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On the nature of medial temporal lobe contributions to the constructive simulation of future events

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A rapidly growing number of studies indicate that imagining or simulating possible future events depends on much of the same neural machinery as does remembering past events. One especially striking finding is that the medial temporal lobe (MTL), which has long been linked to memory function, appears to be similarly engaged during future event simulation. This paper focuses on the role of two MTL regions—the hippocampus and parahippocampal cortex—in thinking about the future and building mental simulations.

Keywords: memory; mental simulation; future thinking; hippocampus; medial temporal lobe; parahippocampal cortex

1. INTRODUCTION

Everyday experience suggests that predictions are about the future, whereas memory is about the past. From this perspective, the two phenomena run on parallel tracks in opposite temporal directions. For example, predictions about the future occur at varying different time scales, ranging from situations where one enters a new setting, such as a school or a museum, and tries to predict what might happen next (e.g. Bar 2007), all the way to predicting how happy one might be years or decades in the future in a marriage or a job (Gilbert 2006). Analogously, memory can operate on the very recent past, as when we use working memory to recall the last few words in a sentence, or the remote past, as when we recall our childhood experiences.

It is becoming increasingly clear, however, that predicting the future and remembering the past may be more closely related than everyday experience might suggest. For example, errors in predicting the future are often based on how we remember the past (for a review, see Gilbert & Wilson 2007). In a related vein, remembering the past recruits many of the same cognitive processes as does imagining or simulating the occurrence of possible events in the future. Consider, for example, a study by D'Argembeau & Van der Linden (2004), in which they asked subjects to either remember a specific event from their past or imagine a specific event that could plausibly happen to them in the future, and rate various attributes of the event. Although remembered past events were associated with more vivid sensory and contextual details than were imagined future events,

there were also strong commonalities between remembering the past and imagining the future. Positive past and future events were rated as more strongly experienced than negative past and future events, temporally close events in either the past or future were more strongly experienced and included more sensory and contextual details than did distant events, and participants were more likely to adopt a first-person than third-person perspective for temporally close than temporally distant events in both the past and the future.

These commonalities in cognitive processes underlying past and future events are complemented by analogous similarities in brain activity: the same 'core network' of brain regions is recruited when people remember the past and imagine the future, including medial prefrontal and frontopolar cortex, medial temporal lobe (MTL), lateral temporal and temporo-polar cortex, medial parietal cortex including posterior cingulate and retrosplenial cortex, and lateral parietal cortex (for reviews, see Schacter *et al.* (2007, 2008) and Buckner *et al.* (2008)). For memory researchers, perhaps the most striking finding from this research is that the MTL, a structure long known to play a critical role in remembering, appears to be similarly involved when individuals imagine or simulate events that might occur in their personal futures.

The purpose of the present paper is to review recent evidence from our laboratory and others that links MTL activity to future event simulation, to consider alternative interpretations of these observations, and to discuss them in relation to other evidence concerning the MTL and constructive memory. Elsewhere, we have provided broad reviews concerning cognitive and neural aspects of future event simulation (Schacter *et al.* 2007, 2008), and focus here instead on the contributions of two regions within the MTL, the hippocampus and parahippocampal cortex.

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One contribution of 18 to a Theme Issue 'Predictions in the brain: using our past to prepare for the future'.

2. REMEMBERING THE PAST AND IMAGINING THE FUTURE: CONCEPTUAL ISSUES AND THE CONSTRUCTIVE EPISODIC SIMULATION HYPOTHESIS

When we use such terms as ‘episodic simulation’ or ‘future event simulation’, we refer to *imaginative constructions of hypothetical events or scenarios that might occur in one’s personal future* (Schacter *et al.* 2008). Although we focus on the idea that simulation is critical for envisaging possible *future* events, we do not restrict our application of simulation to the future. People also engage in simulations of present and past events, a point that will be important to consider in relation to recent empirical observations and theoretical accounts.

Motivated in part by some of the striking commonalities noted earlier between remembering past events and simulating future ones, we advanced the *constructive episodic simulation* hypothesis (Schacter & Addis 2007a,b; for related views, see Suddendorf & Corballis 1997, 2007; Buckner & Carroll 2007; Hassabis & Maguire 2007). By this view, past and future events draw on similar information stored in episodic memory and rely on similar underlying processes: episodic memory supports the construction of future events by extracting and recombining stored information into a simulation of a novel event. Indeed, we have suggested that simulation of future events requires a system that can flexibly recombine details from past events.

