the anterior versus posterior HC. It is possible that we failed to detect differential signal in these regions due to collapsing across too much variance, or that the selected contrasts did not reflect differences in the signal, or perhaps even due to the explicit nature of our task. Either way, one must take caution in interpreting null results (Chen et al., 2017) and note that we were unable to falsify these hypotheses.

In summary, we presented participants with stimuli of different duration and tasked them with detecting a change in duration. We found that participants were sensitive on the order of 0.5 seconds, a finding which was demonstrated in three different groups of participants. We also demonstrate that the left posteromedial entorhinal cortex is differentially involved during the encoding of items such that greater activity in this region is predictive of subsequent Hit versus subsequent Miss. Finally, the left perirhinal cortex was noted to be differentially engaged during successful test performance, being more active during Hits than Correct Rejections, activation which is consistent with previous work demonstrating that this region is sensitive to the conjugation of item and temporal context.

References

Aggleton, J. P. (2012). Multiple anatomical systems embedded within the primate medial temporal lobe: Implications for hippocampal function. *Neuroscience & Biobehavioral Reviews*, *36*(7), 1579–1596. https://doi.org/10.1016/j.neubiorev.2011.09.005

Allen, T. A., Salz, D. M., McKenzie, S., & Fortin, N. J. (2016). Nonspatial sequence coding in CA1 neurons. *Journal of Neuroscience*, *36*(5), 1547–1563. https://doi.org/10.1523/JNEUROSCI.2874-15.2016

Aminoff, E., Gronau, N., & Bar, M. (2007). The parahippocampal cortex mediates spatial and nonspatial associations. *Cerebral Cortex*, *17*(7), 1493–1503. https://doi.org/10.1093/cercor/bhl078

Avants, B. B., Epstein, C. L., Grossman, M., & Gee, J. C. (2008). Symmetric diffeomorphic image registration with cross-correlation: Evaluating automated labeling of elderly and neurodegenerative brain. *Medical Image Analysis*, *12*(1), 26–41.

Avants, B. B., Tustison, N. J., Song, G., Cook, P. A., Klein, A., & Gee, J. C. (2011). A reproducible evaluation of ANTs similarity metric performance in brain image registration. *NeuroImage*, *54*(3), 2033–2044.

Azab, M., Stark, S. M., & Stark, C. E. (2014). Contributions of human hippocampal subfields to spatial and temporal pattern separation. *Hippocampus*, *24*(3), 293–302.

Backus, A. R., Bosch, S. E., Ekman, M., Grabovetsky, A. V., & Doeller, C. F. (2016). Mnemonic convergence in the human hippocampus. *Nature Communications*, *7*, 11991.

Baddeley, A., Eysenck, M. W., & Anderson, M. C. (2009). *Memory* (1 edition). Psychology Press.

Bakker, A., Kirwan, C. B., Miller, M., & Stark, C. E. (2008). Pattern separation in the human hippocampal CA3 and dentate gyrus. *Science*, *319*. https://doi.org/10.1126/science.1152882

Baldassano, C., Esteva, A., Fei-Fei, L., & Beck, D. M. (2016). Two distinct scene-processing networks connecting vision and memory. *ENeuro*, *3*(5). https://doi.org/10.1523/ENEURO.0178-16.2016

Barnett, A. J., O'neil, E. B., Watson, H. C., & Lee, A. C. (2014). The human hippocampus is sensitive to the durations of events and intervals within a sequence. *Neuropsychologia*, *64*, 1–12.

Bruin, J. (n.d.). *newtest: Command to compute new test*. Retrieved September 25, 2018, from http://www.gpower.hhu.de/

Cabeza, R. (2013). Introduction to the special issue on functional neuroimaging of episodic memory. *Neuropsychologia*, *51*(12), 2319–2321.

Cabeza, R., Ciaramelli, E., Olson, I. R., & Moscovitch, M. (2008). The parietal cortex and episodic memory: An attentional account. *Nature Reviews Neuroscience*, *9*(8), 613.

