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## The Hippocampus and Imagining the Future: Where Do We Stand?

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4  
5 **The hippocampus and imagining the future: Where do we stand?**

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24 **Abstract**

25

26 Recent neuroimaging work has demonstrated that the hippocampus is engaged when  
27 imagining the future, in some cases more than when remembering the past. It is possible that  
28 this hippocampal activation reflects recombining details into coherent scenarios and/or the  
29 encoding of these scenarios into memory for later use. However, inconsistent findings have  
30 emerged from recent studies of future simulation in patients with memory loss and  
31 hippocampal damage. Thus, it remains an open question as to whether the hippocampus is  
32 necessary for future simulation. In this review, we consider the findings from patient studies  
33 and the neuroimaging literature with respect to a new framework that highlights three  
34 component processes of simulation: accessing episodic details, recombining details, and  
35 encoding simulations. We attempt to reconcile these discrepancies between neuroimaging  
36 and patient studies by suggesting that different component processes of future simulation may  
37 be differentially affected by hippocampal damage.

38

39 **1. Introduction**

40

41 In daily life, particularly during the unoccupied moments, we often revert to our inner mental  
42 world and engage with our aspects of our lives outside of the present. Mentally projecting  
43 ourselves back into the past or forwards into the future can take make forms – a cursory  
44 thought, a vague image, or a vivid and consuming scenario. There has been increasing  
45 interest in understanding the ways in which remembering and future thinking are similar or  
46 different, both in terms of cognitive and neural processes, and whether such characteristics  
47 are evident for various forms of past and future thinking (for recent reviews, see Schacter,  
48 Addis, & Buckner, 2008; Szpunar, 2010). These studies have been informed by a closely  
49 related line of neuroimaging research showing that when people are consumed by various  
50 forms of thoughts and images, these internally-directed cognitive activities are accompanied  
51 by a characteristic pattern of neural activity - known as the default network (Buckner,  
52 Andrews-Hanna, & Schacter, 2008; Spreng, Mar, & Kim, 2009).

53

54 This network, which includes many regions traditionally associated with memory, such as the  
55 hippocampus, is also up-regulated by tasks that specifically require a focus on remembering  
56 and imagining personal experiences (Buckner & Carroll, 2007; Schacter, Addis, & Buckner,  
57 2007; Spreng et al., 2009). Motivated by findings that remembering and imagining engage  
58 the same ‘common core network’, we advanced the *constructive episodic simulation*  
59 *hypothesis*, which holds that the common neural activity for past and future reflects a reliance  
60 on memory to provide the details comprising both remembered and imagined event  
61 representations (Schacter & Addis, 2007). In that theory, as well as in this review, we focus  
62 on a particularly vivid form of future thinking: the imaginative construction or simulation of  
63 scenarios that might occur in one’s future. We hypothesized that the flexible use of episodic  
64 details from memory during imaginative simulations of the future can help to understand  
65 constructive aspects of memory, such as its susceptibility to distortion (see also Schacter,  
66 Guerin, & St. Jacques, 2011). Like autobiographical memories of past experiences, these  
67 simulations are considered “episodic” in nature because they represent the self engaging in a  
68 specific event in a particular spatiotemporal context. And although the emphasis here is  
69 primarily on simulations located in the imagined future, primarily because of the adaptive  
70 value of such simulations for maximizing future success (Ingvar, 1985; Schacter & Addis,  
71 2007; Suddendorf & Corballis, 1997, 2007; Szpunar, 2010), simulations can also focus on  
72 present or past events; indeed, we have argued that many of the same processes discussed  
73 here are likely also applicable under those conditions (Addis, Pan, Vu, Laiser, & Schacter,  
74 2009).

75

76 One of the more compelling and even unexpected findings from research on the neural  
77 underpinnings of episodic simulations is that the hippocampus, a region traditionally thought  
78 of as a “memory region”, can be engaged to a greater degree when imagining than  
79 remembering (e.g., Addis, Wong, & Schacter, 2007; for reviews, see Buckner, 2010; Schacter  
80 & Addis, 2009). Such findings raise the question of what is unique about episodic simulation  
81 or future thinking that recruits the hippocampus. In very general terms, it would appear that  
82 more intensive processing is required when imagining future events relative to retrieving past  
83 events, because the former requires construction of a novel event, whereas the latter involves  
84 retrieval of an already established event. However, determining what specific component  
85 processes underlie this ‘more intensive processing’, and which such processes rely on the  
86 hippocampus, is necessary to better understand this future>past effect. A number of candidate

87 cognitive processes exist. Although both remembering and imagining typically involve the  
 88 reactivation of memories and episodic details comprising these memories, only imagining  
 89 requires the additional step of recombining such details into a new arrangement – the  
 90 imagined scenario. It is plausible that this recombination process would engage the  
 91 hippocampus, given its role in relational memory processes that link together disparate bits of  
 92 information (Eichenbaum, 2001). Also, if these newly constructed scenarios are ever to be  
 93 accessed in future, they need to be encoded and stored in memory (Ingvar, 1985). In this  
 94 review, we will discuss the conditions under which a hippocampal future>past effect  
 95 emerges, and also consider recent work investigating whether hippocampal activation during  
 96 future thinking reflects access to episodic details, recombining these details to construct  
 97 specific scenarios, and/or the encoding of these scenarios into memory.