Taking an adaptive perspective, we (Schacter & Addis 2007a,b) suggested that a critical function of a constructive memory is to make information available for simulation of future events. Episodic memory thus supports the construction of future events by flexibly recombining stored information into a simulation of a novel event. The adaptive value of such a system is that it enables past information to be used flexibly in simulating alternative future scenarios without engaging in actual behaviour. A potential downside of such a system is that it is vulnerable to memory errors, such as misattribution and false recognition (e.g. Schacter & Addis 2007a,b; see also Suddendorf & Corballis 1997; Dudai & Carruthers 2005).

With respect to the MTL, it has been suggested that the hippocampal region supports relational memory processes that link together disparate bits of information (e.g. Eichenbaum & Cohen 2001). According to the constructive episodic simulation hypothesis, these processes are crucial for recombining stored information into future event simulations. Thus, our hypothesis posits an important link between hippocampal activity and the simulation of future events.

3. NEUROIMAGING OF PAST AND FUTURE EVENTS

A large number of neuroimaging studies have examined brain activity when people remember past autobiographical experiences (for reviews, see Svoboda *et al.* (2006) and Cabeza & St Jacques (2007)). By contrast, only a handful of studies have explored brain activity when people imagine future events. Okuda *et al.* (2003) reported the first such study. During scanning, participants talked freely for 60 s about either the near or distant past (last few days or

years), or the near or distant future (the next few days or years). These critical conditions were compared with a semantic control task involving analysis of the meaning of words. Compared with the control condition, significant levels of activation were observed during both the past and future conditions in the right hippocampus and bilateral parahippocampal cortex. Furthermore, two left parahippocampal areas showed greater activity when individuals were thinking about the future than about the past. Moreover, activity in a number of these MTL regions was modulated by temporal distance. Most of them showed the same neural response to temporal distance for both the past and future events: either increasing or decreasing activity with increasing temporal distance. The only region that exhibited an interaction between temporal direction (i.e. past versus future) and distance (i.e. near versus distant) was an inferior region in the left parahippocampus gyrus (BA 36), one of the two areas noted above that showed greater activity for future than past events. In this region, Okuda *et al.* noted that the increase in brain activity from the near to distant future tasks was smaller than the increase in activity observed from the near to distant past tasks.

These observations are potentially important because they suggest that the parahippocampal and hippocampal regions are at least as active during future event simulation as during remembering of past experiences. Note, however, that because Okuda *et al.* used a relatively unconstrained paradigm that did not probe participants about particular events, it is unclear whether these reports consisted of episodic memories/simulations (unique events specific in time and place), or general semantic information about an individual’s past or future. More recent functional magnetic resonance imaging (fMRI) studies have used event-related designs to yield information regarding the neural bases of specific past and future events.

Addis *et al.* (2007) used event-related fMRI to distinguish between an initial *construction* phase, where participants generated a specific past or future event in response to an event cue (e.g. ‘dress’), making a button press when they had an event in mind, and an *elaboration* phase during which participants generated as much detail as possible about the event. We compared activity during the past and future tasks with control tasks that required semantic and imagery processing, respectively.

We observed evidence of past- and future-related MTL activities during both the construction and elaboration phases. The construction phase was associated with common past–future activity in the posterior left hippocampus, which we suggested might reflect the initial interaction between cues and hippocampally mediated pointers to memory traces. Similarly, the elaboration phase revealed evidence of common past–future activity in the left hippocampus, possibly reflecting the retrieval and/or integration of additional event details into the memorial or imaginal representations, as well as common past–future activity in the bilateral parahippocampal cortex. There was also evidence for differential engagement of MTL activity in the future task: during the construction phase, a region of the right hippocampus showed increased activity

only in the future condition. We suggested that this future-specific hippocampal activity might reflect the novelty of future events and/or additional relational processing required when one must recombine disparate details into a coherent event.

Botzung *et al.* (2008) reported fMRI data that contrast with the aforementioned results showing increased hippocampal activity for future versus past events. One day prior to scanning, subjects described 20 past events from the last week and 20 future events planned for the next week. The subjects constructed cue words for these events that were then presented to them the next day during scanning, when they were instructed to think of past or future events to each cue. Although past and future events produced activation in a similar network to that reported by Okuda *et al.* (2003) and Addis *et al.* (2007), including bilateral MTL, Botzung *et al.* reported no evidence for increased activity in the future condition compared with the past condition. In fact, they noted that both the right and left hippocampus showed greater activity in the past condition than in the future condition.