Cai, D. J., Aharoni, D., Shuman, T., Shobe, J., Biane, J., Song, W., Wei, B., Veshkini, M., La-Vu, M., Lou, J., Flores, S. E., Kim, I., Sano, Y., Zhou, M., Baumgaertel, K., Lavi, A., Kamata, M., Tuszynski, M., Mayford, M., … Silva, A. J. (2016). A shared neural ensemble links distinct contextual memories encoded close in time. *Nature*, *534*(7605), 115–118. https://doi.org/10.1038/nature17955

Chen, G., Taylor, P. A., & Cox, R. W. (2017). Is the statistic value all we should care about in neuroimaging? *NeuroImage*, *147*, 952–959. https://doi.org/10.1016/j.neuroimage.2016.09.066

Clewett, D., & Davachi, L. (2017). The ebb and flow of experience determines the temporal structure of memory. *Current Opinion in Behavioral Sciences*, *17*, 186–193. https://doi.org/10.1016/j.cobeha.2017.08.013

Coull, J. T., Vidal, F., Nazarian, B., & Macar, F. (2004). Functional anatomy of the attentional modulation of time estimation. *Science*, *303*(5663), 1506–1508.

Cox, R. W. (1996). AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research, an International Journal*, *29*(3), 162–173.

Cox, R. W. (2012). AFNI: What a long strange trip it's been. *NeuroImage*, *62*(2), 743–747.

Cox, R. W. (2018). Equitable thresholding and clustering. *BioRxiv*, 295931.

Cox, R. W. (2019). Equitable thresholding and clustering (ETAC): A novel method for fMRI clustering in AFNI. *Brain Connectivity*. https://doi.org/10.1089/brain.2019.0666

Diana, R. A., Yonelinas, A. P., & Ranganath, C. (2013). Parahippocampal cortex activation during context reinstatement predicts item recollection. *Journal of Experimental Psychology: General*, *142*(4), 1287–1297. https://doi.org/10.1037/a0034029

Dimsdale-Zucker, H. R., Ritchey, M., Ekstrom, A. D., Yonelinas, A. P., & Ranganath, C. (2018). CA1 and CA3 differentially support spontaneous retrieval of episodic contexts within human hippocampal subfields. *Nature Communications*, *9*(1), 1–8. https://doi.org/10.1038/s41467-017-02752-1

Doxey, C. R., & Kirwan, C. B. (2015). Structural and functional correlates of behavioral pattern separation in the hippocampus and medial temporal lobe. *Hippocampus*, *25*(4), 524–533.

DuBrow, S., & Davachi, L. (2014). Temporal memory is shaped by encoding stability and intervening item reactivation. *Journal of Neuroscience*, *34*(42), 13998–14005.

Eccles, J. C., Ito, M., & Szentágothai, J. (1967). The mossy fiber input into the cerebellar cortex and its inhibitory control by golgi cells. In *The cerebellum as a neuronal machine* (pp. 116–155). Springer.

Eichenbaum, H., Sauvage, M., Fortin, N., Komorowski, R., & Lipton, P. (2012). Towards a functional organization of episodic memory in the medial temporal lobe. *Neuroscience & Biobehavioral Reviews*, *36*(7), 1597–1608. https://doi.org/10.1016/j.neubiorev.2011.07.006

Eklund, A., Nichols, T. E., & Knutsson, H. (2016). Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates. *Proceedings of the National Academy of Sciences*, *113*(28), 7900–7905. https://doi.org/10.1073/pnas.1602413113

El-Kalliny, M. M., Wittig, J. H., Sheehan, T. C., Sreekumar, V., Inati, S. K., & Zaghloul, K. A. (2019). Changing temporal context in human temporal lobe promotes memory of distinct episodes. *Nature Communications*, *10*(1), 1–10. https://doi.org/10.1038/s41467-018-08189-4

Euston, D. R., Gruber, A. J., & McNaughton, B. L. (2012). The role of medial prefrontal cortex in memory and decision making. *Neuron*, *76*(6), 1057–1070. https://doi.org/10.1016/j.neuron.2012.12.002

Ford, J. H., Verfaellie, M., & Giovanello, K. S. (2010). Neural correlates of familiarity-based associative retrieval. *Neuropsychologia*, *48*(10), 3019–3025. https://doi.org/10.1016/j.neuropsychologia.2010.06.010

Frankó, E., Insausti, A. M., Artacho-Pérula, E., Insausti, R., & Chavoix, C. (2014). Identification of the human medial temporal lobe regions on magnetic resonance images. *Human Brain Mapping*, *35*(1), 248–256. https://doi.org/10.1002/hbm.22170

Geib, B. R., Stanley, M. L., Dennis, N. A., Woldorff, M. G., & Cabeza, R. (2017). From hippocampus to whole-brain: The role of integrative processing in episodic memory retrieval. *Human Brain Mapping*, *38*(4), 2242–2259.

