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Review article

Integration and differentiation of hippocampal memory traces

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ABSTRACT

Prevailing theories of hippocampal function argue that memories are rapidly encoded by non-overlapping memory traces. Concurrently, the hippocampus has been argued to integrate across related experiences, enabling generalization. The cognitive neuroscience of memory has been transformed by the recent proliferation of studies using pattern similarity analyses to investigate the neural substrates of memory in humans, marking an exciting and significant advance in our understanding of population-level neural representations. We provide an overview of hippocampal pattern similarity studies published to date. By considering the effects of stimulus type, time-scale, and hippocampal subregions, we account for both increases and decreases in representational similarity. We argue that hippocampal representations for related memories are not fixed. Instead, the evoked representations are flexibly modulated, depending on whether the current goal is to extract generalities or to reinstate specific experiences. In the first comprehensive review of hippocampal pattern similarity analyses, we provide insight into the mechanisms of memory representation and implications for the interpretation of pattern similarity more generally.

considering hippocampal representations.

uncovering the representations corresponding to memories and de-

termining their relatedness. Both relative increases and decreases in hippocampal pattern similarity have been reported as behaviourally

relevant, leading to difficulties in characterizing how the hippocampus

represents related events in memory. In this paper, we aim to review

and reconcile these findings, to discuss what theories of hippocampal

function would predict about hippocampal similarity patterns, and to

argue for the importance of one's current behavioural goals when

sparse, separated patterns of activity to form memories rapidly and

reduce interference among them (Marr, 1971; McClelland et al., 1995;

O'Reilly et al., 2014; O'Reilly and Norman, 2002). In these models, the

neocortex complements the hippocampus by extracting generalities and

forming representations that abstract commonalities across memories.

A number of recent proposals, however, have suggested that the hip-

pocampus may also play a role in memory integration, forming links

between related memory traces (Horner et al., 2015; Kumaran et al.,

2016; Schapiro et al., 2017). To reconcile these views, several research

According to some models of memory, the hippocampus employs

1. Hippocampal pattern similarity as a measure of representational overlap

Efficient goal-directed behaviour in everyday situations depends on the flexible use of memories at different levels of representation. Depending on the situation, it can be beneficial to represent individual experiences as unique and specific (Richards and Frankland, 2017). After visiting a new city, it is useful to form distinct memories of the different events that took place (e.g., in Toronto, visiting the CN Tower vs. walking around Kensington market). At other times, it can be beneficial to integrate across multiple experiences, e.g. linking the memories of the CN Tower and Kensington market as events from the same visit to Toronto, and keeping these memories separate from the events from a different vacation in Philadelphia (Fig. 1A). It seems likely that both representations latently exist in parallel, but depending on the goal of one's current behaviour, only one of them is activated, or activated more strongly.

Over the past decade or so, researchers using functional magnetic resonance imaging (fMRI) have relied on pattern analyses as a way of

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Fig. 1. A) Example stimuli (e.g. events from a vacation) in two different contexts (e.g. two different cities). B) Within-stimulus similarity can be computed as the pattern overlap between two instances of the same stimulus (e.g., encoding and retrieval of the same experience or repeated presentations of the same stimulus). All models predict that the same experience should be reinstated at retrieval and produce above-baseline similarity between patterns at encoding and retrieval. A relative increase in within-stimulus similarity would be observed if the correlation between the encoding pattern and the retrieval pattern for a particular stimulus was greater than the correlation between the encoding pattern for a particular stimulus and retrieval patterns of all other stimuli. This panel only focuses on within-item similarity, but the off-diagonal could reflect an increase, decrease, or no change in similarity for repeated presentations of different stimuli. C) Patterns of across-stimulus similarity, produced by comparing the activity patterns for each stimulus to every other stimulus, often fall into three categories: i) integration, ii) orthogonalization, and iii) differentiation. i) Integration: Stimuli that share a context (e.g., events 1 and 2 which occurred in the same city) can display increased similarity relative to those that do not (e.g., events 1 and 3, or a study-specific baseline). Such similarity values would suggest that their representations are integrated due to shared features such as spatial, temporal, and/or emotional context. ii) Orthogonalization: Stimuli that share a context may also show no difference in similarity relative to stimuli that do not share a context. This finding would reflect no overlap between the neural populations recruited to represent each stimulus. iii) Differentiation: Stimuli that share a context may show decreased

pattern similarity relative to stimuli that do not share a context. This would suggest that the stimuli are represented not only as unrelated, but as differentiated. That is, voxels responding strongly to the first stimulus become less active for the second stimulus, and voxels responding weakly to the first stimulus become more active for the second stimulus. In all three cases, the predicted similarity between stimuli belonging to different contexts does not change, because no elements are shared.



Fig. 2. Segmentation of subfields along the anterior-posterior hippocampal axis in a representative participant. The inset images represent the corresponding coronal slices on a T2-weighted structural scan. The segmentation depicted here follows the OAP protocol (Olsen et al., 2013; Palombo et al., 2013; Yushkevich et al., 2015), with subfield definitions extended into the anterior hippocampal head. The subfields in the tail are not segmented into separate regions. Studies focusing on the hippocampal long axis typically divide the hippocampus into two segments (anterior vs. posterior to the uncal apex) or three segments (head/body/tail; see above), while those focusing on subfields tend to collapse across the long axis.

groups have suggested that hippocampal function may differ by subfield and/or along its long axis (Fig. 2), with specific subregions differentially contributing to more integrated or differentiated forms of memory. The anterior hippocampus and the cornu ammonis (CA) region 1 have both been proposed to play a role in forms of memory integration, whereas the posterior hippocampus and dentate gyrus (DG) have more consistently been suggested to support sparse and separated representations (Berron et al., 2016; Collin et al., 2017; De Shetler and Rissman, 2017; Duncan and Schlichting, 2018; Morton et al., 2017; Olsen et al., 2012; Poppenk et al., 2013; Robin and Moscovitch, 2017). Recent evidence from high-field fMRI suggests that memory integration can also be observed in CA3 (Grande et al., 2019).

If a brain area employs sparse, separated patterns, unrelated memories should have unrelated neural representations because their content has no (or minimal) overlap. Accordingly, patterns corresponding to individual experiences should be somewhat stable and differentiable from other experiences. Patterns present at encoding should, therefore, be recapitulated at retrieval of the same event, a phenomenon referred to as reinstatement (Fig. 1B). Sparse, orthogonal coding minimizes interference between memories and allows for the coding of specific, episodic memories, a hallmark of hippocampal function (Moscovitch et al., 2016; Tulving, 2002; Yonelinas, 2013). This leaves the question of what occurs when memories are related, sharing some common aspects. One possibility is that related memories may have even more dissimilar patterns than unrelated memories to maximally differentiate similar representations and minimize interference among shared features (Duncan and Schlichting, 2018; McClelland et al., 1995). In contrast, if a brain area is involved in extracting generalities across similar experiences, related memories should have common features in

their neural instantiation. Thus, memories featuring some overlapping content should also entail overlapping memory traces, and the patterns of neural activity corresponding to these memories should be similar to some degree. These competing possibilities entail very different interpretations of the role of the hippocampus in memory organization (Fig. 1C).

