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NOVELTY PREFERENCE IN PATIENTS WITH DEVELOPMENTAL AMNESIA

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Abstract

To re-examine whether or not selective hippocampal damage reduces novelty preference in visual paired comparison (VPC), we presented two different versions of the task to a group of patients with developmental amnesia (DA), each of whom sustained this form of pathology early in life. Compared with normal control participants, the DA group showed a delay-dependent reduction in novelty preference on one version of the task and an overall reduction on both versions combined. Because VPC is widely considered to be a measure of incidental recognition, the results appear to support the view that the hippocampus contributes to recognition memory. A difficulty for this conclusion, however, is that according to one current view the hippocampal contribution to recognition is limited to task conditions that encourage recollection of an item in some associated context, and according to another current view, to recognition of an item with the high confidence judgment that reflects a strong memory. By contrast, VPC, throughout which the participant remains entirely uninstructed other than to view the stimuli, would seem to lack such task conditions and so would likely lead to recognition based on familiarity rather than recollection or, alternatively, weak memories rather than strong. However, before concluding that the VPC impairment therefore contradicts both current views regarding the role of the hippocampus in recognition memory, two possibilities that would resolve this issue need to be investigated. One is that some variable in VPC, such as the extended period of stimulus encoding during familiarization, overrides its incidental nature, and, because this condition promotes either recollection- or strength-based recognition, renders the task hippocampal-dependent. The other possibility is that VPC, rather than providing a measure of incidental recognition, actually assesses an implicit, information-gathering process modulated by habituation, for which the hippocampus is also partly responsible, independent of its role in recognition.

Introduction

Developmental amnesia (DA), a memory disorder associated with relatively selective hippocampal damage sustained early in life (Vargha-Khadem et al., 1997), differs from complete anterograde amnesia in at least two respects. First, whereas memory for everyday

events (episodic memory) is seriously impaired in DA, memory for factual material (semantic memory) is relatively spared. Second, whereas memory retrieved through recall in DA is severely deficient, memory retrieved through recognition is relatively preserved. Neither of these two forms of selective sparing is seen in the profound anterograde amnesia that follows extensive medial temporal lobe damage, i.e. damage that includes the hippocampus but also encompasses large portions of the parahippocampal gyrus (e.g. Scoville and Milner, 1957; Westmacott and Moscovitch, 2001; Bayley and Squire, 2005; Bayley et al., 2008).

The recall-recognition dissociation, first proposed in the initial report of three cases with DA (Vargha-Khadem et al., 1997), was recently confirmed in a large cohort of such patients (Adlam et al., 2009) examined with the Doors and People test (Baddeley et al., 1994, 2006). This test, which allows direct quantitative comparison between recognition and recall for both visual and verbal material, revealed a sharp difference in the effects of early hippocampal damage on these two retrieval processes, with marked impairment in recall but little or none in recognition.

Although DA patients can thus exhibit a surprisingly high level of recognition memory, the sparing of this ability is not complete. For example, unlike item recognition, certain forms of associative recognition, particularly those that involve cross-modal association, reveal a marked deficiency in DA patients (Vargha-Khadem et al., 1997). Moreover, within the category of item recognition, task variables and instructions (such as deep levels of processing, task enactment, or presentation of items in different contexts) known to encourage the encoding of items together with some associative context yield mild but statistically significant impairment (Düzel et al., 2001; Gardiner et al., 2006; Brandt et al., 2009). The recognition tasks that DA patients perform as accurately as their normal controls are those on which the instructions are not conducive to associative encoding, or on which there are no encoding instructions at all, other than that the participant's memory will be tested (Vargha-Khadem et al., 1997; Baddeley et al., 2001; Adlam et al., 2009).