Gilbert, P. E., & Kesner, R. P. (2006). The role of the dorsal CA3 hippocampal subregion in spatial working memory and pattern separation. *Behavioural Brain Research*, *169*(1), 142–149.

Gilbert, P. E., Kesner, R. P., & DeCoteau, W. E. (1998). Memory for spatial location: Role of the hippocampus in mediating spatial pattern separation. *Journal of Neuroscience*, *18*(2), 804–810.

Gilbert, P. E., Kesner, R. P., & Lee, I. (2001). Dissociating hippocampal subregions: A double dissociation between dentate gyrus and CA1. *Hippocampus*, *11*(6), 626–636.

Gilmore, A. W., Nelson, S. M., & McDermott, K. B. (2015). A parietal memory network revealed by multiple MRI methods. *Trends in Cognitive Sciences*, *19*(9), 534–543. https://doi.org/10.1016/j.tics.2015.07.004

Giovanello, K. S., Keane, M. M., & Verfaellie, M. (2006). The contribution of familiarity to associative memory in amnesia. *Neuropsychologia*, *44*(10), 1859–1865. https://doi.org/10.1016/j.neuropsychologia.2006.03.004

Goebel, P. M., & Vincze, M. (2007). Implicit modeling of object topology with guidance from temporal view attention. *Proceedings of the International Cognitive Vision Workshop, ICVW*.

Gold, A. E., & Kesner, R. P. (2005). The role of the CA3 subregion of the dorsal hippocampus in spatial pattern completion in the rat. *Hippocampus*, *15*(6), 808–814.

Grady, C. L., & Ryan, J. D. (2017). Age-related differences in the human hippocampus: Behavioral, structural and functional measures. In *The Hippocampus from Cells to Systems* (pp. 167–208). Springer.

Hanczakowski, M., & Mazzoni, G. (2011). Both differences in encoding processes and monitoring at retrieval reduce false alarms when distinctive information is studied. *Memory*, *19*(3), 280–289.

Hao, X., Wang, X., Song, Y., Kong, X., & Liu, J. (2018). Dual roles of the hippocampus and intraparietal sulcus in network integration and segregation support scene recognition. *Brain Structure & Function*, *223*(3), 1473–1485. https://doi.org/10.1007/s00429-017-1564-2

Heys, J. G., & Dombeck, D. A. (2018). Evidence for a subcircuit in medial entorhinal cortex representing elapsed time during immobility. *Nature Neuroscience*, *21*(11), 1574–1582. https://doi.org/10.1038/s41593-018-0252-8

Howard, M. W., & Eichenbaum, H. (2013). The hippocampus, time, and memory across scales. *Journal of Experimental Psychology: General*, *142*(4), 1211.

Howard, M. W., MacDonald, C. J., Tiganj, Z., Shankar, K. H., Du, Q., Hasselmo, M. E., & Eichenbaum, H. (2014). A unified mathematical framework for coding time, space, and sequences in the hippocampal region. *Journal of Neuroscience*, *34*(13), 4692–4707.

Hsieh, L.-T., Gruber, M. J., Jenkins, L. J., & Ranganath, C. (2014). Hippocampal activity patterns carry information about objects in temporal context. *Neuron*, *81*(5), 1165–1178.

Huffman, D. J., & Stark, C. E. L. (2014). Multivariate pattern analysis of the human medial temporal lobe revealed representationally categorical cortex and representationally

agnostic hippocampus. *Hippocampus*, *24*(11), 1394–1403. https://doi.org/10.1002/hipo.22321

Hunsaker, M. R., & Kesner, R. P. (2013). The operation of pattern separation and pattern completion processes associated with different attributes or domains of memory. *Neuroscience & Biobehavioral Reviews*, *37*(1), 36–58.

Hunsaker, M. R., Rosenberg, J. S., & Kesner, R. P. (2008). The role of the dentate gyrus, CA3a, b, and CA3c for detecting spatial and environmental novelty. *Hippocampus*, *18*(10), 1064–1073.