With the recent development of higher-resolution functional magnetic resonance imaging (fMRI) techniques, protocols for delineating the subfields of the hippocampus (Yushkevich et al., 2015), and techniques for analyzing trial-level multivariate patterns of voxel activity (Haxby, 2012; Haxby et al., 2001; Kriegeskorte and Kievit, 2013; Norman et al., 2006), the past decade has seen a proliferation of human neuroimaging studies examining hippocampal patterns of activity and questions of neural representation. While the term pattern separation typically refers to orthogonalization of representations at the neuronal level (McClelland et al., 1995; Santoro, 2013; Schapiro et al., 2017), the same logic has been applied to the differentiation of patterns at the level of voxels, as macro-scale pattern separation.

The assumption of pattern similarity analyses is that particular patterns of activity across voxels correspond to particular stimuli, shaped by the contexts in which they are embedded (Kriegeskorte et al., 2008; Kriegeskorte and Kievit, 2013). These contexts can be defined by many factors, including temporal and spatial features, perceptual features, goals, memory states, and others. Therefore, the degree of similarity between fMRI patterns corresponding to different stimuli should be informative about the underlying computations. We note that these types of analyses differ from univariate analyses, which focus on the degree of activation rather than the pattern of activation across a population of voxels.

While the present review is focused on the information carried in multi-voxel representations in the hippocampus, repetition suppression or fMRI adaptation is another method used to measure representational overlap. Repetition suppression relies on the reduction or plateauing of neural response following the second presentation of the same stimulus (Barron et al., 2016; Grill-Spector et al., 2006; Krekelberg et al., 2006; Larsson et al., 2015). This measure has been reviewed in detail previously (Barron et al., 2016). Pattern similarity measures and repetition suppression were found to be correlated (Drucker and Aguirre, 2009; Sapountzis et al., 2010), but it has been argued that measures of representational similarity are particularly well-suited for regions with columnar organization (Barron et al., 2016). Repetition suppression and pattern similarity analyses can therefore be thought of as complementary, but not interchangeable. Importantly, repetition suppression does not only operate at the level of single repeated stimuli but can also reveal overlapping neural codes for related stimuli, such as competing activated memories (Barron et al., 2013), non-spatial associative networks of stimuli (Garvert et al., 2017), and may operate at different timescales which reflect different cognitive processes (Epstein et al., 2008).

Studies where both repetition suppression and pattern similarity analyses were applied to the same dataset have revealed partial agreement but also evidence of dissociations between the two methods (Epstein and Morgan, 2012; Ward et al., 2013). Specifically, multivariate approaches are believed to reflect coarser topographical organization, whereas repetition suppression reflects the tuning of individual neurons or cortical columns (Drucker and Aguirre, 2009; Epstein and Morgan, 2012; Hatfield et al., 2016). In one of these studies, pattern similarity in several cortical regions across stimulus repetitions predicted subsequent explicit memory, whereas repetition suppression related to implicit repetition priming (Ward et al., 2013). These studies, however, did not focus on the hippocampus in ROIanalyses and found no evidence of hippocampal clusters in whole-volume searchlight analyses, highlighting the importance of direct comparisons between repetition suppression and pattern similarity analyses for hippocampus-dependent tasks.

terms of stimulus timing. The optimal gap between presentations of related stimuli should be relatively short to obtain a reliable measure of repetition suppression (Brozinsky et al., 2005; Henson et al., 2004), though see Poppenk et al., 2016; van Turennout et al., 2000; Van Turennout et al., 2003). In contrast, pattern similarity comparisons can be made for any pair of stimuli across the entire study and, in fact, greater temporal separation is recommended to enable better detection individual stimulus representations (Dimsdale-Zucker of and Ranganath, 2019; Popal et al., 2019). More studies are necessary to specifically compare hippocampal pattern similarity and repetition suppression measures to determine the degree of sensitivity and specificity offered by each.

fMRI studies comparing the multivariate patterns of hippocampal activity corresponding to different types of related and unrelated stimuli can thus answer the questions of whether, and where, patterns of voxel-level neural activity show signatures of memory differentiation and integration. Insights from these studies can help to resolve the competing, or perhaps complementary, views of the hippocampus playing a role in the differentiation and integration of memories. Here, we provide the first comprehensive review of the literature examining measures of hippocampal pattern similarity, and synthesize the evidence from these studies as it relates to notions of hippocampal integration and differentiation, based on the types of similarity and hippocampal subregions examined.³ In summary, we find evidence for both integration and differentiation of hippocampal patterns, and that the prevalence of each depends on such factors as task demands, the timescale of the comparisons, and hippocampal subregions. While these factors clearly play a role, we argue that disparities in findings may critically depend on whether integrated or differentiated representations were advantageous in a given experimental context, and propose that future studies should focus on parametrically modulating the degree of integration/differentiation necessary to complete a task successfully.

2. Which patterns are being compared and how is pattern overlap interpreted?

An important distinction that exists in studies of hippocampal activity patterns is whether patterns are compared across multiple instances of the same stimulus, or across multiple related, but different, stimuli (Fig. 1A). In this review, within-stimulus similarity refers to comparing the pattern of activity corresponding to a single stimulus at multiple instances, or across encoding and retrieval (Fig. 1B; red circles in Fig. 3). In contrast, across-stimulus similarity refers to comparing

³ Review procedure: To find papers pertaining to hippocampal pattern similarity, we searched the PubMed database in December 2018 using the search terms ["hippocampus" AND "similarity"] and ["hippocampus" and "dissimilarity"]. Initial searches yielded 711 papers. Two independent raters (I.B. and J.R.) screened these papers based on their titles and abstracts for empirical papers using human participants that employed pattern similarity analyses including the hippocampus. We included any papers identified as potentially relevant by either of the raters. This round of screening led to a list of 77 papers. We conducted a second round of screening based on full texts. We screened the papers for empirical studies employing human participants, fMRI methods, and multivariate voxel-wise pattern analyses featuring a hippocampal region of interest (ROI) or searchlight analyses that included the hippocampus. While many of the studies reviewed included analyses of pattern similarity (i.e. representational similarity analysis, RSA), others used multivariate classification techniques (i.e. multi-voxel pattern analysis, MVPA). In cases of MVPA, successful classification of an item or category suggests that the instances of this item/category had similar patterns, allowing for accurate classification, and therefore we interpret these results to mean higher similarity within successfully-classified categories. Based on the second round of screening, and the inclusion of additional papers found in the reference sections and subsequent searches (last updated in May 2020), our final list included 104 relevant papers (Fig. 3A).