Findings similar to those described above have also been obtained in some patients with amnesia resulting from selective hippocampal pathology sustained in adulthood (Aggleton & Shaw, 1996; Holdstock et al., 2000; Mayes et al., 2004; Yonelinas et al., 2002), suggesting that when examples of both spared and impaired recognition are observed in the very same cases, it is due to the selectivity of the hippocampal injury, not to the age at which the injury occurred (Brandt et al., 2009). This possibility – that the hippocampus participates in some but not all forms of recognition memory – has generated two alternative explanations concerning the specific form of recognition to which the hippocampus contributes. One of these proposals, which is based on the division of recognition ability into two qualitatively different processes, viz. familiarity and context-based recollection (Jacoby, 1991), hypothesizes that only recollection is dependent on the hippocampus (Aggleton & Brown, 1999; Diana et al., 2007). The other proposal, though not denying the existence of two different recognition processes, views medial-temporal-lobe-dependent recognition as varying along the single dimension of memory strength, reflected in different levels of confidence, with the hippocampus mediating only the higher confidence judgments (Squire et al., 2007). Despite the considerable research effort that has recently been invested in attempts to test these alternative hypotheses directly, no consensus has yet been reached (Eichenbaum et al., 2007; Mayes et al., 2007; Brandt et al., 2009; Kirwan et al., 2010; Diana et al., 2009). Additional direct tests would clearly be valuable, but perhaps the indirect approach of exploring further those conditions under which recognition in patients with selective hippocampal damage is either intact or impaired can also advance our understanding of the role of the hippocampus in recognition memory.

One condition that has not yet been explored in DA is incidental recognition memory. A laboratory task that is widely accepted as a valid measure of this form of memory – across different species and developmental ages (Fagan, 1973; Bachevalier, 1990; Manns et al., 2000) – is visual paired comparison (VPC). In the standard version of VPC, participants are presented with a pair of identical stimuli (such as a face or a scene) for a short period of time, and then, after a delay, one member of the pair is presented again alongside a new one. Without any instruction during either familiarization or test, normal participants almost invariably look longer at the new stimulus, a spontaneous preference for novelty that is presumed to signal their recognition of the stimulus presented previously.

Two different outcomes on this task might be predicted for patients with DA. On the one hand, superficially at least, uninstructed viewing of an item during familiarization and test is the opposite of instructions conducive to encoding that item plus its associative context with the explicit intent to remember the item later, the condition under which DA patients show significantly impaired recognition; indeed, uninstructed viewing in the incidental memory conditions of VPC should promote even less encoding than instructed processing in an explicit recognition task, the situation in which they are most often *unimpaired*. Consequently, item recognition tested with the VPC task might also be expected to reveal normal levels of performance in DA. On the other hand, uninstructed viewing closely resembles the condition under which DA patients show such severely impaired memory for the stimuli encountered in the events of everyday life (i.e. episodic memory). On this basis, patients with DA might be expected to show a clear-cut impairment in VPC.

That impairment as the more likely outcome is suggested by the positive results from two studies of VPC in patients with adult-onset amnesia (McKee and Squire, 1993; Pascalis et al., 2004), although in neither study could the impairment be attributed with high confidence to selective hippocampal damage. The first of those two reports presented the mean score for a single group of 11 highly diverse amnesic cases, only two of whom had pathology that appeared to be limited to the hippocampus (Kritchevsky and Squire, 1993); two of the other cases had hippocampal plus either extrahippocampal or white matter damage, five had diencephalic pathology, and in the remaining two the pathology was unknown. The second report (Pascalis et al., 2004) was of a single case (patient YR) whose pathology was hippocampus-selective initially but whose cognitive functions began to deteriorate around the time of the VPC study, raising the possibility that the neuropathology had begun to spread.

The present study was therefore undertaken in an attempt to obtain a more definitive answer to whether or not selective hippocampal damage impairs performance on the VPC task. To this end, we compared DA patients with normal controls on two different versions of the task.

Methods

Participants

The five patients who took part in this study had each been diagnosed with developmental amnesia (DA), a disorder caused by hippocampal atrophy that is sometimes sustained in infancy or childhood consequent to episodes of hypoxia/ischaemia. As indicated above, this disorder is characterized by severe and chronic loss of episodic memory but relative preservation of both IQ and semantic memory (Vargha-Khadem et al., 1997). Details of the five patients (2 females) are listed in Table 1. Their mean age ($\pm$ SD) at the time of the current study was 25 ($\pm$ 6.3) years, and their mean percent reduction ($\pm$ SD) in hippocampal volume relative to the hippocampal volume of normal controls was 38.7 ($\pm$ 4.9) on the left, 42.1 ($\pm$ 14.5) on the right, and 40.4 ($\pm$ 9.5) percent bilaterally.

University College London (UCL) students and staff members served as the control group. In Experiment 1, there were 29 such participants (18 females), also with a mean age of $25 (\pm 3.2)$ years; and 23 of these participants (mean age, 25 ± 3.5 years; 13 females) formed the control group in Experiment 2. A separate group of 32 UCL students and staff (23.6 ± 4.6 years of age; 18 females) took part in a pre-experiment procedure for selecting the stimuli.