Jenkins, L. J., & Ranganath, C. (2010). Prefrontal and medial temporal lobe activity at encoding predicts temporal context memory. *Journal of Neuroscience*, *30*(46), 15558–15565.

Jenkins, L. J., & Ranganath, C. (2016). Distinct neural mechanisms for remembering when an event occurred. *Hippocampus*, *26*(5), 554–559. https://doi.org/10.1002/hipo.22571

Jou, J., Flores, S., Cortes, H. M., & Leka, B. G. (2016). The effects of weak versus strong relational judgments on response bias in two-alternative-forced-choice recognition: Is the test criterion-free? *Acta Psychologica*, *167*, 30–44. https://doi.org/10.1016/j.actpsy.2016.03.014

Kesner, R. P. (2007a). A behavioral analysis of dentate gyrus function. *Progress in Brain Research*, *163*, 567–576.

Kesner, R. P. (2007b). Behavioral functions of the CA3 subregion of the hippocampus. *Learning & Memory*, *14*(11), 771–781.

Kesner, R. P., Gilbert, P. E., & Barua, L. A. (2002). The role of the hippocampus in memory for the temporal order of a sequence of odors. *Behavioral Neuroscience*, *116*(2), 286.

Kim, H. (2010). Dissociating the roles of the default-mode, dorsal, and ventral networks in episodic memory retrieval. *NeuroImage*, *50*(4), 1648–1657. https://doi.org/10.1016/j.neuroimage.2010.01.051

Kim, H. (2011). Neural activity that predicts subsequent memory and forgetting: A meta-analysis of 74 fMRI studies. *NeuroImage*, *54*(3), 2446–2461.

Kim, J., & Yassa, M. A. (2013). Assessing recollection and familiarity of similar lures in a behavioral pattern separation task. *Hippocampus*, *23*(4), 287–294.

Kirwan, C. B., Hartshorn, A., Stark, S. M., Goodrich-Hunsaker, N. J., Hopkins, R. O., & Stark, C. E. (2012). Pattern separation deficits following damage to the hippocampus. *Neuropsychologia*, *50*(10), 2408–2414.

Kirwan, C. B., & Stark, C. E. (2007). Overcoming interference: An fMRI investigation of pattern separation in the medial temporal lobe. *Learn Mem*, *14*. https://doi.org/10.1101/lm.663507

Kitamura, T., Pignatelli, M., Suh, J., Kohara, K., Yoshiki, A., Abe, K., & Tonegawa, S. (2014). Island cells control temporal association memory. *Science*, *343*(6173), 896–901. https://doi.org/10.1126/science.1244634

Kraus, B. J., Brandon, M. P., Robinson, R. J., Connerney, M. A., Hasselmo, M. E., & Eichenbaum, H. (2015). During running in place, grid cells integrate elapsed time and distance run. *Neuron*, *88*(3), 578–589. https://doi.org/10.1016/j.neuron.2015.09.031

Kubota, Y., Toichi, M., Shimizu, M., Mason, R. A., Findling, R. L., Yamamoto, K., & Calabrese, J. R. (2006). Prefrontal hemodynamic activity predicts false memory—A near-infrared spectroscopy study. *Neuroimage*, *31*(4), 1783–1789.

Lacy, J. W., Yassa, M. A., Stark, S. M., Muftuler, L. T., & Stark, C. E. (2011). Distinct pattern separation related transfer functions in human CA3/dentate and CA1 revealed using high-resolution fMRI and variable mnemonic similarity. *Learning & Memory*, *18*(1), 15–18.

Lancaster, J. L., Laird, A. R., Eickhoff, S. B., Martinez, M. J., Fox, P. M., & Fox, P. T. (2012). Automated regional behavioral analysis for human brain images. *Frontiers in Neuroinformatics*, *6*, 23.

Leal, S. L., & Yassa, M. A. (2014). Effects of aging on mnemonic discrimination of emotional information. *Behavioral Neuroscience*, *128*(5), 539.

Leutgeb, J. K., Leutgeb, S., Moser, M.-B., & Moser, E. I. (2007). Pattern separation in the dentate gyrus and CA3 of the hippocampus. *Science*, *315*(5814), 961–966.