As we have pointed out elsewhere (Schacter *et al.* 2008), however, participants in the Botzung *et al.* (2008) study initially carried out their simulations of future events in a separate session prior to scanning, they thus may have recalled their prior simulation during scanning, rather than constructing it for the first time, as subjects did in the earlier studies. Although Botzung *et al.* excluded those trials in which subjects stated that they produced an event from the pre-scan interview, it is unclear how reliably subjects can make the requested discrimination. Moreover, since subjects had previously encoded their future event simulation, rather than constructing it anew during scanning as in previous studies, there may have been less recruitment of processes involved in recombining details from past experiences. Similar findings have been reported in other studies examining the retrieval of previously constructed imaginary events (Hassabis *et al.* 2007a; D'Argembeau *et al.* 2008).

Two more recent studies from our laboratory have further examined the nature of hippocampal activations observed during the construction and elaboration stages of event remembering and simulation, respectively. Addis & Schacter (2008) further analysed the elaboration-stage data reported initially by Addis *et al.* (2007), using parametric modulation analyses to examine MTL activity according to the amount of detail generated and the temporal distance of each event from the present. We suggested that *reintegrating* increasing amounts of detail for either a past or future event would be associated with increasing levels of hippocampal activity. However, future events should require more intensive *recombining* of disparate details into a coherent event, so the hippocampal response to increasing amounts of future event detail should be larger than that for past event detail. Consistent with these predictions, the analysis showed that the left posterior hippocampus was responsive to the amount of detail for both the past and future events, probably reflecting the retrieval of details from episodic memory that is required for both tasks. By contrast, a distinct region in the left anterior hippocampus responded

differentially to the amount of detail comprising future events, possibly reflecting the recombination of details into a novel future event.

The parametric modulation analysis of temporal distance revealed that the increasing recency of past events was associated with activity in the right parahippocampus gyrus (BA 35/36), while activity in the bilateral hippocampus was associated with the increasing remoteness of future events. We proposed that the hippocampal response to the distance of future events reflects the increasing disparateness of details probably included in remote future events, and the intensive relational processing required for integrating such details into a coherent episodic simulation of the future. Overall, these results suggest that, although MTL regions supporting past and future event simulation show impressive commonalities during event elaboration, they can be recruited in different ways depending on whether the generated event is in the past or future.

A study by Addis *et al.* (2008a) provides additional insight into the nature of MTL activity during the construction phase. Participants were cued to either remember specific past events or imagine specific future events, as in Addis *et al.* (2007). In addition, they were also cued to remember general routine events (e.g. having brunch after attending church) or to imagine generic events that might occur in their personal futures (e.g. reading the newspaper each morning). We reasoned that in a region that is responsive to the amount of detail recombined into a coherent imagined episode, as we suggested with respect to the hippocampus (Addis & Schacter 2008), more activity should be evident when constructing specific future events relative to general future events (as well as specific and generic past events). By contrast, if the hippocampal region is simply responsive to the prospective nature of future events, then it should be more engaged during the construction of both types of future events relative to past events, irrespective of specificity.

We replicated the aforementioned findings of equivalent left hippocampal activity during the construction of past and future events, and greater right hippocampal activity for future than past event construction. Importantly, though, the increased right hippocampal activity was evident only for specific events; in fact, there was no evidence for right hippocampal activity during construction of generic future events. Thus, the results appear to provide evidence against the idea that right hippocampal activation for specific future events indicates a uniquely prospective function for this region. Importantly, there were regions that did show activation patterns that could be interpreted as reflecting a prospective function, such as the left frontopolar cortex, in which construction of future events resulted in greater activity than past events, irrespective of the specificity of the event.

An event-related fMRI study by Hassabis *et al.* (2007a) also provides data that call into question the idea that MTL activation during event simulation is tied specifically to thinking about events in one's future. Participants were asked to imagine novel, fictitious scenes, without explicit reference to whether those

scenes should be placed in the past, present or future. Subjects were then scanned in a subsequent session in which they were cued to remember the previously constructed fictitious scenes, construct additional novel fictitious scenes or recall real episodic memories from their personal pasts. Hassabis *et al.* found that all three conditions were associated with activations in the hippocampus, parahippocampal gyrus and several other regions in the core network. The results thus indicate that activity in these regions is not restricted to conditions that explicitly require imagining future events.