Apparatus

Subjects sat with their heads on a chin rest facing a 43-inch computer screen placed at a viewing distance of 61 cm while their eye position and duration of eye fixations were recorded with an eye-tracking system (Model SLA R6.1 Applied Science Laboratories, Bedford, MA, USA) equipped with digital and infrared cameras. The eye tracker recorded fixations at a frequency of 50 Hz and sent the signals to a control unit that displayed the online data on two video monitors (one for the eye image and the other for the scene display overlapped with eye fixations). The signals were also sent to a computer equipped with software (Eyenal, version 2.66), which automatically extracted the participant's fixations on the stimuli for offline analysis.

Stimuli

Stimuli consisted of coloured renditions of natural landscapes and fractal images downloaded from the internet. These stimuli were always presented in pairs of the same type. Each stimulus was 22 cm high by 16 cm wide, and the two members of the pair were placed side-by-side, 15 cm apart.

To select pairs of stimuli that engaged comparable looking times, we recorded spontaneous eye movements in the separate group of *pre-experiment participants* during an observation period in which they viewed a total of 184 pairs of stimuli (92 pairs of landscapes and 92 pairs of fractal images) for 8 s each, with interpair intervals of 2 s. To avoid causing fatigue, we divided the observation period into three 30-min sessions. An ANOVA with left-right position as the factor was used to detect significant differences ($p < 0.05$) in time spent looking at the two members of the pair. On the basis of that analysis, we selected 128 pairs of stimuli (64 pairs of landscapes and 64 pairs of fractal images) that engaged similar viewing times by both members of the pair.

Procedure

As noted above, two experiments were conducted, each with a different version of VPC.

Experiment 1—The two types of stimuli, fractals and landscapes, were each presented in a separate 32-trial session. As illustrated in Figure 1, on each trial of a session, two identical stimuli were presented for 8 s (familiarization), and, following a variable intratrial delay, one of these stimuli was shown again for 8 s, but this time appearing with the novel member of its pair (test). This sequence of familiarization followed by test was repeated for each of the 32 trial-unique stimulus pairs of a given type, with 8 such trials at each of 4 different delays (0, 5, 30, or 120 s) intermixed pseudorandomly. The intertrial interval (ITI) was 2 s, and the intratrial delays and left-right position of the novel stimulus in the test phase were counterbalanced across trials. Each of the two sessions (one with fractals, and one with landscapes) lasted ~35 min, and the order of the two, which were separated by 4–5 hours, was counterbalanced across participants. This version of the VPC task, in which each stimulus familiarization period was followed, after a variable delay, by a test trial, is referred to here as the standard version.

Experiment 2—The 32 remaining pairs of stimuli of each type (fractals and landscapes) were used in the second experiment. As before, the stimuli of one type were presented for

familiarization for 8 s each followed by the test. In this version of VPC, however, the 32 pairs of identical stimuli were presented for familiarization sequentially, with interpair intervals (IPIs) of 2 s (Fig. 1). Two seconds after familiarization of all 32 stimulus pairs was complete, the 32 stimuli, each now appearing with the novel member of its pair, were presented for test, but in reverse order, i.e. with the last familiarized stimulus appearing first, and the first familiarized stimulus appearing last, again with IPIs of 2 s. This reverse-order testing procedure resulted in delays between familiarization and test that varied from 2 s to 622 s, at delay increments of 20 s. Thus, most of the retention intervals in this experiment (maximum, about 10 min) exceeded the 2-min maximum in Experiment 1, although the entire session in Experiment 2 lasted only about 10 min, compared with 35 min for Experiment 1. As before, the left-right position of the novel stimulus at test was counterbalanced across trials. The same procedure was later repeated with the second stimulus type. Presentation of one stimulus type began 5-10 min after the end of the first session of Experiment 1, and presentation of the other type ended 5-10 min before the start of the second session of Experiment 1. Across the two experiments (1 and 2), the counterbalanced order of fractals (F) and landscapes (L) alternated in one of two sequences, either 1F-2L-2F-1 L o r 1 L-2F-2L-1F, with the order determined pseudorandomly across participants.