Li, X., Morgan, P. S., Ashburner, J., Smith, J., & Rorden, C. (2016). The first step for neuroimaging data analysis: DICOM to NIfTI conversion. *Journal of Neuroscience Methods*, *264*, 47–56.

Maass, A., Berron, D., Libby, L. A., Ranganath, C., & Düzel, E. (2015). Functional subregions of the human entorhinal cortex. *ELife*, *4*, e06426. https://doi.org/10.7554/eLife.06426

MacDonald, C. J., Lepage, K. Q., Eden, U. T., & Eichenbaum, H. (2011). Hippocampal "time cells" bridge the gap in memory for discontiguous events. *Neuron*, *71*(4), 737–749.

Mankin, E. A., Sparks, F. T., Slayyeh, B., Sutherland, R. J., Leutgeb, S., & Leutgeb, J. K. (2012). Neuronal code for extended time in the hippocampus. *Proceedings of the National Academy of Sciences*, *109*(47), 19462–19467. https://doi.org/10.1073/pnas.1214107109

Marr, D. (1969). A theory of cerebellar cortex. *The Journal of Physiology*, *202*(2), 437–470.

Marr, D. (1971). A theory of archicortical function. *Proc R Soc Lond B Biol Sci*, *262*, 23–81.

Marshall, A. C., Cooper, N. R., & Geeraert, N. (2016). The impact of experienced stress on aged spatial discrimination: Cortical overreliance as a result of hippocampal impairment. *Hippocampus*, *26*(3), 329–340.

Mayes, A., Montaldi, D., & Migo, E. (2007). Associative memory and the medial temporal lobes. *Trends in Cognitive Sciences*, *11*(3), 126–135. https://doi.org/10.1016/j.tics.2006.12.003

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: A network model of insula function. *Brain Structure and Function*, *214*(5–6), 655–667.

Montchal, M. E., Reagh, Z. M., & Yassa, M. A. (2019). Precise temporal memories are supported by the lateral entorhinal cortex in humans. *Nature Neuroscience*, 1.

Moritz, S., Gläscher, J., Sommer, T., Büchel, C., & Braus, D. F. (2006). Neural correlates of memory confidence. *Neuroimage*, *33*(4), 1188–1193.

Mueller, S. G., Chao, L. L., Berman, B., & Weiner, M. W. (2011). Evidence for functional specialization of hippocampal subfields detected by MR subfield volumetry on high resolution images at 4T. *NeuroImage*, *56*(3), 851–857.

Naya, Y., Chen, H., Yang, C., & Suzuki, W. A. (2017). Contributions of primate prefrontal cortex and medial temporal lobe to temporal-order memory. *Proceedings of the National Academy of Sciences*, *114*(51), 13555–13560. https://doi.org/10.1073/pnas.1712711114

Okado, Y., & Stark, C. E. (2005). Neural activity during encoding predicts false memories created by misinformation. *Learning & Memory*, *12*(1), 3–11.

Olsen, R. K., Nichols, E. A., Chen, J., Hunt, J. F., Glover, G. H., Gabrieli, J. D. E., & Wagner, A. D. (2009). Performance-related sustained and anticipatory activity in human medial

temporal lobe during delayed match-to-sample. *Journal of Neuroscience*, *29*(38), 11880–11890. https://doi.org/10.1523/JNEUROSCI.2245-09.2009

Palombo, D. J., Reid, A. G., Thavabalasingam, S., Hunsberger, R., Lee, A. C. H., & Verfaellie, M. (2019). The human medial temporal lobe is necessary for remembering durations within a sequence of events but not durations of individual events. *Journal of Cognitive Neuroscience*, 1–11. https://doi.org/10.1162/jocn_a_01489

Pastalkova, E., Itskov, V., Amarasingham, A., & Buzsáki, G. (2008). Internally generated cell assembly sequences in the rat hippocampus. *Science (New York, N.Y.)*, *321*(5894), 1322–1327. https://doi.org/10.1126/science.1159775

Philippi, C. L., Tranel, D., Duff, M., & Rudrauf, D. (2015). Damage to the default mode network disrupts autobiographical memory retrieval. *Social Cognitive and Affective Neuroscience*, *10*(3), 318–326. https://doi.org/10.1093/scan/nsu070

Phillips, J. S., Velanova, K., Wolk, D. A., & Wheeler, M. E. (2009). Left posterior parietal cortex participates in both task preparation and episodic retrieval. *NeuroImage*, *46*(4), 1209–1221. https://doi.org/10.1016/j.neuroimage.2009.02.044

Pidgeon, L. M., & Morcom, A. M. (2016). Cortical pattern separation and item-specific memory encoding. *Neuropsychologia*, *85*, 256–271.