98  
 99 A related line of enquiry is to determine not only whether the hippocampus is active during  
 100 future simulation but whether it makes a critical and necessary contribution. While it has  
 101 been long established that a functioning hippocampus is necessary for the retrieval of detailed  
 102 autobiographical memories (for a review, see Moscovitch et al., 2005), it is less clear whether  
 103 this is the case for future simulation (see Table 1 for a summary of patient cases discussed  
 104 herein). While some patients with hippocampal damage and impaired episodic memory also  
 105 exhibit difficulties in imagining detailed and coherent future events (Andelman, Hoofien,  
 106 Goldberg, Aizenstein, & Neufeld, 2010; Hassabis, Kumaran, Vann, & Maguire, 2007; Race,  
 107 Keane, & Verfaellie, 2011), other studies do not report imagination deficits in such patients.  
 108 Spared simulation abilities in the context of hippocampal damage and memory loss have been  
 109 reported in an adult developmental amnesic patient (Maguire, Vargha-Khadem, & Hassabis,  
 110 2010), a group of developmental amnesic school-aged children (Cooper, Vargha-Khadem,  
 111 Gadian, & Maguire, 2011; see also, Hurley, Maguire, & Vargha-Khadem, in press), and a  
 112 group of adult patients with bilateral hippocampal damage (Squire et al., 2010).

113  
 114 --Insert Table 1 about here--  
 115

116 Such findings imply that a fully intact hippocampus may not be required for future  
 117 simulation. However, the inconsistent results yielded from these studies raise a number of  
 118 important questions. Does the temporal extent of amnesia influence the degree to which  
 119 imagined scenarios can be constructed? Does the age of onset of hippocampal damage affect  
 120 the degree of impairment? Does the location of the damage within the hippocampus influence  
 121 the pattern of spared and impaired abilities? Can residual hippocampal tissue support future  
 122 simulation? Are particular simulation tasks better able to detect deficits? In considering the  
 123 findings from patient studies in conjunction with those from neuroimaging literature, we will  
 124 attempt to reconcile these discrepant results by suggesting that different component processes  
 125 of future simulation may be differentially affected by hippocampal damage: although the  
 126 processes of accessing and recombining details to construct and encode a future event are  
 127 inherently related processes in healthy individuals, it is possible that in the damaged brain  
 128 these processes are, to some extent, dissociable.

129

## 130 **2. Access to memory details: the episodic fodder for future simulations**

131

132 In recent years, neuroimaging has provided evidence to suggest that imagining the future  
 133 relies on much of the same neural machinery as remembering the past. One hypothesis that  
 134 such findings motivate is that memories must be reactivated in order to extract the  
 135 information needed to ‘flesh out’ detailed simulations. Indeed, if simulations involve the

136 projection of the self in time beyond the present (Buckner & Carroll, 2007) and are to be  
137 meaningful for that individual, then personally-relevant episodic details from memory are  
138 needed. Such elements would include the major components of an episode, including the  
139 people, places and objects previously encountered by the individual. In their scene  
140 construction hypothesis, Hassabis and Maguire (2007) argue that spatial information is  
141 particularly important. A spatial framework provides a platform upon which to build the  
142 scenario, and without this, an imagined event would likely lack a sense of coherence.

143

144 Although common hippocampal activity for past and future events is suggestive of access to  
145 mnemonic information during both tasks, it is not conclusive. Addis and Schacter (2008)  
146 examined whether hippocampal responses during remembering and imagining were  
147 modulated by subjective ratings of the detail comprising these events. Activity in the  
148 posterior hippocampus correlated with detail ratings for both past and future events,  
149 consistent with the idea that both tasks require access to episodic details. Moreover, Weiler,  
150 Suchan and Daum (2010b) found activity in the posterior hippocampus was associated with  
151 both past and future events, though the responses had differing timecourses. Nevertheless, the  
152 location of this neural response dovetails with studies implicating the posterior hippocampus  
153 in retrieval as opposed to encoding (Lepage, Habib, & Tulving, 1998; Prince, Daselaar, &  
154 Cabeza, 2005; Schacter & Wagner, 1999), in the reinstatement of previous conditions  
155 (Giovanello, Schnyer, & Verfaellie, 2009; Preston, Shrager, Dudukovic, & Gabrieli, 2004),  
156 and in the amount of detail comprising autobiographical memory (Addis, Moscovitch,  
157 Crawley, & McAndrews, 2004).

158

159 However, the most convincing evidence that access to episodic details may be *necessary* for  
160 future simulations comes from studies of patients with memory loss (see Table 1). One of the  
161 early observations of a link between past and future thinking came from Tulving (1985). In a  
162 discussion of K.C., a patient with dense autobiographical amnesia resulting from a head  
163 injury, it was also noted that K.C. exhibited difficulties in imagining specific episodes in his  
164 personal future. Similarly, amnesic patient D.B., who sustained brain damage as a result of  
165 cardiac arrest and anoxia, cannot remember or imagine personal events (Klein, Loftus, &  
166 Kihlstrom, 2002). In both cases, the neuroanatomical damage is not restricted to the  
167 hippocampus (patient KC has damage in and beyond the hippocampus, including extensive  
168 prefrontal damage, Rosenbaum et al., 2005; no neuroanatomical findings have been reported  
169 for patient D.B.). Nevertheless, these reports raised the possibility that there is a link between  
170 remembering and imagining – that being able to access details from episodic memory may be  
171 an important and perhaps necessary condition of the successful construction of episodic  
172 simulations.