To keep the eye-tracking system calibrated in both experiments, participants were instructed to fixate on a central fixation point on the blank screen during the ITI (Experiment 1) or IPI (Experiment 2). To increase the likelihood that subsequent stimulus recognition memory would be incidental, participants were asked at the start of each session simply to look at the stimuli. In both experiments, the eye recordings were used to determine the total time a participant spent looking at one or the other identical stimuli during the 8 s of familiarization, as well as the amount of time spent looking at each of the different stimuli during the 8 s of test. The percent novelty preference at test was defined as the time the participant viewed the new stimulus divided by the total time the participant spent viewing both the old and the new stimuli.

Results

Experiment 1

During the *familiarization* periods of *Experiment 1*, mean looking times per stimulus ($\pm$ SDs) across stimulus types for the control and patient groups were 5.6 ($\pm$ 1.05) and 5.9 ($\pm$ 0.85) s, respectively (Fig. 2a). An analysis of variance (ANOVA) indicated that neither the Group factor (DA, NC), the Stimulus factor (fractals, landscapes), nor the interaction between the two attained significance (all p s $>$ 0.05). The possibility of group differences in fatigue over the 35 min/session was examined by comparing looking time during the first 10 and last 10 of the 32 familiarization periods, but the comparison failed to detect any evidence of fatigue in either group ($p >$ 0.05).

During the *test* periods of *Experiment 1*, both the NC and DA groups showed a novelty preference (Fig. 2b). Mean novelty preferences, averaged across delays and stimulus types, were 72.6 ($\pm$ 6.9) and 65.6 ($\pm$ 10.0) percent for the NC and DA groups, respectively, both values being well above chance (NC: $t[28] = 17.48$, $p <$ 0.001; DA: $t[4] = 3.48$, $p = 0.025$).

An ANOVA with the factors of Group (DA, NC) and Stimulus type (fractals, landscapes) showed a Group effect that fell just short of significance ($F[1,32] = 3.74$, $p = 0.062$), but no effect of Stimulus type ($F_{\text{HUYNH-FELDT}}[1,32] = 1.05$, $p = 0.314$) or of its interaction with Group. The two stimulus types were therefore collapsed (Fig. 2b), and a second ANOVA was performed with the factors of Group (DA, NC) and Delay (0, 5, 30, 120 s). This analysis revealed significant forgetting over time ($F_{\text{HUYNH-FELDT}}[3,96] = 32.42$, $p <$

0.0001), with, critically, a significant interaction of Group $\times$ Delay ($F_{\text{HUYNH-FELDT}[3,96]} = 3.27, p = 0.025$). The within-subjects contrasts revealed that the Group $\times$ Delay interaction was linear ($F[1,32] = 5.08, p = 0.031$). As illustrated in the figure, the mean percent novelty preference in the DA group was comparable to that in the controls at the 0 and 5 s delays, but was significantly shorter than the control values at both the 30-s delay ($t[32] = 2.71, p = 0.011$) and the 120-s delay ($t[32] = 2.37, p = 0.024$), at which point the DA group's differential viewing of the two stimuli, unlike that of the controls, no longer differed from chance (30-s delay: $t[4] = 1.15, p = 0.313$; 120-s delay: $t[4] = 1.76, p = 0.153$).

Experiment 2

In the *familiarization* periods of *Experiment 2*, the mean looking times ($\pm$ SDs) per stimulus across both stimulus types for the control and patient groups were 6.0 ($\pm$ 1.1) and 5.5 ($\pm$ 1.2) s, respectively (Fig. 3a). These values were comparable to those in Experiment 1, and an ANOVA indicated that, as before, there were no significant Group, Stimulus type, or interaction effects (all $ps > 0.05$). Also as in Experiment 1, a comparison of looking times during the first 10 and last 10 of the 32 familiarization periods uncovered no evidence of fatigue in either group.

During the *test* periods in *Experiment 2*, despite a progression of delays that greatly exceeded those in the first experiment, the NC group ($n = 23$; see *Participants* section) again showed an overall novelty preference. Mean ($\pm$ SD) percent time spent looking at the novel stimulus, averaged across delays and stimulus types, was 61.1 ($\pm$ 8.6). Although this overall value fell more than 10 percent below the value for Experiment 1, it remained significantly above chance ($t[22] = 6.22, p < 0.001$). By contrast, the DA Group's overall novelty preference of 54.9 percent ($\pm$ 6.2), which also fell more than 10 percent below that of Experiment 1, did not differ from chance ($t[4] = 1.44, p = 0.222$).