PsychoPy v2.0. (n.d.). Retrieved January 31, 2019, from https://www.psychopy.org/

Qin, S., Duan, X., Supekar, K., Chen, H., Chen, T., & Menon, V. (2016). Large-scale intrinsic functional network organization along the long axis of the human medial temporal lobe. *Brain Structure and Function*, *221*(6), 3237–3258. https://doi.org/10.1007/s00429-015-1098-4

Radua, J., Del Pozo, N. O., Gomez, J., Guillen-Grima, F., & Ortuno, F. (2014). Meta-analysis of functional neuroimaging studies indicates that an increase of cognitive difficulty during executive tasks engages brain regions associated with time perception. *Neuropsychologia*, *58*, 14–22. https://doi.org/10.1016/j.neuropsychologia.2014.03.016

Reagh, Z. M., Ho, H. D., Leal, S. L., Noche, J. A., Chun, A., Murray, E. A., & Yassa, M. A. (2016). Greater loss of object than spatial mnemonic discrimination in aged adults. *Hippocampus*, *26*(4), 417–422.

Reagh, Z. M., Roberts, J. M., Ly, M., DiProspero, N., Murray, E., & Yassa, M. A. (2014). Spatial discrimination deficits as a function of mnemonic interference in aged adults with and without memory impairment. *Hippocampus*, *24*(3), 303–314.

Reagh, Z. M., & Yassa, M. A. (2014). Object and spatial mnemonic interference differentially engage lateral and medial entorhinal cortex in humans. *Proceedings of the National Academy of Sciences*, *111*(40), E4264–E4273.

Roberts, J. M., Ly, M., Murray, E., & Yassa, M. A. (2014). Temporal discrimination deficits as a function of lag interference in older adults. *Hippocampus*, *24*(10), 1189–1196.

Robinson, N. T. M., Priestley, J. B., Rueckemann, J. W., Garcia, A. D., Smeglin, V. A., Marino, F. A., & Eichenbaum, H. (2017). Medial entorhinal cortex selectively supports temporal coding by hippocampal neurons. *Neuron*, *94*(3), 677-688.e6. https://doi.org/10.1016/j.neuron.2017.04.003

Rockland, K. S., & Van Hoesen, G. W. (1999). Some temporal and parietal cortical connections converge in CA1 of the primate hippocampus. *Cerebral Cortex*, *9*(3), 232–237. https://doi.org/10.1093/cercor/9.3.232

Rolls, E. T. (1989). Functions of neuronal networks in the hippocampus and neocortex in memory. In *Neural models of plasticity* (pp. 240–265). Elsevier.

Rolls, E. T. (1991). Functions of the primate hippocampus in spatial and nonspatial memory. *Hippocampus*, *1*(3), 258–261.

Rolls, E. T. (1996). A theory of hippocampal function in memory. *Hippocampus*, *6*(6), 601–620.

Rolls, E. T. (2010). A computational theory of episodic memory formation in the hippocampus. *Behavioural Brain Research*, *215*(2), 180–196.

Rolls, E. T. (2013). The mechanisms for pattern completion and pattern separation in the hippocampus. *Frontiers in Systems Neuroscience*, *7*.

Rolls, E. T., & Kesner, R. P. (2016). *Pattern separation and pattern completion in the hippocampal system. Introduction to the Special Issue*. Elsevier.

Rolls, E. T., & Treves, A. (1994). Neural networks in the brain involved in memory and recall. In *Progress in brain research* (Vol. 102, pp. 335–341). Elsevier.

Rumelhart, D. E., Hinton, G. E., & Williams, R. J. (1986). Learning representations by back-propagating errors. *Nature*, *323*(6088), 533.

Salz, D. M., Tiganj, Z., Khasnabish, S., Kohley, A., Sheehan, D., Howard, M. W., & Eichenbaum, H. (2016). Time cells in hippocampal area CA3. *Journal of Neuroscience*, *36*(28), 7476–7484. https://doi.org/10.1523/JNEUROSCI.0087-16.2016

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.