Additional evidence on this point is provided by another recent study from our laboratory. Addis *et al.* (in press) approached the question of whether future event-related activity is specifically associated with prospective thinking, or with the more general demands of imagining an episodic event in either temporal direction, by instructing subjects to imagine events that might occur in their personal future or events that might have occurred in their personal pasts but did not. Prior to scanning, participants provided episodic memories of actual experiences that included details about a *person, object and place* involved in that event. During scanning, the subjects were cued to recall some of the events that had actually occurred, and for the conditions in which they imagined events, the experimenters randomly recombined details concerning person, object and place from separate episodes. Participants were thus presented with cues for a person, object and place taken from multiple episodes, and were instructed to imagine a single, novel episode that included the specified details.

With respect to the MTL, Addis *et al.* (in press) reported that both the hippocampus and parahippocampal cortex were similarly engaged when participants imagined future and past events, suggesting that these regions (as well as others in the core network that showed the same pattern) can be used for event simulation regardless of the temporal location of the event.

This study also allowed us to address an issue that is particularly relevant to the constructive episodic simulation hypothesis discussed earlier, which emphasizes that future event simulations are built by flexibly recombining details from past experiences, probably engaging the relational processes supported by the hippocampus. However, our previous studies on imagining future events did not provide direct evidence that subjects recombine details from multiple past events into novel future simulations. An alternative possibility is that participants simply recast their memories of individual past experiences as imagined future events, especially when they are thinking about events that might plausibly occur in the near future. For example, when given the cue 'car' and asked to imagine an event that might occur in the next few weeks involving a car, participants might simply recall a recent episode in which they saw a car cross a red light, and imagine that such an incident might occur in the next few weeks. When this kind of recasting process occurs, there is little or no recombination of details of past events into imagined future scenarios. However, the

finding that the hippocampus was robustly activated during event simulation when we experimentally recombined details concerning person, object and place from different episodes provides evidence against this recasting hypothesis. Although we would not rule out the possibility that recasting occurs on some test trials, the finding of hippocampal activation in this paradigm, which should minimize or eliminate recasting, is consistent with the claim from the constructive episodic simulation hypothesis, that activity in the hippocampus during event simulation reflects the recombination of details from different episodes.

One feature common to the neuroimaging studies reviewed so far is that each one provided some evidence for activity in both the hippocampal and parahippocampal regions in conditions designed to elicit future event simulation (Okuda *et al.* 2003; Addis *et al.* 2007, in press; Botzung *et al.* 2008) or imagination (Hassabis *et al.* 2007a). Szpunar *et al.* (2007) reported a contrasting pattern of results. In their fMRI study, participants were given event cues, such as *past birthday* or *retirement party*, and were instructed to remember specific events from their personal pasts, imagine specific events that might reasonably occur in their personal futures or imagine specific events that could involve a familiar individual (Bill Clinton). Compared with the latter condition, remembering one's personal past or simulating one's personal future was associated with significant and comparable levels of activity in the bilateral parahippocampal cortex, as well as other regions activated in other studies, including other posterior regions such as posterior cingulate and anterior regions such as the frontopolar cortex. By contrast, no evidence for hippocampal activation was reported in the personal past or future conditions relative to the 'Bill Clinton' control. We will return to this observation later when considering theoretical implications of the aforementioned results.

Szpunar *et al.* (in press) sought to characterize the nature of activity they had observed in the parahippocampal and related posterior regions. They noted previous work from Bar & Aminoff (2003), suggesting that the parahippocampal cortex and posterior cingulate are involved in processing contextual associations, thus suggesting that these regions may be responsible for generating the familiar contexts in which future event simulations are situated (Addis *et al.* 2007; Szpunar *et al.* 2007). To test the idea, Szpunar *et al.* asked participants to imagine themselves in future scenarios involving either a familiar or an unfamiliar context; they also asked participants to remember past experiences involving familiar contexts. They carried out region-of-interest analyses focused on the areas within the bilateral parahippocampal cortex and posterior cingulate that had been activated in their previous study. Consistent with the hypothesis that these regions are important for instantiating contextual information, both regions showed robust activity in the past and future conditions that required generating a familiar context, and significantly less activity in the future condition that required generating an unfamiliar context.