An ANOVA with the factors of Group (DA, NC) and Stimulus type (fractals, landscapes) revealed a significant effect of Stimulus type ($F_{\text{HUYNH-FELDT}[1,26]} = 9.52, p = 0.004$), but no effect of Group ($F[1,26] = 2.33, p = 0.139$) or of its interaction with Stimulus type ($F_{\text{HUYNH-FELDT}[1,26]} = 0.07, p = 0.794$). To analyze novelty preference as a function of delay, the 32 different delays were collapsed into four blocks of eight successive delays each: i.e. the first eight, or shortest, delays; the next eight, longer delays; and so on (Fig. 3b). A three-way ANOVA with the factors of Group, Stimulus type, and Delay confirmed the results of the two-way ANOVA and also revealed a significant effect of Delay ($F_{\text{HUYNH-FELDT}[3,78]} = 3.98, p = 0.011$). The significant effect of Stimulus type reflected a greater overall novelty preference for fractals than for landscapes across both groups, while the significant Delay factor reflected a gradual decrease in the novelty preference of both groups as the delays increased gradually to more than 10 min. Despite the delay-dependent decrease in preferential looking to the novel stimulus, the NC group's values remained above chance at all four delay-blocks (all $ps < 0.0001$), whereas the values for the DA group were above chance only for the first block of delays (2-142 s, $t[4] = 4.09, p = 0.015$).

A separate analysis was then performed on just this first block of delays divided into four smaller blocks (2-22, 42-62, 82-102, and 122-142 s), as these were the delays most comparable to those used in Experiment 1. None of the main factors (Group, Stimulus type, or Delay) attained significance, nor did any of the interactions. It should be noted that statistically significant differences were less likely to be observed in this analysis than in the others, inasmuch as the number of observations was reduced to one quarter of the total number, and the variance was increased accordingly.

Comparison of Experiments 1 and 2

In order to compare the outcomes of Experiments 1 and 2, we collapsed scores across all delays in each experiment (excluding the 0-s condition of Experiment 1) and compared the novelty preference scores of the five DA patients with those of the 23 normal control participants who took part in both experiments (see *Participants*). A three-way ANOVA with the factors of Group (DA, NC), Experiment (1, 2) and Stimulus type (fractals, landscapes) indicated that all three main effects were significant (Group: $F[1,26] = 4.67$, $p = 0.040$; Experiment: ($F_{\text{HUYNH-FELDT}}[1,26] = 22.49$, $p < 0.001$; Stimulus type: $F_{\text{HUYNH-FELDT}}[1,26] = 7.43$, $p = 0.011$), but none of interactions. As illustrated in Figure 4, novelty preference in Experiment 1 exceeded that in Experiment 2, an expected outcome given the much shorter delays that were used in Experiment 1 (maxima of 2 min vs. 10 min). More interestingly, novelty preference for fractals exceeded that for landscapes across both experiments, even though this factor did not reach significance in Experiment 1 alone.

To determine whether the greater novelty preference for fractals than for landscapes across both groups might have been associated with more time spent viewing the fractals than the landscapes during familiarization, we performed an ANOVA on the familiarization data using the same three factors as before (i.e. Group, Experiment, and Stimulus type). Only the Stimulus factor was significant ($F_{\text{HUYNH-FELDT}}[1,26] = 4.91$, $p = 0.036$), and, although the difference was small in magnitude (fractals, 5.88 ± 0.6 s; landscapes, 5.54 ± 0.8 s), the finding suggests that this difference was sufficient to yield better encoding of the fractals, leading, in turn, to the greater novelty preference for this stimulus type.

To examine the above possibility directly, we examined whether percent novelty preference at test across participants was correlated with amount of time they spent looking at the (old) stimulus during familiarization. Although we expected that such a correlation might be found for the seemingly better-encoded fractals, no reliable correlation was obtained for either group or both combined in any condition.

An important final result is that the impairment in the DA group across the two experiments was not due to any group difference in time spent viewing the stimuli during the familiarization periods; rather, the mean familiarization looking times per pair of identical stimuli, collapsed across experiments and stimulus types, were exactly the same for the two groups: 5.7 s out of the 8 s familiarization period.