Schröder, T. N., Haak, K. V., Zaragoza Jimenez, N. I., Beckmann, C. F., & Doeller, C. F. (2015). Functional topography of the human entorhinal cortex. *ELife*, *4*, e06738. https://doi.org/10.7554/eLife.06738

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., Kenna, H., Reiss, A. L., & Greicius, M. D. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *Journal of Neuroscience*, *27*(9), 2349–2356. https://doi.org/10.1523/JNEUROSCI.5587-06.2007

Sestieri, C., Corbetta, M., Romani, G. L., & Shulman, G. L. (2011). Episodic memory retrieval, parietal cortex, and the default mode network: Functional and topographic analyses. *Journal of Neuroscience*, *31*(12), 4407–4420. https://doi.org/10.1523/JNEUROSCI.3335-10.2011

Sheppard, D. P., Graves, L. V., Holden, H. M., Delano-Wood, L., Bondi, M. W., & Gilbert, P. E. (2016). Spatial pattern separation differences in older adult carriers and non-carriers for the apolipoprotein E epsilon 4 allele. *Neurobiology of Learning and Memory*, *129*, 113–119.

Shirer, W. R., Ryali, S., Rykhlevskaia, E., Menon, V., & Greicius, M. D. (2012). Decoding subject-driven cognitive states with whole-brain connectivity patterns. *Cerebral Cortex*, *22*(1), 158–165. https://doi.org/10.1093/cercor/bhr099

Shrager, Y., Kirwan, C. B., & Squire, L. R. (2008). Activity in both hippocampus and perirhinal cortex predicts the memory strength of subsequently remembered information. *Neuron*, *59*(4), 547–553.

Small, S. A., Schobel, S. A., Buxton, R. B., Witter, M. P., & Barnes, C. A. (2011). A pathophysiological framework of hippocampal dysfunction in ageing and disease. *Nature Reviews Neuroscience*, *12*(10), 585–601.

Staresina, B. P., & Davachi, L. (2009). Mind the gap: Binding experiences across space and time in the human hippocampus. *Neuron*, *63*(2), 267–276.

Stark, S. M., Kirwan, C. B., & Stark, C. E. L. (2019). Mnemonic similarity task: A tool for assessing hippocampal integrity. *Trends in Cognitive Sciences*, *23*(11), 938–951. https://doi.org/10.1016/j.tics.2019.08.003

Stark, S. M., Yassa, M. A., Lacy, J. W., & Stark, C. E. (2013). A task to assess behavioral pattern separation (BPS) in humans: Data from healthy aging and mild cognitive impairment. *Neuropsychologia*, *51*(12), 2442–2449.

Steemers, B., Vicente-Grabovetsky, A., Barry, C., Smulders, P., Schröder, T. N., Burgess, N., & Doeller, C. F. (2016). Hippocampal attractor dynamics predict memory-based decision making. *Current Biology*, *26*(13), 1750–1757.

Strange, B. A., Witter, M. P., Lein, E. S., & Moser, E. I. (2014). Functional organization of the hippocampal longitudinal axis. *Nature Reviews. Neuroscience*, *15*(10), 655–669. https://doi.org/10.1038/nrn3785

Sugar, J., & Moser, M.-B. (2019). Episodic memory: Neuronal codes for what, where, and when. *Hippocampus*, *29*(12), 1190–1205. https://doi.org/10.1002/hipo.23132

Suh, J., Rivest, A. J., Nakashiba, T., Tominaga, T., & Tonegawa, S. (2011). Entorhinal cortex layer III input to the hippocampus is crucial for temporal association memory. *Science*, *334*(6061), 1415–1420. https://doi.org/10.1126/science.1210125

Suzuki, C., Tsukiura, T., Mochizuki-Kawai, H., Shigemune, Y., & Iijima, T. (2009). Prefrontal and medial temporal contributions to episodic memory-based reasoning. *Neuroscience Research*, *63*(3), 177–183. https://doi.org/10.1016/j.neures.2008.11.010

Suzuki, W. A., & Naya, Y. (2014). The perirhinal cortex. *Annual Review of Neuroscience*, *37*, 39–53. https://doi.org/10.1146/annurev-neuro-071013-014207

Thavabalasingam, S., O'Neil, E. B., & Lee, A. C. (2018). Multivoxel pattern similarity suggests the integration of temporal duration in hippocampal event sequence representations. *NeuroImage*, *178*, 136–146.