173

174 Similar results have been reported in patients with damage reported to be limited to the  
175 hippocampus. Hassabis et al. (2007) found that four out of five patients with hippocampal  
176 amnesia could not construct imaginary scenarios of everyday scenes: their constructions  
177 contained significantly less content than those of controls, and the details that were generated  
178 were not well integrated. Although the authors also found that providing patients with details  
179 did not improve their performance, the provided information was semantic in nature and  
180 therefore may not have been sufficient to support imaginings that have an episodic basis. One  
181 critical issue is whether these patients have damage circumscribed to the hippocampus.  
182 Although Maguire and Hassabis (2011) state these patients were “specifically selected” for  
183 damaged restricted to the hippocampus, Squire and colleagues (Squire, McDuff, & Frascino,  
184 2011) disagree with this assessment. They argue that aspects of the clinical profiles of these

185 patients (e.g., generalized atrophy, seizures, personality change) suggest the presence of  
186 damage outside of the hippocampus. They also note that the one patient in the Hassabis et al.  
187 (2007) study who did not exhibit imagination deficits had a different etiology  
188 (meningoencephalitis and recurrent meningitis, versus limbic encephalitis in the four other  
189 patients), as well as residual hippocampal tissue and function (Hassabis et al., 2007).

190

191 Race and colleagues (2011) examined the ability to remember and imagine in a group of  
192 eight amnesic patients with medial temporal damage. This study is important for two reasons.  
193 First, the paradigm included a condition in which participants were required to construct  
194 narratives when the details did not have to be retrieved from memory but were presented as  
195 pictures (also see Gaesser, Sacchetti, Addis, & Schacter, 2011). When completing the past  
196 and future tasks, amnesic patients generated significantly fewer episodic details than did  
197 controls, and the number of episodic details for past and future narratives was correlated.  
198 Critically, hippocampal damage did not disrupt the ability to construct a narrative in the  
199 picture condition, where access to episodic memory was not required. Moreover,  
200 performance on the picture narrative task was not correlated with performance on the future  
201 task. Second, although the etiology and extent of damage varied across the eight patients,  
202 there was one patient in whom damage was confirmed as being limited to the hippocampus.  
203 Importantly, the performance of this patient mirrored that of the other patients who had some  
204 degree of extra-hippocampal temporal damage, suggesting that damage to the hippocampus  
205 alone is sufficient to disrupt future simulation. Together, the observations from this study  
206 further support the notion that in the context of hippocampal damage, it is an inability to  
207 access details in episodic memory, and not more general deficits in narrative ability, that  
208 underlies deficient episodic simulation performance.

209

210 While studies of amnesia give insight into the ability to simulate when there is little, or no,  
211 access to episodic details, studies of aging -- where deficits in accessing past events are  
212 present but comparatively milder -- have also provided relevant evidence. In a series of  
213 studies, we have examined the ability to remember and imagine in healthy and also in  
214 pathological aging (i.e., patients in the early stages of Alzheimer's disease), in which  
215 autobiographical memory is typically affected (Levine, Svoboda, Hay, Winocur, &  
216 Moscovitch, 2002), and hippocampal atrophy and dysfunction are also evident (Hedden &  
217 Gabrieli, 2004). In these studies, we had participants generate memories of past events and  
218 simulations of future events in response to word cues and found that the number of episodic  
219 details comprising events in older or demented adults was reduced relative to appropriate  
220 control groups (for a review, see Schacter, Gaesser, & Addis, 2010). Moreover, the number  
221 of episodic details for past events is strongly correlated with the number of details comprising  
222 future events. These correlations are consistently evident across old and young (Addis,  
223 Musicaro, Pan, & Schacter, 2010; Addis, Wong, & Schacter, 2008), and across demented and  
224 healthy older adults (Addis, Sacchetti, Ally, Budson, & Schacter, 2009), and exist even when  
225 controlling other factors that may more generally influence the detail of narratives, such as  
226 cognitive decline and verbal fluency (Addis, Sacchetti, et al., 2009). The deficits in episodic  
227 remembering and imagining that we have documented in older adults do also extend to a  
228 picture description task that does not require episodic memory (Gaesser et al., 2011).  
229 Nonetheless, we also found that the age deficits in remembering and imagining were still  
230 observed after controlling for general narrative abilities, as measured by this picture  
231 description task. Neuroimaging evidence suggests that the reduction in episodic detail when  
232 older adults describe past and future events may be related to dysfunction in the regions  
233 supporting episodic detail, including the hippocampus (Addis, Roberts, & Schacter, 2011).

234

235 What is to be made, then, of patients with memory loss who can still imagine the future?  
236 Such findings appear to speak against the idea that access to memories is a critical precursor  
237 to future simulation. As noted earlier, Squire et al. (2010) reported that a group of patients  
238 with damage to the hippocampus showed an intact ability to create detailed imaginary future  
239 events. However, although these patients have hippocampal damage, it is notable that their  
240 degree of retrograde amnesia is minimal: these patients can retrieve events from the remote  
241 past, and only exhibit a mild (and non-significant) deficit for retrieving memories from the  
242 recent past. Thus, the results of this study could also be interpreted as supporting the notion  
243 that access to the past – even in the context of hippocampal damage – can provide a basis for  
244 imagining the future.

245

246 However, there are reported cases of hippocampal damage that has differentially affected  
247 remembering but not imagining. For instance, Maguire and colleagues reported that  
248 developmentally amnesic patients who sustained hippocampal damage early in life can  
249 construct imaginary scenarios (Maguire et al., 2010; Hurley et al., in press; but see, Kwan,  
250 Carson, Addis, & Rosenbaum, 2010). Moreover, as noted earlier, one of the patients from the  
251 Hassabis et al. (2007) study could also complete their scene construction task. Interestingly,  
252 some of these patients have been noted to have residual hippocampal tissue that appears to be  
253 functional, in that it is activated during memory tasks (Maguire et al., 2010), although such  
254 activation has not yet been shown during future simulation. These researchers also report  
255 normal imagination abilities in a group of children with hippocampal damage and amnesia  
256 (Cooper et al., 2011), further suggesting that the time of onset of the amnesia may be an  
257 important consideration. It is possible that with early damage, these patients develop other  
258 strategies or rely either on residual episodic memories or detailed semantic information to  
259 construct scenarios (Cooper et al., 2011).