Fig. 3. Dot matrix representing the A) total number of papers in each category and B) pattern similarity findings within each category. The majority of these papers reported an increase in pattern similarity between related stimuli relative to either unrelated stimuli or an otherwise-defined study-specific baseline. The half-circles represent papers in which findings were mixed (for example, some findings reflected no change in similarity and others reflected an increase).

patterns of activity corresponding to multiple stimuli, usually computed between distinct stimuli that share a common feature such as a shared context, semantic category or memory outcome (Fig. 1C; green circles in Fig. 3). Findings of increased pattern similarity have very different implications for theories of hippocampal function depending on whether a relative increase is found within or across stimuli (Fig. 3). Here, we use the term "stimulus" to refer to a single encounter (i.e. trial) with a distinct stimulus or event, but these may be complex and associative in nature, such as word-picture pairs, items in a spatial/temporal context, film clips, or everyday episodes. Thus, within-stimulus similarity may refer to multiple encoding instances of a word-picture association, a repeatedly navigated route, or an episodic event. Within-stimulus similarity is also frequently computed between encoding and retrieval of the same stimulus (Fig. 1B). In contrast, across-stimulus similarity may be computed between a class of stimuli associated with a common context, such as words or images associated with a shared spatial context, events within the same narrative context, or even across sets of remembered or forgotten stimuli (Fig. 1C).

It is important to note that throughout this review we interpret "similarity" in terms of assessing *relative* increases and decreases in similarity, rather than in terms of a comparison to a true numerical value of zero. In the case of across-stimulus comparisons, *increased* similarity, for example, would reflect greater similarity between stimuli belonging to a particular category, relative to those belonging to a different category. In the case of within-stimulus comparisons, *increased* similarity, for example, would reflect higher encoding-retrieval pattern similarity for remembered but not forgotten items. The observation of 'null' effects does not imply that the raw correlation between individual patterns is zero, but rather that the correlation between patterns of interest

does not differ between conditions. The range of raw similarity values also differs between experiments, but the interpretation of the relative values is the same across studies.

In each section, we provide a representative study to illustrate each type of finding.

3. Consistency of within-stimulus representations with repetition

A finding of increased similarity for repeated presentations of the same stimulus, relative to other stimuli, demonstrates that repeated instances of a single stimulus can be consistent in their hippocampal patterns of activity. This suggests that there are stable stimulus-specific representations in the hippocampus, and that these stimulus-specific patterns can be reinstated. The fact that reinstatement can be observed across multiple timepoints suggests that pattern differentiation is not so extreme that changing temporal context would lead to unrelated patterns of representation for the same item. The timescale at which patterns might be transformed or overwritten has been discussed previously (Frankland and Bontempi, 2005; Moscovitch et al., 2016; Richards and Frankland, 2017; Sekeres et al., 2018; Winocur and Moscovitch, 2011) and will not be a focus of the present review.

Several studies provide evidence for within-stimulus similarity in the hippocampus by demonstrating increased similarity between encoding and/or retrieval patterns corresponding to associations between images of objects and/or scenes (Alm et al., 2018; Backus et al., 2016; Jonker et al., 2018; Lee et al., 2018; Liang and Preston, 2017; Mack and Preston, 2016; Tompary et al., 2016; Tompary and Davachi, 2017) (Fig. 3B). One such representative study examined encoding-retrieval similarity object pairs, splitting them according to whether the entire pair was subsequently remembered or not (Tompary et al., 2016). The results suggested that subsequently remembered pairs had significantly higher within-stimulus (encoding-retrieval) similarity than forgotten ones. Interestingly, even single visually similar images of scenes evoked within-stimulus similarity making it possible to use brain activity patterns to correctly classify scenes judged by participants as identical to one another (Bonnici et al., 2012a,b). In separate studies, patterns evoked by individual scenes could reliably be differentiated (Fandakova et al., 2019) and participants' memory could be predicted by scenespecific encoding patterns (Lee et al., 2013). Other studies have shown evidence for increased hippocampal similarity between repeated instances of stimuli that include specific spatial and temporal contexts (Hassabis et al., 2009; Hsieh et al., 2014; Kalm et al., 2013; Kok and Turk-Browne, 2018; Libby et al., 2014; Thavabalasingam et al., 2018). Studies using more complex stimuli including film clips, person-sceneobject associations and real autobiographical memories also report increased within-stimulus similarity in the hippocampus (Bonnici et al., 2012c, 2013; Bonnici and Maguire, 2018; Chadwick et al., 2010, 2011; Oedekoven et al., 2017; St-Laurent et al., 2014, 2015; van den Honert et al., 2017).

Of the studies listed above, three reported correlations with behaviour (Fandakova et al., 2019; Thavabalasingam et al., 2018; Tompary et al., 2016). Greater within-stimulus pattern similarity was related to greater recall accuracy (Fandakova et al., 2019; Tompary et al., 2016), and memory for their duration and order (Thavabalasingam et al., 2018). In one study, correctly, but not incorrectly, recalled images were accurately classified (Liang and Preston, 2017). In several other studies, no correlations with behaviour were reported, but the representational similarity analyses were weighted by recall vividness (St-Laurent et al., 2014, 2015) or richness (Oedekoven et al., 2017).

Taken together, these studies support the notion of differentiated stimulus-level representations in the hippocampus that can be distinguished from one another based on higher similarity values for the same stimulus relative to other stimuli (see Fig. 1B). In the few studies to examine within-stimulus similarity in hippocampal subfields, similarity was found across multiple subfields including subiculum, CA1, and CA2/3/DG (Bonnici et al., 2012b; Bonnici et al., 2013; Tompary et al., 2016). It is noteworthy that most studies reporting within-stimulus similarity employed complex items, such as multi-element associations between visual stimuli, stimuli embedded within specific spatial/temporal contexts, and complex episodic events such as film clips or autobiographical memories. In contrast to the evidence reviewed above, one study showed that the first and second presentation of an object could be distinguished based on hippocampal patterns, suggesting that stimulus-level hippocampal representations may not be completely stable with repetition and that differentiation may occur at the level of unique encounters even with identical stimuli (Manelis et al., 2011). More research is needed to provide further evidence for this possibility.