4. STUDIES OF AMNESIC PATIENTS AND OLDER ADULTS

Although most of the evidence linking future event simulation with MTL activity comes from neuroimaging studies, additional evidence is provided by studies of amnesic patients, who exhibit an impairment in the ability to remember past experiences as a result of bilateral damage to the MTLs and related structures. Tulving (1985) reported that the severely amnesic patient K. C., who cannot remember any specific episodes from his past (for a review of K. C., see Rosenbaum *et al.* 2005), exhibits similar problems envisioning any specific episodes in his future. K. C. is characterized by bilateral MTL damage, but also has extensive prefrontal damage, and in other regions (see Rosenbaum *et al.* 2005), so it is unclear whether his problems imagining the future are associated specifically with the MTL. A similar caveat applies to a more recent study concerning patient D. B., who became amnesic as a result of cardiac arrest and consequent anoxia (Klein *et al.* 2002). D. B. showed clear deficits on a 10-item questionnaire probing past and future personal events that were matched for temporal distance from the present. However, even though anoxia is typically associated with MTL damage, no neuroanatomical findings were reported concerning patient D. B.

Hassabis *et al.* (2007b) examined the ability of five patients with documented bilateral hippocampal amnesia to imagine novel experiences, such as 'imagine you're lying on a white sandy beach in a beautiful tropical bay'. The experimenters scored the constructions of patients and controls based on the content, spatial coherence and subjective qualities of the imagined scenarios. Four of the five hippocampal patients produced constructions that were significantly reduced in richness and content, and especially, the spatial coherence of the scenarios, relative to scenarios constructed by controls. The single patient who performed normally on the imaginary scene task maintained some residual hippocampal tissue. Since the lesions in the other cases appear to be restricted to hippocampal formation, this study strengthens the link between event simulation and hippocampal function.

We also note that a recent study by Addis *et al.* (2008b) provides evidence that future event simulation is impaired in older adults, who also exhibit memory impairments, albeit considerably milder than those seen in amnesic patients. Young and older participants generated memories of past events and simulations of future events in response to individual word cues, and transcriptions of the events were segmented into distinct details that were classified as either internal (episodic) or external (semantic; cf. Levine *et al.* 2002). The key finding was that older adults generated fewer internal (but not external) details than younger adults; importantly, this effect was observed to the same extent for future events as for past events. Although there is no direct evidence from this study linking the age-related deficits to MTL dysfunction, two kinds of indirect evidence suggest that such a link may exist. First, we reported that the internal (but not external) detail score in older adults correlated significantly with a measure of relational memory (paired-associate learning) that is

known to be dependent on the hippocampus. Second, hippocampal atrophy has been documented in older adults (e.g. Driscoll *et al.* 2003).

5. MTL AND FUTURE EVENT SIMULATION: SUMMARY, EXTENSIONS AND THEORETICAL IMPLICATIONS

The studies reviewed in the preceding sections are broadly consistent with the idea that regions within the MTL are associated with constructing simulations of future events. We discuss now a number of points regarding these studies and related research that has characterized MTL function in different domains.

First, consider the neuroimaging studies that we reviewed. On balance, the most consistent feature of the neuroimaging data is that both the hippocampus and parahippocampal cortices are similarly active during the simulation of future events and the remembering of past events, in agreement with a meta-analysis by Spreng *et al.* (in press). In addition, however, it is clear that this common activation of the hippocampus and parahippocampus is not restricted to conditions requiring prospective event simulation: the same regions are engaged when individuals are instructed to simulate events that might have occurred in their pasts (Addis *et al.* in press) or when asked to imagine scenes without a specific temporal reference (Hassabis *et al.* 2007a). This latter finding fits well with the related observations that both regions show similarly increased activity during tasks involving spatial navigation (for a review, see Buckner & Carroll 2007; Spreng *et al.* in press) and, under some conditions, during tasks requiring theory of mind judgements, which commonly activate medial prefrontal and parietal regions of the core network (Buckner & Carroll 2007; Spreng *et al.* in press; but these structures are probably not necessary for some theory of mind tasks on which amnesic patients perform well; see Rosenbaum *et al.* 2007).

Even though more evidence is required given the relatively small database, in general, extant results support the view that the hippocampal and parahippocampal regions are engaged when individuals build simulations of events located in the future, past or present. Thus, although our focus in the present paper remains on the simulation of future events, it seems likely that ideas concerning the role of MTL regions apply more broadly to other kinds of simulations.