260

261 It is also notable that these findings have emerged using the scene construction task. Hassabis  
262 et al. (2007) mention that this task was designed to “increase the dependence of constructions  
263 on generalized semantic memory representations”. On each trial, a sentence cue (e.g.,  
264 “Imagine you are lying on a white sandy beach”) is provided to take participants into a  
265 generic scene; it is very likely that this scene can then be fleshed out with semantic detail.  
266 Thus, it is possible that these patients are able to complete this particular imagination task  
267 using detailed yet semantic representations of how certain scenes or episodes unfold, rather  
268 than extracting information from their own experiences. However, when the task requires  
269 creation of a specific and novel episode, similar patients (e.g., with developmental amnesia)  
270 show simulation deficits – particularly in the amount of episodic detail generated (Kwan et  
271 al., 2010). Although amnesics may generate fewer episodic details relative to controls, they  
272 sometimes show little or no reduction in the number of semantic details comprising their  
273 event narratives (Race et al., 2011). It has also been shown in other studies that patients with  
274 episodic, but not semantic, memory deficits can successfully complete future thinking tasks  
275 that are based primarily on general knowledge (e.g., non-personal future tasks; Klein et al.,  
276 2002).

277

278 When faced with reduced or no access to episodic memory, it may be a natural compensation  
279 strategy to rely on semantic information to aid in describing autobiographical events. Using a  
280 scoring technique that specifically parses episodic from non-episodic information (Levine et  
281 al., 2002), we have also found that although older adults show a decline in the amount of  
282 episodic detail comprising their past and future events, they show a corresponding increase in

283 the amount of non-episodic, conceptual information (Addis et al., 2010; Addis et al., 2008;  
 284 note also that this pattern extends to picture description; Gaesser et al., 2011). In line with  
 285 this finding, older adults also show an increase, relative to young, in their recruitment of  
 286 lateral temporal regions during autobiographical tasks (Addis et al., in revision); these regions  
 287 are thought to mediate semantic and conceptual autobiographical information (Addis,  
 288 McIntosh, Moscovitch, Crawley, & McAndrews, 2004; Graham, Lee, Brett, & Patterson,  
 289 2003).

290

291 Another key question is whether access to episodic details is *sufficient* for future simulation  
 292 to occur. It is likely that this ability is only a starting point; once episodic details are  
 293 extracted, they still have to be used in a meaningful way, which we have argued requires  
 294 additional processes such as detail recombination (e.g., Addis & Schacter, 2008; Schacter &  
 295 Addis, 2009). Nonetheless, the findings discussed earlier of intact future simulation  
 296 performance in hippocampal amnesics with relatively preserved autobiographical memories  
 297 (Squire et al., 2010) suggests that access to episodic details may be sufficient for future  
 298 simulation. By contrast, Andelman et al. (2010) reported a case study of a patient, M.C., with  
 299 a bilateral hippocampal lesion and loss of autobiographical memory restricted only to the past  
 300 3 years. Thus, at 27 years of age, she still had approximately 20 years of episodic memories  
 301 to draw upon when completing a future simulation task. M.C. was, however, unable to do so:  
 302 when asked to describe her personal future, her responses were vague and general, or she  
 303 reported that she simply didn't know. Because there was no quantitative assessment of future  
 304 simulation performance in this case, the results must be interpreted cautiously. Still, they  
 305 raise the possibility that while access to episodic details may be necessary in order to  
 306 construct episodic simulations, it may not be sufficient.

307

### 308 **3. Detail recombination: constructing a coherent scenario**

309

310 As we have reviewed above, being able to access details from episodic memory can be  
 311 conceptualized as an initial stage in the process of episodic simulation. Of course, having a  
 312 jumble of details is useless if they cannot be recombined and integrated appropriately. We  
 313 have argued that 'detail recombination' is critical to imagining coherent scenarios – the kinds  
 314 of simulations one creates when thinking about experiences relevant in their daily lives.  
 315 Given the role of the hippocampus, particularly the anterior hippocampus, in relational  
 316 processing, we have argued that this region is likely critical in the ability to form coherent  
 317 scenarios (e.g., Addis & Schacter, 2008; Schacter & Addis, 2009).

318

319 This proposal is based on an integration of findings from various neuroimaging studies. An  
 320 early meta-analysis of medial temporal activity during memory tasks reported that the  
 321 anterior portion of the hippocampus appears to be particularly responsive to tasks with  
 322 relational demands (Schacter & Wagner, 1999); subsequent work has further supported this  
 323 anterior localization of relational memory processes (e.g., Chua, Schacter, Rand-Giovannetti,  
 324 & Sperling, 2007; Giovanello, Schnyer, & Verfaellie, 2004; Jackson & Schacter, 2004;  
 325 Kirwan & Stark, 2004; Staresina & Davachi, 2008, 2009). The role of this region within the  
 326 realm of relational memory may be further refined, based on findings from Preston et al.  
 327 (2004; see also Heckers, Zalesak, Weiss, Ditman, & Titone, 2004). This work suggests that  
 328 the anterior hippocampus may be particularly involved in the recombination of details  
 329 extracted from various memories. Using a transitive inference paradigm, participants first  
 330 learned to associate one set of items (faces, A) with another set of items (houses, B). They  
 331 then learned to associate those same houses (B) with a new set of items (novel faces, C).