Thierry, A.-M., Gioanni, Y., Dégénétais, E., & Glowinski, J. (2000). Hippocampo-prefrontal cortex pathway: Anatomical and electrophysiological characteristics. *Hippocampus*, *10*(4), 411–419.

Treves, A., & Rolls, E. T. (1992). Computational constraints suggest the need for two distinct input systems to the hippocampal CA3 network. *Hippocampus*, *2*(2), 189–199.

Treves, A., & Rolls, E. T. (1994). Computational analysis of the role of the hippocampus in memory. *Hippocampus*, *4*. https://doi.org/10.1002/hipo.450040319

Tustison, N. J., Cook, P. A., Klein, A., Song, G., Das, S. R., Duda, J. T., Kandel, B. M., van Strien, N., Stone, J. R., Gee, J. C., & Avants, B. B. (2014). Large-scale evaluation of ANTs and FreeSurfer cortical thickness measurements. *NeuroImage*, *99*(0), 166–179. http://dx.doi.org/10.1016/j.neuroimage.2014.05.044

Uncapher, M. R., & Wagner, A. D. (2009). Posterior parietal cortex and episodic encoding: Insights from fMRI subsequent memory effects and dual-attention theory. *Neurobiology of Learning and Memory*, *91*(2), 139–154.

van den Honert, R. N., McCarthy, G., & Johnson, M. K. (2016). Reactivation during encoding supports the later discrimination of similar episodic memories. *Hippocampus*, *26*(9), 1168–1178.

Wais, P. E., Jahanikia, S., Steiner, D., Stark, C. E. L., & Gazzaley, A. (2017). Retrieval of high-fidelity memory arises from distributed cortical networks. *NeuroImage*, *149*, 178–189. https://doi.org/10.1016/j.neuroimage.2017.01.062

Wang, F., & Diana, R. A. (2017). Neural correlates of temporal context retrieval for abstract scrambled phrases: Reducing narrative and familiarity-based strategies. *Brain Research*, *1655*, 128–137.

Wang, H., Suh, J. W., Das, S. R., Pluta, J., Craige, C., & Yushkevich, P. A. (2013). Multi-atlas segmentation with joint label fusion. *IEEE Transactions on Pattern Analysis and Machine Intelligence*, *35*(3), 611–623. https://doi.org/10.1109/TPAMI.2012.143

Wang, Y., Romani, S., Lustig, B., Leonardo, A., & Pastalkova, E. (2015). Theta sequences are essential for internally generated hippocampal firing fields. *Nature Neuroscience*, *18*(2), 282–288. https://doi.org/10.1038/nn.3904

Wickelgren, W. A. (1968). Unidimensional strength theory and component analysis of noise in absolute and comparative judgments. *Journal of Mathematical Psychology*, *5*(1), 102–122.

Wickens, T. D. (2002). *Elementary signal detection theory*. Oxford University Press, USA.

Wigström, H. (1977). Spatial propagation of associations in a cortex-like neural network model. *Journal of Neuroscience Research*, *3*(4), 301–319.

Yassa, M. A., & Stark, C. E. (2011). Pattern separation in the hippocampus. *Trends in Neurosciences*, *34*(10), 515–525. https://doi.org/10.1016/j.tins.2011.06.006

Yushkevich, P. A., Piven, J., Hazlett, H. C., Smith, R. G., Ho, S., Gee, J. C., & Gerig, G. (2006). User-guided 3D active contour segmentation of anatomical structures: Significantly improved efficiency and reliability. *Neuroimage*, *31*(3), 1116–1128.

Yushkevich, P. A., Pluta, J. B., Wang, H., Xie, L., Ding, S.-L., Gertje, E. C., Mancuso, L., Kliot, D., Das, S. R., & Wolk, D. A. (2015). Automated volumetry and regional thickness analysis of hippocampal subfields and medial temporal cortical structures in mild

cognitive impairment. *Human Brain Mapping*, *36*(1), 258–287.

https://doi.org/10.1002/hbm.22627