Five studies reported no within-stimulus similarity in the hippocampus (Ferreira et al., 2019; Robin et al., 2018; Staresina et al., 2012; Wang et al., 2018; Xiao et al., 2017; Fig. 3B). Most of these studies used word cues to elicit memory for associations (with scenes, other words, or imagined events), raising the possibility that hippocampal reinstatement partly depends on stimulus type, with verbal cues les;s likely to show evidence for stimulus-level reinstatement. We note that by including the term *hippocampus* in the search methodology for this review, the papers reviewed may over-represent the number of positive hippocampal results, and under-represent the number of null findings of within-stimulus similarity in the hippocampus.

The majority of these findings suggest that unique stimuli and their features are maintained as distinct hippocampal representations. However, this does not necessarily constitute evidence as to whether stimulus-specific representations can be differentiated from one another. Evidence of within-stimulus similarity is not informative about how that stimulus is represented relative to other stimuli with shared content. If stimulus-level representations must be differentiable from other stimuli despite shared aspects, they should elicit *decreased* similarity values relative to stimuli with no shared aspects. In contrast, if stimulus-level representations are linked by virtue of shared content, we would expect *increased* similarity values when related stimuli are compared.

4. Flexibility of across-stimulus representations

When examining across-stimulus similarity, that is, patterns of representation corresponding to distinct but related stimuli, there are three possible predictions with different implications for hippocampal mechanisms (Fig. 1C). The simplest view to take when comparing across stimulus-level fMRI patterns is that they are a linear combination of their constituent parts. For example, if two events are paired with the same city (Fig. 1A), the two corresponding representations should both carry the same amount of 'city' information, and the remaining unexplained pattern corresponds to the specifics of each event. This process would produce increased similarity between stimulus-level representations, because each event-city pairing would require a representation only partially overlapping with other event-city pairings (integration). Such a finding would suggest that the hippocampus plays a role in representing the integration of distinct events by virtue of overlapping content. A second possibility is that that the specific eventcity bindings would correspond to new, independent representations, specific to only that particular event-city combination. Thus, distinct but related stimuli might have unrelated patterns of hippocampal representation, consistent with sparse coding (orthogonalization - no shared similarity). The third possibility is that related items have decreased similarity to one another compared with unrelated items, indicating not just a lack of a relationship between related stimuli but repulsion (differentiation; Duncan and Schlichting, 2018). Differentiated memory traces may facilitate the separation of related stimuli and reduce interference between them to promote learning of individual items. We review evidence for each of these three types of findings in turn and provide an illustrative example for each type.

4.1. Integrated representations: increased across-stimulus similarity

The majority of the papers in this review provided evidence for increased similarity between hippocampal patterns of activity for related stimuli (Fig. 3B). A major factor leading to across-stimulus similarity appeared to be common spatial content, including those in which stimuli were associated with a common spatial context, scene, location or direction in space (Kim et al., 2017; Kim and Maguire, 2018; Kyle et al., 2015a,b; Libby et al., 2014; Ritchey et al., 2015; Robin et al., 2018; Stokes et al., 2015; Sulpizio et al., 2014; Tompary and Davachi, 2017; Wagner et al., 2016; Xiao et al., 2017). Another common aspect was shared temporal context or temporal proximity of stimuli (Ezzvat and Davachi, 2014: Hsieh et al., 2014: Kyle et al., 2015a, b: Schapiro et al., 2012, 2016). Some studies reported that the unique combination of temporal and spatial context, or more complex forms of event or associative context, drove increased similarity between stimuli in memory (Deuker et al., 2016; Dimsdale-Zucker et al., 2018; Hannula et al., 2013; Jiang et al., 2015; Libby et al., 2019; Milivojevic et al., 2015, 2016; Nielson et al., 2015; Schlichting et al., 2015). These studies suggest that while the hippocampus may have unique patterns of activity corresponding to stimuli, those with shared content (especially temporal and spatial) have some overlap in their neural representation. Such findings support the conclusion that the hippocampus plays a role in representing forms of context in its patterns of neural activity.

Across-stimulus similarity in the hippocampus, however, is not limited to stimuli with a common spatial-temporal context. Several studies report evidence for increased hippocampal similarity between stimuli that share more abstract elements or processes, such as attentional state, reward status, or emotional state, relative to stimuli that do not (2016a; Cordova et al., 2019; Mack et al., 2016; Wagner et al., 2020; Wolosin et al., 2013; Zeithamova et al., 2018) (Fig. 3B). In one such representative study, participants viewed paintings and were instructed to pay attention to either the room the painting was in or the art style of the painting (Aly and Turk-Browne, 2016a). Higher hippocampal pattern similarity was observed for paintings encoded in the same attentional state, relative to those encoded in different attentional states. These results suggest that similar contexts, even those determined purely by the current experimental task, drive similarity between otherwise equally related stimuli (paintings). In addition, there is evidence from a number of studies that items with a common memory outcome (e.g. recollected vs. familiar, remembered vs. forgotten, high vs. low vividness) have increased across-item similarity (Dandolo and Schwabe, 2018; Doxey et al., 2018; Kirwan et al., 2014; Kragel and Polyn, 2016; Rissman et al., 2016; Schlichting et al., 2014; Thakral et al., 2020; Uncapher et al., 2015; van den Honert et al., 2016; van Dongen et al., 2016; Wagner et al., 2016). These results in particular seem to be at odds with studies reported above showing decreased similarity between related items over the course of learning, an issue to which we will return below. Finally, a number of studies also report that stimuli with common semantic and visual features show increased similarity of hippocampal patterns (Blumenthal et al., 2018; Boccia et al., 2019; Huffman and Stark, 2014; Kuhl et al., 2012; Liang et al., 2012; Wagner et al., 2016; Xiao et al., 2016), suggesting that even properties of solitary stimuli might lead to similarities in the hippocampal neural representations corresponding to those stimuli.

Of the papers reporting increased across-stimulus similarity, eight reported correlations showing that behavioural performance scaled with the extent of pattern similarity (Alm et al., 2018; Aly and Turk-Browne, 2016a; Hsieh et al., 2014; Kyle et al., 2015b; Libby et al., 2014; Schlichting et al., 2014; Wolosin et al., 2013; Zeithamova et al., 2018). For example, greater pattern similarity was associated with sequence memory (Hsieh et al., 2014), the ability to recall competing spatial contexts (Kyle et al., 2015b), recognition of stimuli bound to different contexts (Libby et al., 2014) or associates (Schlichting et al., 2014), reward value (Wolosin et al., 2013; Zeithamova et al., 2018), and the ability to retrieve task features accurately depending on attentional state (Aly and Turk-Browne, 2016a). Interestingly, one study reported a benefit of similarity during delayed retrieval, but *diss*imilarity during encoding, suggesting that different mnemonic demands may differentially benefit from pattern (dis-)similarity (Alm et al., 2018). Another study reported that only memories successfully retrieved after a delay showed a significant *negative* relationship between stimulus-specific encoding-retrieval similarity and similarity among stimuli at retrieval (Tompary and Davachi, 2017). Several other studies reported results split according to categorical behavioural measures, again consistently highlighting an effect of higher pattern similarity. Stimuli judged as closer together in time tended to have higher pattern similarity (Deuker et al., 2016; Ezzyat and Davachi, 2014; Kyle et al., 2015b; Nielson et al., 2015; Schapiro et al., 2013), although in one case, stimuli judged as close in space were found to have lower pattern similarity (Kyle et al., 2015a).