332 During the scanning session, seeing items (A, B, or C) taken from any of the memories (A-B,  
333 B-C) resulted in posterior hippocampal activity, further implicating the posterior  
334 hippocampus in retrieval or reinstatement. However, seeing novel rearrangements of such  
335 details (A-C) resulted in selective anterior hippocampal activity. This recombination process  
336 can be considered analogous to future simulation, where we argue details extracted from  
337 different memories that may have not been encountered together in reality, are rearranged in  
338 imagination – and similarly, this recombination process should also engage the anterior  
339 hippocampus.

340

341 More recently, Staresina and Davachi (2009) investigated hippocampal responses to the  
342 process of integrating details across time and space. They identified a region in the anterior  
343 hippocampus that was more responsive when details were presented in a spatiotemporally  
344 discontinuous manner (i.e., separated across time and space) and required integration, relative  
345 to when details were presented in a contiguous, integrated form. Conceptually, we suggest  
346 that this process again maps onto the kind of recombination thought to occur during  
347 simulation: an integration of details from memories formed in different spatiotemporal  
348 contexts.

349

350 The findings of Preston et al. (2004) and Staresina and Davachi (2009) dovetail with those  
351 from a neuroimaging study of past and future detail. In that study, we (Addis & Schacter,  
352 2008) found common responses to detail of past and future events in posterior hippocampus,  
353 but the anterior hippocampus was responsive only to the amount of detail comprising future  
354 events – which are presumably recombined across spatiotemporally distinct experiences.  
355 Interestingly, we have replicated the finding of differential future activity within the anterior  
356 hippocampus across a number of studies using autobiographical cuing (e.g., Addis, Wong, et  
357 al., 2007; adapted from Crovitz & Schiffman, 1974) and experimental recombination  
358 paradigms (Addis, Pan, et al., 2009). While the cuing task requires an individual to generate  
359 future events from generic cues (nouns), the experimental recombination paradigm uses  
360 random rearrangements of episodic details (persons, places, objects) taken from the  
361 individual's own memories, thus ensuring that detail recombination occurs. Moreover, these  
362 paradigms enable examination of activity during the initial construction of the future event  
363 when the cue is presented, and the subsequent elaboration of the event once it is in mind.  
364 With this approach, we have found that over the course of a simulation trial, this activity  
365 typically emerges during the initial construction phase rather than being evident throughout  
366 the duration of a simulation trial (Addis, Cheng, Roberts, & Schacter, 2011; Addis, Pan, et  
367 al., 2009; Addis, Wong, et al., 2007; Martin, Schacter, Corballis, & Addis, 2011). This  
368 temporal pattern suggests that the differential future-related activity is associated with  
369 processes occurring early in the construction of future events, when detail recombination  
370 would be expected to occur. Other labs have also reported similar future>past effects in the  
371 anterior hippocampus. For instance, Weiler and colleagues (Weiler, Suchan, & Daum, 2010a)  
372 found that imagining future events that had a low probability of occurring during the  
373 upcoming holidays was associated with more anterior hippocampal activity than events with  
374 a higher probability of occurring. The authors suggested that perhaps low probability events  
375 place a higher demand on the binding of disparate event features relative to high probability  
376 events that may be already planned.

377

378 Determining the boundary conditions of the future>past effect will provide a better  
379 understanding of whether detail recombination is important for engaging the anterior aspect  
380 of the hippocampus. Importantly, we have recently shown that this effect is limited to certain

381 types of future events. We examined hippocampal activity when imagining specific (unique)  
382 and general (routine) future events, hypothesizing that constructing a specific future event  
383 should place greater demand on recombining details and hippocampal resources relative to  
384 constructing a generic future event that more closely relies on conceptual knowledge about  
385 routines (Addis et al., 2011). Indeed, our analysis supported this hypothesis, demonstrating  
386 that hippocampal activity was strongest when imagining specific future events relative to  
387 more generic and routinized ones. Participant ratings confirmed that specific future events  
388 were more detailed and novel than general future events, further suggesting that the process  
389 of constructing an event that is both detailed *and* novel engages the anterior hippocampal  
390 region. Additionally, because these findings suggest that the hippocampus is not strongly  
391 engaged by constructing generic future events, it may not be surprising that patients with  
392 hippocampal damage can imagine the future in a gist-like, conceptual manner.

393

394 These observations from neuroimaging studies suggest that dysfunction in the hippocampus  
395 may result in deficits in recombining details. Several findings suggest the presence of such  
396 difficulties. Hassabis et al. (2007) found that not only did the events constructed by  
397 hippocampal amnesics lack content overall, but the details they did generate were not well  
398 integrated and lacked a spatial coherence. In healthy older adults who show some degree of  
399 structural and functional dysfunction in the hippocampus (Hedden & Gabrieli, 2004), we  
400 found that the integration of memory details into simulations was reduced relative to young  
401 adults (Addis et al., 2010). Using the experimental recombination paradigm, we  
402 experimentally ‘extracted’ person, place and object details from different past events; random  
403 recombinations of a participant’s memory details were later presented during a future  
404 simulation task. Importantly, each future simulation was required to include the person, place  
405 and object details presented. While both groups were able to include all three details in the  
406 simulations, the young group was better able to integrate these three details into the same  
407 imagined spatiotemporal context. In contrast, older adults integrated on average two of the  
408 three details into the same spatiotemporal context, and then often touched on the third detail  
409 in a separate context, essentially resulting in a series of ‘mini-events’. These findings  
410 suggests that even with experimental support to access details from various episodic  
411 memories, the ability to integrate these details into a coherent scenario with a specific  
412 temporal and spatial context may be reduced in populations with compromised hippocampal  
413 function.