Discussion

The results of Experiment 1, obtained with the standard version of VPC, demonstrated that whereas the DA patients had novelty preference scores comparable to those of the normal controls at 0- and 5-s delays, they were deficient at 30- and 120-s delays, and showed a delay-dependent deficit in incidental recognition memory. Although significant impairment was not observed on the version of VPC that was used in Experiment 2, that negative finding was likely due to a floor effect (i.e. mean novelty-preference scores fell to 61 and 55% in the NC and DA groups, respectively), caused by a combination of long delays and proactive interference from intervening stimuli, both of which were consequences of the reversed-order-testing paradigm adopted for this experiment. This modified version of VPC may therefore not be as sensitive a measure of novelty preference as the standard version. However, despite the floor effect, the results obtained on the two very different versions of the VPC task in the two experiments were nearly identical in their patterns (see Fig. 4), and the statistical analysis of the combined results indicates that the DA group had deficient novelty preference overall.

This positive finding in the DA group, which sustained substantial yet relatively selective hippocampal damage early in life, increases confidence that in some of the patients with adult-onset amnesia referred to earlier (McKee and Squire, 1993; Pascalis et al., 2004), the delay-dependent deficit on the VPC task is likewise attributable to their hippocampal pathology. The positive finding is consistent as well with the delay-dependent deficits on the VPC task that have been observed in monkeys given selective hippocampal lesions (Zola et al., 2000; Nemanic et al., 2004) and with the recent demonstration of a neural signal in the monkey's hippocampus that is likely to support novelty preference in VPC (Jutras and Buffalo, 2010). The combined evidence suggests that this task may well prove to be a singularly effective measure of hippocampal-based item recognition, a measure that reveals impairment consistently across species and irrespective of age at hippocampal damage. The conclusion regarding age at injury, derived from the present results in comparison with those of the cases with adult-acquired hippocampal damage (McKee and Squire, 1993; Pascalis et al., 2004), also receives tentative support from work in nonhuman primates, based on findings of impairment on the VPC task in adult monkeys given hippocampal lesions in infancy (Pascalis and Bachevalier, 1999); that evidence, however, is complicated by the fact that the hippocampal removals were accompanied by aspiration of posterior parahippocampal cortical areas TH and TF, and thus the conclusion awaits confirmation in animals that have sustained more selective hippocampal damage early in life.

Having obtained evidence that helps confirm the ubiquity of reduced novelty preference after selective hippocampal damage, we are faced with the puzzle implied at the outset, namely, the inconsistent or nonmonotonic relationship between encoding conditions in various tasks and lesion effects on those tasks. As noted earlier, uninstructed viewing during both familiarization and test in VPC seems to be the direct opposite of instructions conducive to the effective encoding of items plus their context for later retrieval in an explicit recognition test; yet DA patients are impaired under both of these conditions, which appear to be at opposite extremes. By contrast, in explicit recognition tasks on which the instructions do not promote encoding items with associated context, or on which there are no processing instructions at all, just as in VPC, DA patients are commonly unimpaired.

This inconsistent relationship between encoding conditions and lesion effects has implications for understanding the specific role of the hippocampus in recognition memory. Within the category of explicit recognition tasks, it is reasonable to assume that the deeper the processing and encoding of a studied item to generate associative context, the greater the likelihood of item recollection and, in parallel with that, the greater the item's memory strength. Thus, both of the competing views regarding the participation of the hippocampus in recognition memory – that it contributes selectively either to recollection as opposed to familiarity, or to high confidence as opposed to low confidence judgments (paralleling level of memory strength) – find support in the impairments produced by hippocampal damage on deep-processing tasks. But then the opposite should be inferred from the DA group's impairment on VPC, where incidental encoding would seem to promote neither the generation of associative context nor particularly strong memories, and to result rather in relatively weak and nonassociative memories. Here neither of the competing theoretical views appears to be supported, and, indeed, both would seem to be contradicted.