Evidence pertaining to subfield specificity for across-stimulus similarity is mixed, but broadly consistent with a role for CA1 in integration. Several of the studies examining hippocampal subfields found comparable increases in pattern similarity in all subfields (Aly and Turk-Browne, 2016b; Schapiro et al., 2016; Wolosin et al., 2013). One study reported more distinctive coding for different spatial environments in CA3/DG compared to CA1 (Kyle et al., 2015a). Three studies investigating navigation in 3D virtual environments reported that the subiculum specifically coded for similar heading directions (Chadwick et al., 2015; Kim and Maguire, 2018; Shine et al., 2019), and in one case, the amount of heading information in the entorhinal-subicular region related to participants' performance (Chadwick et al., 2015). The CA1 was implicated in integrating across unrelated stimuli linked by a common stimulus (Schlichting et al., 2014), consistent with its proposed role in comparing current inputs with stored, related representations (Chen et al., 2015; Duncan et al., 2012; Olsen et al., 2012). Another study found increased similarity in CA1 and subiculum when participants compared temporal relations compared to a non-relational task (Cordova et al., 2019), suggesting these regions may be involved preferentially in coding temporal information. Because relatively few studies have sufficient spatial resolution to examine subfields, and because many studies collapse across DG, CA2 and CA3, future high-resolution investigations are needed to resolve the conditions under which similar vs. dissimilar coding in hippocampal subfields can be observed.

The majority of studies examining the hippocampal long axis provide evidence of pattern similarity in the anterior, compared to the posterior hippocampus, consistent with the notion that the anterior hippocampus represents global contexts and integrates across individual stimuli. Anterior hippocampal patterns tended to be more similar for stimuli with shared spatial contexts than those with nonshared contexts (Hannula et al., 2013; Kim et al., 2017; Libby et al., 2014, 2019; Ritchey et al., 2015; Wagner et al., 2016). More broadly, the anterior hippocampus represented spatiotemporal distances between items or events (Deuker et al., 2016; Nielson et al., 2015), even conceptual distances based on abstract dimensions, and was also found to represent the updating of conceptual knowledge and formation of associations (Mack et al., 2016; Schlichting et al., 2015; Theves et al., 2019). One study found evidence for representation of more abstract, integrative associations in the anterior hippocampus, and simpler associations in the posterior hippocampus (Collin et al., 2015). Interestingly, the opposite pattern has also been reported in two studies which found greater similarity for stimuli with shared spatial contexts in the posterior, relative to anterior, hippocampus (Robin et al., 2018; Tompary and Davachi, 2017). One study also reported greater similarity for exemplars from the same category in the posterior, relative to anterior, hippocampus (Dandolo and Schwabe, 2018).

Recent studies have leveraged the observation that similar clusters in the brain represent stimuli in a similar manner across participants to derive *across-participant* measures of representational similarity. Such approaches include inter-subject alignment based on representational and functional connectivity patterns (Conroy et al., 2013; Guntupalli et al., 2016; Haxby et al., 2011; Koch et al., 2020). Across-participant representations were found to be aligned while participants followed the same narrative (Hasson, 2004; Hasson et al., 2010) and even when they recalled it (Chen et al., 2017; Heusser et al., 2018). This correspondence in evoked patterns was found to be schema-dependent in the medial prefrontal cortex (Baldassano et al., 2018) and segmented by event boundaries (Baldassano et al., 2017). Interestingly, none of these studies reported evidence of across-participant pattern similarity in the hippocampus, but rather in a network of regions consisting of the medial prefrontal and posterior cingulate cortices. The absence of such a hippocampal effect suggests that hippocampal codes are participantunique, and shared experience may be dependent on cortical modulation, activation of schemas, and anticipation of upcoming events. It may also be that due to the nature of the method, which has relied exclusively on temporally-extended, naturalistic stimuli, hippocampal contributions are less crucial (Zuo et al., 2020), compared to explicit encoding and retrieval. From a methodological standpoint, it is also worth noting that the medial temporal lobes, especially anterior and ventral aspects, tend to have lower signal-to-noise ratio than many cortical regions. Segmenting the hippocampus into subfields results in further signal reduction (Hrybouski et al., 2019; Nau, 2020). The resulting increase in noise may obscure any effects that might otherwise be present in the hippocampus. However, signal could be boosted by only averaging over regions that respond similarly - if subfield-specific effects are present, averaging across the entire hippocampus could reduce signals associated with effects of interest.

4.2. Orthogonal representations: no difference in across-stimulus similarity

In contrast to the studies reviewed above, a number of studies reported no difference in similarity between related stimuli relative to unrelated stimuli, or chance-level classification (Ferreira et al., 2019; Huffman and Stark, 2017; Kafkas et al., 2017; Kluen et al., 2019; LaRocque et al., 2013; Lee et al., 2018; Liuzzi et al., 2019; Martin et al., 2013; Morgan et al., 2011; Raykov et al., 2020; Ren et al., 2020; Robin et al., 2018; Senoussi et al., 2016; van den Honert et al., 2017) (Fig. 3B, open green circles). Many of these studies involved classification of visual/semantic categories of images, including faces, objects, and scenes, and failed to find reliable differentiation of these categories based on hippocampal patterns of activity. This pattern of hippocampal results often contrasts with findings from nearby neocortical regions which show stimulus specificity (Liang et al., 2012; LaRocque et al., 2013; Martin et al., 2013). Despite not finding any changes in representational similarity overall, one study reported a significant negative correlation between memory for individual faces, scenes, and objects and representational overlap in the hippocampus, suggesting that lower similarity was beneficial to memory for individual stimuli (LaRocque et al., 2013).

While it is difficult to draw conclusions based on null findings, this lack of similarity between categories of stimuli is predicted by pattern separation accounts of hippocampal function. If related items are encoded by sparse, differentiated patterns of activity, we predict no increase in similarity between two exemplars of a given category (e.g. two human faces) compared with exemplars from different categories (e.g. a face and an object). A representative example of this pattern of findings was observed in a study which reported no difference in hippocampal similarity between stimuli belonging to the same category, relative to those belonging to different categories (LaRocque et al., 2013). Despite the null effect of category overall, however, greater dissimilarity between a particular stimulus and other stimuli in the same category was predictive of better memory. These results support the notion that hippocampal representations are orthogonal, and that greater differentiation may support the ability to recall them. An alternative interpretation is that the hippocampus is not sensitive to these categories of stimuli, and therefore does not have discernible representations at the stimulus or category level. Again, we note that our search procedure likely underrepresented the number of studies with null findings in the hippocampus so we highlight the studies above as a sample of studies demonstrating a lack of similarity between representations in the hippocampus.