414

415 Again, one might raise the question that if the hippocampus is necessary for detail  
416 recombination, how is it that some patients with hippocampal damage can imagine seemingly  
417 coherent future events? One issue is that not every study of future simulation in patients  
418 includes a measure of detail integration or spatial coherence and thus in instances where  
419 hippocampal patients can successfully imagine, it can be difficult to determine whether the  
420 scenarios constructed were in fact coherent. Maguire and Hassabis (2011) argue that the  
421 number of spatial references produced by the patients studied by Squire et al. (2010) appear  
422 reduced relative to the typical level of controls, suggesting that these patients may have been  
423 creating primarily semantic representations. Moreover, it is possible to imagine a future event  
424 with minimal, if any, detail recombination: one can “recast” past events into the future. It is  
425 possible that paradigms using single cues may elicit recasting. For instance, if shown the cue  
426 word “car”, one might recall a relevant experience (“my car breaking down and my husband  
427 picking me up”) and then imagine that experience unfolding in the same way in future. In  
428 many protocols, it is ensured that participants are generated novel scenarios (e.g., Addis,  
429 Wong, et al., 2007, 2008; Hassabis et al., 2007), but this is not always done or reported. In

430 order to circumvent this possibility, we designed an experimental recombination paradigm in  
 431 which participants are required to recombine details extracted from their own past events  
 432 (Addis et al., 2009). Although this paradigm has been employed with older adults (Addis et  
 433 al., 2010), replicating our findings using the cue word paradigm, it has not yet been used to  
 434 assess recombination abilities in patients with circumscribed hippocampal damage. The  
 435 results of such a study would be of considerable interest.

436

#### 437 **4. Memory for the future: encoding future simulations**

438

439 Differential engagement of the anterior hippocampus may also reflect the process of encoding  
 440 newly-imagined scenarios. Indeed, the anterior portion of the hippocampus has been  
 441 implicated in encoding (Schacter & Wagner, 1999; Spaniol et al., 2009), particularly for  
 442 relational (e.g., Chua et al., 2007; Jackson & Schacter, 2004; Kirwan & Stark, 2004;  
 443 Staresina & Davachi, 2008, 2009) and novel (Kohler, Danckert, Gati, & Menon, 2005)  
 444 information. If the adaptive significance of simulating several alternative “behavioral modes”  
 445 is to maximize success in anticipated situations (Ingvar, 1985) and flexible planning (Boyer,  
 446 2008), then retaining this “fitness-relevant” information in memory for future reference is a  
 447 necessary step. Nairne, Thompson and Pandeirada (2007) investigated whether information  
 448 relevant to survival is remembered better than survival-irrelevant information. In that study,  
 449 participants judged whether items were relevant to survival (having provisions and  
 450 protection) or moving (moving to a foreign country) situations, or judged the items for  
 451 pleasantness. In line with the idea that we are tuned to remember fitness-relevant information,  
 452 subsequent memory performance was boosted for items rated as survival-relevant.  
 453 Interestingly, more recent work using a variant of the paradigm developed by Nairne and  
 454 colleagues suggests that the much of the benefit of “survival processing” may be attributable  
 455 to the engagement of encoding processes that support planning for the future (Klein,  
 456 Robertson, & Delton, 2010).

457

458 Three kinds of evidence demonstrate the adaptive value of simulations. First, it is well  
 459 established that simulations play an important role in psychological well-being. Being able to  
 460 generate specific and detailed simulations of future events can enhance one’s ability to cope  
 461 with upcoming situations (Brown, MacLeod, Tata, & Goddard, 2002; Taylor, Pham, Rivkin,  
 462 & Armor, 1998; Taylor & Schneider, 1989). For instance, creating simulations about positive  
 463 future outcomes can improve emotion regulation, resulting in decreased amounts of worry  
 464 related to upcoming future events (Brown et al., 2002). In addition to helping one cope with  
 465 the prospect of an upcoming event, mentally simulating appropriate actions for future  
 466 stressful situations can enhance one’s ability to cope if and when those situations arise  
 467 (Taylor & Schneider, 1989).

468

469 Second, simulations are used when attempting to solve open-ended or ill-defined problems,  
 470 where different possible solution paths need to be mentally evaluated. Using the Means-Ends  
 471 Problem Solving Test, Sheldon and colleagues (Sheldon, McAndrews, & Moscovitch, 2011)  
 472 examined the ability of older adults and patients with temporal lobe epilepsy to solve open-  
 473 ended social problems. Both of these groups are known to have some degree of impairment  
 474 on tasks of autobiographical memory (Addis, Moscovitch, & McAndrews, 2007; Levine et  
 475 al., 2002; St-Laurent, Moscovitch, Levine, & McAndrews, 2009); older adults are also known  
 476 to show reduced performance on episodic simulation tasks (Addis et al., 2008). It was found  
 477 that when simulating solutions to ill-defined problems, both groups generated fewer relevant  
 478 steps than controls. This finding suggests that without full access to episodic memory and the

479 ability to generate detailed simulations, the effectiveness of problem solving is reduced (for  
480 relevant neuroimaging evidence, see Gerlach, Spreng, Gilmore, & Schacter, 2011; Spreng,  
481 Stevens, Chamberlain, Gilmore, & Schacter, 2010).