Another issue raised by neuroimaging studies concerns the evidence that the hippocampal and parahippocampal regions can be differentially engaged by tasks requiring future event simulation compared with autobiographical remembering. Addis *et al.* (2007) reported that the right hippocampus shows greater activity during construction of future than past events, a finding that we subsequently replicated when demonstrating that the effect occurs for specific but not general future events. By contrast, Okuda *et al.* (2003) reported greater future than past activity for two areas within the left parahippocampal gyrus. The contrasting results suggest that interpretive caution must be exercised regarding a possible difference between the hippocampal and parahippocampal regions in this

respect, but given that the right hippocampal effect has been replicated, and the methodological concerns noted earlier regarding the Okuda *et al.* (2003) study, we are inclined to assign more weight at the present time to the hippocampal than the parahippocampal finding.

We have suggested that the future greater than past activity in the right hippocampus could reflect the more intensive constructive activity associated with recombining details of past events to generate a novel future event (Addis *et al.* 2007). Note that this effect was observed in the right anterior hippocampus (Talairach *xyz* coordinate = 40, -22, -11 for the peak voxel in Addis *et al.* (2007)). This idea fits nicely with our thinking about the finding reported by Addis & Schacter (2008) during event elaboration, where activity in a left anterior hippocampal region (*xyz* = -20, -22, -6) correlated with the amount of detail in future but not past events, while left posterior hippocampal activity (*xyz* = -18, -34, 1) correlated with both the future and past details. This latter region is quite close to the posterior hippocampal region associated with the amount of retrieved detail in an earlier study of autobiographical memory (*xyz* = -20, -37, 0; Addis *et al.* 2004). These observations led us to propose that the anterior hippocampal region is specifically involved in recombining details from past events, converging with our account of the future greater than past activity during construction in the right anterior hippocampus.

These ideas also fit with findings from other memory paradigms. In a meta-analysis of MTL activations during encoding and retrieval, Schacter & Wagner (1999) noted evidence linking anterior hippocampal activity with relational or associative processing at both encoding and retrieval. Subsequent research has been largely consistent with this observation, as anterior regions of the hippocampus showed preferential activation in conditions requiring relational processing at both encoding (e.g. Giovanello *et al.* 2004; Jackson & Schacter 2004; Kirwan & Stark 2004; Chua *et al.* 2007) and retrieval (Giovanello *et al.* 2004; Kirwan & Stark 2004). Recent work using functional connectivity analyses of rest fMRI data has suggested that the anterior and posterior hippocampus are connected with distinct cortical systems (Kahn *et al.* 2008).

Findings reported by Preston *et al.* (2004; see also Heckers *et al.* 2004) point towards an even further possible refinement of the foregoing ideas, suggesting that left anterior hippocampal activity (*y* = -22) is associated specifically with recombining elements from previously learned associations. They used a transitive inference design in which participants first learned to associate specific faces (stimuli A) with specific houses (stimuli B), and then learned to associate another set of faces (stimuli C) with the same houses (stimuli B). Critically, the A and C faces were not shown together during training, but were related to one another through their overlapping associations with the same house (B). During scanning, correctly recognizing that the A-C face pair contained related elements significantly engaged the left anterior hippocampus relative to all other recognition conditions, including successful recognition of A-B and B-C face-house pairs as 'old'.

By contrast, a region of the left posterior hippocampus (*y* = 30) was engaged by all tasks requiring the retrieval of relational information (i.e. correct recognition of A-B, B-C and A-C pairs). Linking these observations with the aforementioned data from Addis & Schacter (2008), perhaps both the past and future events require the retrieval of some form of relational information (i.e. details that were encoded as part of a complex autobiographical memory) and commonly engage the posterior hippocampus, whereas only future events require recombining such details, and thus, as in Preston *et al.*'s study, recruit the anterior hippocampus.

The foregoing observations might be useful in thinking about one of the puzzling findings from neuroimaging research noted earlier: in contrast to other studies, Szpunar *et al.* (2007) did not report evidence of hippocampal activation when individuals simulated events in their personal futures, compared with when they imagined Bill Clinton participating in similar kinds of events. We suggested that both of these tasks probably involve the kind of relational processing and recombining of event details thought to elicit hippocampal activation. If so, significant hippocampal activation during each task would not be evident in a comparison between tasks.