4.3. Differentiated representations: decreased across-stimulus similarity

Finally, a number of papers have also demonstrated decreased similarity between related stimuli in the hippocampus, consistent with a differentiation account of hippocampal patterns (Berens et al., 2018; Chanales et al., 2017; Copara et al., 2014; Dimsdale-Zucker et al., 2018; Ezzvat et al., 2018: Favila et al., 2016: Hulbert and Norman, 2014: Jenkins and Ranganath, 2016; Koolschijn et al., 2019; Kyle et al., 2015b; LaRocque et al., 2013; Schlichting et al., 2015; Wing et al., 2020) (Fig. 3B, darker green circles). The majority of studies showing a relative decrease in similarity involved stimuli with large degrees of overlap in content or context. These studies included stimuli that share temporal or spatial context such as overlapping routes, room sequences, or object sequences, all showing decreased representational similarity compared to unrelated stimuli (Chanales et al., 2017; Dimsdale-Zucker et al., 2018; Jenkins and Ranganath, 2016; Kyle et al., 2015a). Even more abstract sets of related associations, such as multiple objects with overlapping associations, have shown decreased similarity relative to baseline measures (Ezzyat et al., 2018; Favila et al., 2016; Hulbert and Norman, 2014; LaRocque et al., 2013; Schlichting et al., 2015). Studies reported that participants with greater learning-related pattern differentiation showed greater improvements in behavioural discrimination (Hulbert and Norman, 2014), and another study showed a similar nonsignificant trend at delayed recall (Ezzyat et al., 2018). Three studies also provided evidence that pattern dissimilarity predicted memory for event order (Jenkins and Ranganath, 2016), knowledge structure (Koolschijn et al., 2019) and model-weighted novel learning (Berens et al., 2018).

This collection of results suggests that learning stimuli with a high degree of overlap in their episodic content and context leads to differentiation of neural patterns in the hippocampus. Several of these studies reported an increase in pattern differentiation over time, including reconfiguration related to changes in the learned relational structure (Koolschijn et al., 2019), overnight (Ezzyat et al., 2018), and over the course of learning (Berens et al., 2018; Chanales et al., 2017; Favila et al., 2016; Hulbert and Norman, 2014). In one such representative study, experimenters used pairs of similar scenes. The scenes belonging to each pair were then presented to participants alongside the same face, or different faces. After learning these associations, hippocampal patterns for scenes paired with the same face were significantly less similar to one another, relative to those for scenes paired with different faces (Favila et al., 2016). This evidence further supports the notion that hippocampal dissimilarity is related to learning and reducing interference between related stimuli. In the three studies in this subset that examined hippocampal subfields, all found evidence for differentiation in regions including CA2/3/DG (Copara et al., 2014; Dimsdale-Zucker et al., 2018; Kyle et al., 2015b), though in one study the cluster of interest also overlapped with the subiculum and CA1 (Kyle et al., 2015b). These findings are consistent with a specialized role for DG in pattern separation, as predicted by anatomical models. In some cases, both relative decreases and increases in similarity can be observed, depending on the subfield. For example, one study found that stimuli with shared spatial context were represented more similarly in CA1, but were differentiated in CA2/3/DG (Dimsdale-Zucker et al., 2018).

Few studies have systematically examined hippocampal pattern differentiation along its anteroposterior axis. One study reported that both same-day and overnight pattern differentiation was greater in the anterior, compared to the posterior hippocampus (Ezzyat et al., 2018). Another study reported a significant decrease in pattern similarity after

participants connected previously unrelated story elements in the posterior, but not anterior, hippocampus (Milivojevic et al., 2015). Two studies using searchlight analyses investigating learning-related pattern differentiation found posterior hippocampal clusters (Berens et al., 2018; Schlichting et al., 2015). While the evidence is still preliminary, these studies suggest that the posterior hippocampus shows a lower degree of similarity between related items relative to the anterior hippocampus. The conditions under which anterior vs. posterior hippocampal representations diverge should continue to be investigated in future experiments.

5. Reconciling pattern similarity findings

The evidence compiled here suggests that perceiving and remembering related items can result in both higher and lower hippocampal pattern similarity. While task-specific aspects and different hippocampal subregions undoubtedly contributed to the variability in results, it is possible that integrated/differentiated representations could be uncovered in the same studies if different behavioural outcomes were optimal. When examining within-stimulus similarity values, a clear pattern of findings emerged: most of the studies we examined found evidence for the reinstatement of encoding patterns associated with specific stimuli at retrieval. Similarity values for the same item at encoding vs. retrieval tended to be significantly greater than the similarity between the same item at encoding vs. other items at retrieval. Stability of single-stimulus representations is beneficial because it would imply processing efficiency: the recruitment of the same neural population for the same stimulus suggests that it was successfully encoded and not perceived as novel on the second presentation. This conclusion is supported by several studies which found that greater encoding-retrieval similarity was related to better memory performance (Alm et al., 2018; Tompary et al., 2016; Tompary and Davachi, 2017). That said, stable single-stimulus representations may not be detectable in the hippocampus for all types of stimuli, particularly if the task is not associative (LaRocque et al., 2013; Staresina et al., 2012).

Most of the studies examining pattern similarity across stimuli have reported increased pattern similarity among stimuli with shared content, such as spatial, temporal, encoding context, relative to stimuli with no shared content. Many of these studies have also reported that higher across-stimulus pattern similarity was associated with better memory performance (Aly and Turk-Browne, 2016a; Kuhl et al., 2012; Schlichting et al., 2014; Zeithamova et al., 2018), suggesting that higher similarity was advantageous in the specific tasks used. Another group of studies, however, has reported lower across-item pattern similarity for stimuli with overlapping content. Many of these studies reported that better behavioural performance was associated with lower pattern similarity (Favila et al., 2016; Hulbert and Norman, 2014; LaRocque et al., 2013). Interestingly, many studies reporting both higher and lower across-stimulus pattern similarity used, on the surface level, similar paradigms, including repetitive presentations of the same stimuli.