482

483 Third, recent studies have demonstrated that episodic simulation has a significant impact on  
484 temporal discounting of future rewards: when people imagine experiencing a reward in the  
485 future, they show an increased tendency to favor rewards that produce greater long-term  
486 payoffs, thereby countering the normal tendency to devalue delayed rewards (Benoit, Gilbert,  
487 & Burgess, 2011; Peters & Büchel, 2010). Interestingly, fMRI data reveal that these effects  
488 of episodic simulation on temporal discounting are associated with increased coupling  
489 between activity in the hippocampus and prefrontal regions involved in reward representation  
490 (Benoit et al., 2011; Peters & Büchel, 2010). Related studies have shown that varying the  
491 manner in which memory is queried can also influence temporal discounting toward long-  
492 term payoffs when memory queries emphasize the production of patient (vs. impatient)  
493 thoughts (Weber et al., 2007). It would be interesting to approach effects of episodic  
494 simulation on temporal discounting from the theoretical perspective of query theory  
495 (Johnson, Haubl, & Keinan, 2007) and to determine whether the memory-based effects on  
496 temporal discounting have a similar neural basis to those shown for episodic simulation.

497

498 In order to influence future behaviors and realize these adaptive benefits of simulation, it is  
499 important that simulations are encoded and maintained in memory (Ingvar, 1985; Szpunar,  
500 Addis, & Schacter, in press). There is indirect evidence to support this idea. For instance,  
501 individuals tend to act in a way that is consistent with or constrained by how they have  
502 imagined themselves in those situations (Johnson & Sherman, 1990), implying that some  
503 record of that simulation influences later behavior. There is typically a high correspondence  
504 of stated intentions and subsequent behavior (Fishbein & Ajzen, 1980). Consider also  
505 prospective memory, where an intention is encoded into memory and later accessed and  
506 implemented when triggered by a target event or time cue. It is likely that the intentions  
507 involved in prospective memory range in the degree to which they draw upon simulations.  
508 Particularly relevant to the idea of episodic simulation is the process of forming  
509 “implementation intentions” (Gollwitzer, 1999) which involve imagining and rehearsing a  
510 plan with reference to the specific future context in which it will be executed. Research has  
511 shown that creating implementation intentions significantly increases the likelihood of  
512 carrying out that intention (Chasteen, Park, & Schwarz, 2001; Orbell, Hodgkins, & Sheeran,  
513 1997), again suggesting that these simulations are not only stored in memory but do influence  
514 future behavior. Poppenk and colleagues (Poppenk, Moscovitch, McIntosh, Ozcelik, & Craik,  
515 2010) directly investigated the process of encoding intentions, using fMRI to see whether  
516 later memory for intentions was associated with hippocampal activity during encoding. They  
517 found that successful encoding of intentions engaged the hippocampus, as did the encoding of  
518 other forms of information, such as present actions. But unique to the prospective task was  
519 the recruitment of frontopolar cortex, consistent with finding that damage to this region  
520 results in deficits of prospective memory (e.g., Burgess, Veitch, de Lacy Costello, & Shallice,  
521 2000).

522

523 If the involvement of the hippocampus in future simulation is only to encode imagined  
524 scenarios, then hippocampal damage would not necessarily result in an inability to construct  
525 simulations – just an inability to encode and retain them. There are some data to suggest that  
526 this might be the case (see Table 1). For instance, although children with hippocampal  
527 damage can imagine scenarios, when asked to recall them the following day, they do so with

528 less accuracy and consistency than healthy controls (Cooper et al., 2011). Additionally, adults  
 529 with hippocampal damage appear to repeat themselves more than controls when describing  
 530 future events, possibly indicative of a failure to sufficiently encode the scenario as it is  
 531 constructed (Squire et al., 2010).

532

533 We conducted an fMRI study (Martin et al., 2011) to investigate whether hippocampal  
 534 activity during future simulation is indeed related to successful encoding by incorporating the  
 535 experimental recombination (Addis, Pan, et al., 2009) and subsequent memory (e.g., Wagner  
 536 et al., 1998) paradigms. During scanning, participants were presented with random  
 537 recombinations of person, location, and object details taken from their own memories and for  
 538 each set of details, they imagined a novel future event involving all three details. After  
 539 scanning, participants completed an unexpected cued recall test, in which they were showed  
 540 two details and had to recall the third. By this design, we had an objective measure of  
 541 whether the critical details comprising each simulation were successfully encoded. As  
 542 predicted, successfully encoded simulations were associated with greater activity in the  
 543 anterior right hippocampus than simulations that were later forgotten. Moreover, the posterior  
 544 right hippocampus was also modulated by encoding success. A functional connectivity  
 545 analysis revealed that both the anterior and posterior hippocampus exhibited connectivity  
 546 with each other and a wider brain network (including medial prefrontal and medial parietal  
 547 regions) during successful encoding. When encoding was not successful, the posterior  
 548 hippocampus did not show this pattern of connectivity. However, it is interesting to note that  
 549 during unsuccessful encoding, the anterior region still exhibited connectivity with the wider  
 550 core network. It is possible that this neural pattern reflects the attempt to construct a  
 551 simulation, even if it is ultimately not encoded sufficiently to be recalled later. We also  
 552 found that the imagined events that were later-remembered were on average more detailed  
 553 than later-forgotten ones, and activity in regions exhibiting an encoding effect was also  
 554 modulated by the level of detail. Together, these observations suggest that constructing a  
 555 memorable scenario may be related, at least in part, to how well the composite details were  
 556 retrieved from memory and recombined.