Of course, the question of whether hippocampal regions are *necessary* for simulating future events cannot be answered by neuroimaging studies alone, which are necessarily correlational in nature. Moreover, the imaging evidence leaves open the question of whether hippocampal activity during future event simulation reflects retrieval and/or recombination of event details, as we have suggested, versus the encoding and storage of novel information. As we have stressed, future event simulations involve the construction of novel scenarios, and the hippocampus appears to play a role in the encoding of novel events (e.g. Ranganath & Rainer 2003). Evidence reviewed earlier indicating impaired future event simulation in amnesic patients is consistent with the idea that the hippocampal region is indeed necessary for retrieving and/or recombining event details into a representation that supports simulation of the future, but further studies of amnesic patients are required to understand more fully the nature and extent of their simulation deficits.

Intriguingly, several recent studies of rodents have shown that hippocampal neurons code for prospective information concerning where the rat needs to go in the immediate future (e.g. Ferbinteanu & Shapiro 2003; Foster & Wilson 2007; Johnson & Redish 2007). For instance, Johnson & Redish (2007) recorded from ensembles of neurons with place fields in the CA3 region of the hippocampus, allowing them to analyse activity during choices made by rats in a spatial decision task. On some trials, the spatial representation reconstructed from the neural ensemble appeared to indicate possible future paths, leading Johnson and Redish to suggest that the hippocampus may be a source of prospective memory signals. It will be important to investigate whether and to what extent such findings are related to the observations on future event simulation in humans considered here.

Let us also consider the role of the parahippocampal region in future event simulation. As we have seen, this region is activated consistently in neuroimaging studies as part of a more general core network. Although hippocampal and parahippocampal regions generally show similar activity patterns, there are reasons to posit that they play different roles within the network. Evidence discussed earlier from Szpunar *et al.* (in press) suggests that the parahippocampal region (along with posterior cingulate) is important for generating familiar contexts that contribute to future event simulations. This idea fits well with the previously mentioned studies of Bar & Aminoff (2003; see also, Bar 2007), which have independently implicated the parahippocampal cortex (and posterior cingulate/retrosplenial cortex) in contextual processing. Strong evidence that the parahippocampal region contributes specifically to the generation of contextual associations comes from a recent study by Bar *et al.* (2008), who showed that it responds more strongly to scenes with strong contextual associations (e.g. scenes involving objects such as a traffic light, which are strongly associated with a particular context) when compared with scenes that are matched with respect to visual qualities but have weaker contextual associations (e.g. scenes involving objects such as a water bottle, which are not strongly associated with a particular context). It therefore makes both theoretical and empirical sense to suggest that the parahippocampal region may allow access to contextual associations that are recombined by the hippocampus with other kinds of event details to create a full-blown episodic simulation.

Finally, we note that the research considered here also raises important issues regarding *reality monitoring* processes that allow us to distinguish between remembered and imagined events (Johnson & Raye 1981). If, as we have seen, remembering past events and imagining future or novel events recruit largely overlapping brain networks, including the MTL, then how do individuals distinguish mental simulations from memories of real events? There is probably no simple answer to this question (for a recent discussion see Hassabis *et al.* (2007a)), but we think there is a role for the well-known idea from research on reality monitoring that remembering events that one has actually experienced is associated with greater sensory and perceptual details than remembering previously imagined events (e.g. Johnson & Raye 1981). This idea has received support from behavioural studies (e.g. Johnson *et al.* 1988) as well as neuroimaging research (Kensinger & Schacter 2006; see also, Slotnick & Schacter 2004).

More directly related to the present concerns, in our previously discussed study using experimental recombination of event details (Addis *et al.* in press), we found evidence suggesting the existence of distinct remembering and imagining subsystems within the core network. Remembering actual autobiographical events was preferentially associated with activity in the parahippocampal cortex and posterior visual regions, whereas imagining future or past events was preferentially associated with a subsystem including the anterior hippocampus. In our study, remembered events were rated as significantly more detailed than imagined

events, so it would make sense from the perspective of the reality monitoring framework that regions associated with processing of sensory and contextual details would show greater activity for real than imagined events.

Although much work remains to be done, we believe that the research considered here has the potential to enrich, broaden and, perhaps, alter our ideas about the nature and functions of memory, as well as our thinking about how the MTL allows us to stay connected with both the past and the future.

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