An important open question, therefore, concerns the conditions under which stimuli show a relative increase or decrease in similarity. We will discuss these conditions in turn below, but we would like to acknowledge a baseline degree of noise in fMRI data and studies with small samples (which is the case in a majority of fMRI studies published to date), so no explanation will fully account for every study published in the field. We would also like to note that in the approximately 100 studies we reviewed, no two studies had identical fMRI acquisition and preprocessing parameters. We do not aim to critique any acquisition or preprocessing schemes because parameters at both of these steps are tailored to the experimental question, but different temporal and spatial resolutions of the datasets may have contributed to discrepancies in the observed results.

6. What determines whether representations are integrated or not?

The studies reporting increased and decreased similarity between related stimuli may seem to offer competing evidence for the nature of hippocampal representations. Despite the broad range of paradigms and analytic parameters, we propose that findings of increased and decreased similarity in the hippocampus may in fact be complementary, and vary based on several key factors. These factors include the degree of similarity between the stimuli, the goal of the experimental task, the amount of time since learning and degree of experience with the stimuli, and the anatomical subregion of the hippocampus.

6.1. How do task factors shape hippocampal representations?

What factors determine whether stimulus representations are similar (integrated)? Increased across-stimulus similarity between stimuli with the same context relative to different contexts suggests that the representations of individual stimuli include contextual information. It is possible that different types of context differentially bias towards integration vs. differentiation. For example, relating multiple stimuli to the same spatial context is an efficient manner of relating overlapping mnemonic representations and integrating them (Copara et al., 2014; Kyle et al., 2015b; Libby et al., 2014, 2019; Tompary and Davachi, 2017). Similarly, linking stimuli in time may give rise to memory for temporal context and the ability to judge the order of events (DuBrow and Davachi, 2014; Ezzyat and Davachi, 2014; Hsieh et al., 2014), especially for stimuli that share both temporal and spatial context (Dimsdale-Zucker et al., 2018). In contrast, hippocampal pattern dissimilarity has been observed for similar scenes paired with the same face (Favila et al., 2016). Integrating multiple stimuli linked to the same spatiotemporal context may be advantageous because the scene can activate a distributed representation (thinking of one restaurant can activate all events that had occurred there). In contrast, differentiating multiple presentations of the same face (person) may be advantageous as it affords higher memory specificity (similar experiences with the same person). These same principles may apply more generally to the differing demands of other tasks, depending on whether it is advantageous to have integrated or distinct memory representations. Distinctiveness, however, can result from patterns that share no overlap (orthogonal), or that are dissimilar (differentiated).

What determines whether stimulus representations are unrelated (orthogonal) or dissimilar (differentiated)? While some studies found increased similarity, discussed above, others reported 'null' findings - no evidence of increased or decreased similarity across stimuli with shared content. There are two possibilities that could produce these results, which are not mutually exclusive. First, it is possible that only stimuli with a large degree of overlap need to be representationally repelled (Hulbert and Norman, 2014; Ritvo et al., 2019). Second, it is possible that dissimilarity is only measurable with fMRI for stimuli with a large degree of overlap. With high degrees of stimulus overlap, the activity of neurons supporting the representation of one stimulus should be decreased when a second, highly overlapping stimulus is encountered. Stimuli with small degrees of overlap might be dissimilar but not detectable due to the resolution of fMRI, producing null findings.

It is important to note, however, that the correspondence between hippocampal fMRI signal and local field potentials measured by depth electrodes is weak (Ekstrom, 2010; Ekstrom et al., 2009). While hippocampal activity patterns provide meaningful insight into cognition in humans, as reviewed here, it is unclear how these patterns emerge from hippocampal cellular firing. Nonetheless, analogous representational similarity analyses have been applied to recordings of single neurons in rodents, providing a converging approach and evidence for contextspecific coding in electrophysiological data (McKenzie et al., 2014, 2016). Future investigations are needed to establish how responses of single neurons translate into population-level responses measured by fMRI.

6.2. How stable are hippocampal representations over time?

An outstanding question is how stable within- or across-stimulus representations are over longer periods of time. One study found that only object-scene pairs that were remembered after a 1-week period, but not those that were forgotten, showed encoding-retrieval similarity (Tompary and Davachi, 2017). Another study reported successful classification of different highly memorable autobiographical memories years after they were first encoded (Bonnici et al., 2012a; Bonnici and Maguire, 2018). The stability of patterns corresponding to different memories over the years is difficult to establish because the precise localization of individual voxels over multiple years may be impossible, but these data suggest that even if the patterns corresponding to different memories are transformed to an extent, they remain differentiated.

Items that share no content tend to show no similarity at any time point (Dandolo and Schwabe, 2018). Studies that investigated stimuli with shared content reported both decreases and increases in similarity over time. Decreases in similarity were observed over the course of learning within the experiment (Berens et al., 2018; Chanales et al., 2017) and overnight (Ezzyat et al., 2018; Ritchey et al., 2015), and increases were observed after a week (Tompary and Davachi, 2017). Thus, there may be a trade-off between decreasing similarity over the course of learning distinct representations, but increases over longer timescales as memories become more generalized. Behavioural findings seem to support this trade-off, with some studies showing increased differentiation relating to better behavioural performance during learning, and others showing increased similarity relating to better memory performance at retrieval. Thus, it is possible that differentiation is initially advantageous when encoding partially overlapping stimuli, but that over time the similarities between stimuli are represented, perhaps reflecting transformation of representations with time (Robin and Moscovitch, 2017; Winocur and Moscovitch, 2011; Sekeres et al., 2018). Future studies are needed to examine hippocampal representations at different degrees of remoteness.

A related question concerns the relationship between the dynamics during ongoing processing and patterns evoked when retrieving the formed memories. A recent study suggests that more dissimilarity in hippocampal voxelwise timecourses while participants were navigating to a familiar goal was related to a more efficient navigational strategy (Brunec, Bellana et al., 2018). Hippocampal patterns corresponding to overlapping routes were found to diverge over the course of experience (Chanales et al., 2017). Similarly, divergence between stimulus-level patterns over the course of learning was found to correspond to an efficient learning model (Berens et al., 2018) and to better behavioural performance (Hulbert and Norman, 2014). However, patterns of similarity (and dissimilarity) during ongoing processing may be unrelated to patterns at delayed testing. It is possible, for example, that some tasks elicit similarity between related stimuli during learning, but that these patterns diverge over time (or vice versa). It would be important to relate moment-to-moment dynamics during encoding to pattern similarity at retrieval to establish whether specific activation states support better encoding or influence the way memories are formed.

The degree of overlap between pre-encoding and encoding timepoints predicts later memory (Sadeh et al., 2019), suggesting that greater stability of neural patterns during encoding may enable more integration. Further, the persistence and reactivation of patterns across rest predicted later memory performance (Gruber et al., 2016; Schapiro et al., 2018; Schuck and Niv, 2019; Tambini and Davachi, 2013). Along similar lines, an intracranial EEG study reported that the speed at which participants were able to name pictures following sentences was predicted by the degree of pattern overlap in hippocampal field potentials between the sentence and picture intervals (Jafarpour et al., 2017).