557

## 558 **5. Future directions: mapping component processes to hippocampal regions**

559

560 Considering together the patient and neuroimaging data reviewed here, there appears to be  
 561 evidence supporting the idea that there are three important component processes involved in  
 562 the simulation of episodic future events. First, details stored in episodic memory with which  
 563 to furnish the simulation must be accessed. Second, the details extracted from various  
 564 memories need to be recombined and integrated into a spatiotemporal context in order imbue  
 565 a simulation with a sense of coherence. Third, if a simulation is to influence and guide future  
 566 behaviours, it needs to be successfully encoded into memory. The evidence reviewed herein  
 567 suggests that these different processes all rely, to some extent, on the hippocampus. It  
 568 remains an open and important question as to whether different subregions of the  
 569 hippocampus are specifically associated with specific component processes. While the  
 570 posterior hippocampus likely supports the retrieval of previously experienced details,  
 571 particularly those spatial in nature, the anterior hippocampus supports the recombination of  
 572 extracted details into a coherent scenario, and both regions support successful encoding.

573

574 This framework may be able to inform the debate on whether hippocampal damage disrupts  
 575 the ability to imagine the future (Maguire & Hassabis, 2011; Squire et al., 2010). It is critical  
 576 that future research on patients with hippocampal damage employ more refined experimental

577 designs to probe whether detail access, detail recombination and/or encoding of simulations  
578 is disrupted. The case study approach may particularly important here. There is considerable  
579 variance of performance across patients with hippocampal damage, and it will be important to  
580 understand the specific patterns of spared and impaired sub-processes within each case.  
581 Moreover, it is likely that the nature and location of damage to the hippocampus is critical.  
582 Differential impairments of the construction and/or encoding of future simulations may  
583 emerge depending on the nature of the hippocampal damage: whether it is confined to the  
584 anterior and/or posterior aspects, affects primarily the right hippocampus, affects the entirety  
585 of the structure, or extends beyond its boundaries. Moreover, it will be critical in future  
586 studies to ascertain whether damage in amnesic patients is restricted to the hippocampus or  
587 extends more broadly.

588  
589 Another challenge will be to find ways in which to differentiate the process of recombining  
590 details to construct a simulation and the encoding of those simulations. These processes are  
591 closely related in two ways: cognitively, with more detailed simulations being more  
592 successfully encoded; and neurally, with both processes engaging the anterior right  
593 hippocampus. As such, they may be difficult to disentangle. One fruitful avenue may be to  
594 investigate whether detail recombination and successful encoding are mediated by specific  
595 hippocampal subfields. The hippocampal formation is a circuit comprised of several  
596 anatomically-distinct subregions, including the dentate gyrus, three cornu ammonis  
597 (CA<sub>1</sub>/CA<sub>2</sub>/CA<sub>3</sub>) areas, and the subiculum. Recent work suggests a functional distinction  
598 between the input structures into the hippocampus (dentate gyrus/CA<sub>2</sub>/CA<sub>3</sub>) and the output  
599 (subiculum/CA<sub>1</sub>). Specifically, while the input structures appear to be involved in encoding,  
600 the output structures may be more involved in binding (Carr, Rissman, & Wagner, 2010).  
601 Moreover, the finding that the dentate gyrus is involved in encoding is consistent with the  
602 hypothesis that the ability to form temporal associations among new experiences that happen  
603 close together in time is ultimately dependent upon the continuous production of new-born  
604 granule cells in the dentate gyrus (Aimone, Wiles, & Gage, 2006; Deng, Aimone, & Gage,  
605 2010). Extrapolating these findings to the realm of future simulation, it is possible that detail  
606 recombination during future simulation may be differentially associated with CA<sub>1</sub>/subiculum,  
607 and successful encoding with dentate gyrus/CA<sub>2</sub>/CA<sub>3</sub>. Recent developments in ultra-high-  
608 field 7T MRI to obtain exceptionally high resolution images of hippocampal subfield  
609 anatomy – including distinct layers within subfields (e.g. Kerchner et al., 2010) – will no  
610 doubt facilitate more detailed investigations of the roles of different hippocampal subfields.

611  
612 Neuroimaging studies to date suggest there may also be lateralization effects in the  
613 hippocampal activity that is differentially associated with future thinking. Specifically, we  
614 initially reported that hippocampal activity common to past and future events was evident in  
615 the left hippocampus, but that the future>past effect was specific to the right hippocampus  
616 (Addis, Wong, et al., 2007). A number of other studies finding future-related activity also  
617 report a right lateralization (Addis et al., 2011; Martin et al., 2011; Weiler et al., 2010a,  
618 2010b), although some studies report such activity is bilateral (Addis, Pan, et al., 2009).  
619 Interestingly, a patient with damage that affected only the right hippocampus exhibited  
620 difficulties in generating detailed future simulations (Race et al., 2011), suggesting the right  
621 hippocampus may indeed be critical to this ability. However, it remains to be determined  
622 what specific contribution the right hippocampus might be making to future simulation.

623  
624 The research considered here is in an early stage of development. It is only during the past  
625 few years that studies examining the contribution of the hippocampus to imagining the future

626 have begun in earnest, and it is clear that much remains to be learned. Further integration of  
 627 this new line of work with more firmly established research on hippocampal contributions to  
 628 memory encoding and retrieval will be critical to advancing our understanding, as will  
 629 integration with animal studies of such related phenomena as prospective coding in the  
 630 hippocampus (e.g., Ferbinteanu & Shapiro, 2003; Foster & Wilson, 2006; Johnson & Redish,  
 631 2007; for discussion, see Buckner, 2010). We are hopeful that these kinds of studies will  
 632 help to increase our understanding of the neural and cognitive processes that link memory  
 633 and imagination, and in so doing, provide new insights into how the future depends on the  
 634 past.

635

636

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644

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