We would like to note that we intentionally focused only on studies

Integration: Representation of global structure





Fig. 4. The same experiences can be retrieved in a flexible manner. In some cases, integration is beneficial, as it enables us to extract the generalities across experiences and shape our future behaviour. Increased similarity would be expected between all related experiences in such cases as activation would spread from the target event to related events. At other times, the representation of specific instances is beneficial, as it enables us to retrieve precise, detailed memories. In this case, increased similarity would be expected between elements of the target experience (red nodes), while nonrelevant elements would be inhibited, resulting in decreased similarity (blue nodes).

reporting *hippocampal* pattern similarity findings. Several researchers have also reported on interactions between hippocampal univariate activity and cortical voxelwise representations. These studies highlight the key role of the link between hippocampal univariate responses and cortical pattern changes in both novel memory formation and reactivation at retrieval (Cooper and Ritchey, 2020; Long et al., 2016; Ritchey et al., 2013; St-Laurent et al., 2015). Reconciling the evidence for univariate vs. multivariate hippocampal effects, and further exploring hippocampal-cortical interactions, are key avenues for future work in this field.

6.3. How do hippocampal representations differ by subregion?

Studies examining differences along the anteroposterior axis of the hippocampus offer more evidence for integration in the anterior relative to the posterior hippocampus. Integration was found based on shared spatiotemporal content and more abstract association formation (Collin et al., 2015; Deuker et al., 2016; Nielson et al., 2015; Ritchey et al., 2015; Schlichting et al., 2014; Theves et al., 2019). These findings suggest that the anterior hippocampus is involved in more generalized or conceptual representations (Collin et al., 2017; Poppenk et al., 2013; Robin and Moscovitch, 2017; Sheldon and Levine, 2016). Evidence regarding the nature of representations in the posterior hippocampus is less conclusive, but several studies reported evidence for differentiation (Berens et al., 2018; Milivojevic et al., 2015; Schlichting et al., 2015). These patterns are consistent with a recent study showing higher similarity between voxel patterns in the anterior relative to the posterior hippocampus, suggesting that intrinsic hippocampal dynamics could support this difference (Brunec, Bellana et al., 2018). Interestingly, three studies have shown that after various delays, pattern similarity tends to be higher in the posterior relative to the anterior hippocampus (Dandolo and Schwabe, 2018; Ezzyat et al., 2018; Tompary and Davachi, 2017), meriting further investigation into memory transformation along the long axis.

Consistent with theoretical predictions, a number of studies reported differentiation in regions including DG (Copara et al., 2014; Kyle et al., 2015b), though these regions also included areas CA2/3 which remain very difficult to differentiate from DG in human neuroimaging at 3 T (Olsen et al., 2019; Wisse et al., 2017; Yushkevich et al., 2015). One high-resolution study reported successful decoding of highly similar lures in the DG (Berron et al., 2016). Some evidence points to a role for CA1 in integration (Schlichting et al., 2014), consistent with its hypothesized role as a comparator (Chen et al., 2015; Duncan et al.,

2012; Olsen et al., 2012). One study found dissociable patterns in different subfields such that CA1 had increased similarity and CA2/3/DG had decreased similarity between closely related events (Dimsdale-Zucker et al., 2018). Most of the reviewed studies, however, did not have sufficient resolution to examine differences in hippocampal subfields and often collapsed across them. Based on the finding of opposite patterns in different subfields, collapsing across these may result in null findings in the hippocampus overall.

7. Hippocampal representations underlie flexible memory use

The hippocampal capacity to integrate and differentiate experiences may be crucial to adaptive goal-directed behaviour. Different situations in our lives necessitate shifts between integrative and distinctive forms of encoding and retrieval. For example, when driving along a familiar street to a new goal, it would be adaptive to inhibit representations of competing routes that encompass that same familiar street. Similarly, when attempting to remember a friend's most recent birthday party, retrieving all birthday party memories would be detrimental, as it would produce interference. In contrast, when a detour during navigation is necessary, retrieving an integrated representation of an entire neighbourhood would be beneficial, as would being able to draw on multiple memories when planning a future birthday party. In the real world, therefore, adaptive behaviour in different situations might require varying degrees of similarity between hippocampal patterns corresponding to related experiences (Fig. 4). Evidence for switches between pattern reinstatement and separation depending on trial-wise changes in task demands have been reported in high-frequency activity measured by intracranial electrocorticography in humans (Lohnas et al., 2018). These data provide converging conclusions with fMRI findings and highlight the importance of considering what constitutes an adaptive response at each point in time.

The notion that situation-specific goals can shape neural responses is also consistent with a recent theoretical framework which highlights the importance of distinguishing between the neurocomputational operations and the representational content that underlie a given cognitive process (Cowell et al., 2019). Evidence suggests that the hippocampus preferentially represents high-dimensional, complex associative information, constructed from simpler, lower-dimensional single-item/ feature representations supported by cortical regions in the ventral visual stream and medial temporal lobe. This account could explain some of the 'null' results discussed above (e.g. LaRocque et al., 2013; Martin et al., 2013). In these studies, participants were presented with single objects with no associative demand, and thus task demands may not have recruited hippocampal representations in the first place. Importantly, the view presented in Cowell et al. (2019) holds that a brain region's representational content is dissociable from the operations applied to it; the same operation (e.g., pattern completion) is recapitulated across the different types of content represented throughout the ventral visual stream and MTL. In the hippocampus, a pattern completion operation applied to the high-dimensional associative representations enables the recollection of a complex episode when presented with a partial cue of that episode. Likewise, a pattern separation operation applied at encoding would support differentiation of the high-dimensional associative representations in the hippocampus. Thus, depending on the optimal behavioural strategy in a given situation, the operations can switch flexibly, but the underlying high-dimensional associative hippocampal representations to which these operations are applied remain the same.

8. Conclusions

In this review, we discussed the findings from a wide range of studies reporting differential similarity and dissimilarity effects in the hippocampus relating to varied paradigms. To reconcile this diverse body of research, future studies should test whether increases and decreases in similarity can both facilitate memory depending on different experimental parameters, such as stimulus characteristics, task demands, time of testing and precise hippocampal localization. This approach would also allow us to test intra-individual hippocampal pattern flexibility to determine if certain individuals are biased towards integration vs. differentiation, regardless of the task. More broadly, this line of research would provide some insight into perhaps one of the most critical issues regarding this field of study: how the same realworld experience is represented depending on whether we are attempting to extract generalities or to draw on specific experiences.

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