Such a conclusion, however, could be premature for either one of two very different reasons. First, VPC and intentional or explicit recognition tasks that have been given to patients with selective hippocampal lesions differ in numerous ways besides encoding and retrieval instructions, and these other variables could well override any effects that such differential instructions might have. For example, in explicit recognition tasks, stimulus type alone can determine the presence or absence of impairment in DA; in one study at least (Bird et al., 2008), scene stimuli revealed impairment whereas face stimuli did not. Although stimulus

type did not determine lesion effects in our VPC task, neither did the two stimulus categories yield identical outcomes, the fractals having elicited longer viewing times during familiarization and greater novelty preference during test than the landscapes did. Indeed, familiarization time itself could be an important variable, one that may often be overlooked. Although it is known that increasing familiarization periods increases novelty preference (Richmond et al., 2004), explicit recognition studies rarely manipulate this particular encoding variable, and they also rarely extend familiarization periods for as long as the 8 s that were allowed in the current VPC task. Two additional critical variables, of course, are the length of the delays between study and test and how the delays are filled. In short, until patients with selective hippocampal lesions and their normal controls are compared directly on intentional and incidental recognition tasks in which all these other variables are controlled (e.g. see Naveh-Benjamin et al., 2009), no conclusions can be drawn about the interacting effects of differential encoding instructions and hippocampal lesions on recognition. In light of the presents results, however, just such direct comparisons are clearly needed, as they may well show that, under otherwise comparable conditions, impairment on intentional recognition tasks is always greater than that on incidental recognition tasks, a result indicative of a monotonic relationship between encoding instructions and effect of hippocampal lesions.

The second reason we cannot yet conclude that our results contradict current views of hippocampal-dependent recognition concerns the VPC task itself. Nearly all of our discussion thus far rests on the widely-shared assumption that, in the VPC test period, viewing the old stimulus less than the new one is driven by the same cognitive memory process that supports explicit recognition of the old stimulus (e.g. Manns et al., 2000). However, this assumption has not gone unquestioned. From time to time, since its inception as a memory measure in preverbal infants (Fantz, 1964), VPC has been posited to tap instead an implicit, attention-based process or an implicit, information-gathering process modulated by habituation, both of which differ qualitatively from explicit recognition memory (e.g. Schacter and Moscovitch, 1984). Recently, this view received empirical support from a study (Snyder et al., 2008) showing a double dissociation between the effects of stimulus likability and complexity on novelty preference, on the one hand, and explicit recognition, on the other. This same study also showed a lack of correlation between degree of stimulus recognizability in an explicit task and degree of novelty preference away from stimuli with increasing recognizability. If confirmed, these findings would suggest that the impairment in DA on both explicit recognition and VPC, although seeming to result from one and the same disordered memory process, actually reflects disorders in two quite different processes, for both of which the hippocampus is normally responsible. Paradoxical as such a possibility may be, it cannot be dismissed without further study.

The finding that patients with developmental amnesia do show reduced novelty preference in VPC has thus raised many complex questions in place of the straightforward one with which this study began. However, until these new questions are answered, it may not be possible to identify the specific contribution that the hippocampus makes to recognition memory.

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Figure 1.

The VPC paradigms in Experiments 1 and 2 are illustrated with fractals and landscapes, respectively (though both types of stimuli were used in separate sessions in each experiment). In Experiment 1 (top row, which represents any two successive trials), we used the standard version of the task: A pair of identical stimuli was presented for familiarization, and this was followed after a variable delay by presentation of the test pair, composed of a familiarized and a novel stimulus; this sequence of familiarization followed by test was repeated for each of the 32 stimulus pairs. In Experiment 2 (bottom row, which represents familiarization trials 31 and 32 followed by test trials 1 and 2), we used a paradigm that differed from the standard version in two respects: (i) All 32 pairs of identical stimuli were sequentially presented for familiarization first, and only then were the test pairs presented, each composed as before of a familiarized and a novel stimulus; (ii) these 32 test pairs were presented sequentially in an order that was the reverse of the familiarization sequence, i.e. the last familiarized stimulus was tested first, and the first familiarized stimulus was tested last. The delays between familiarization and test in Experiment 1 were 0, 5, 30, and 120s in pseudorandom order, whereas in Experiment 2, they increased progressively from 2 s to > 10 minutes.

Figure 2.

(a) Mean time spent viewing the pairs of identical stimuli during the 8-s familiarization period. (b) Mean percent novelty preference during the 8-s test period. NC, normal control participants (N = 29); DA, patients with developmental amnesia (N = 5). Error bars, SEs.

*Significant group difference at the 0.05 level.

Figure 3.

(a) Mean time spent viewing the pairs of identical stimuli during the 8-s familiarization period. (b) Mean percent novelty preference stimuli during the 8-s test period. Each delay category includes 8 delays, increasing progressively in 20-s steps. NC, normal control participants ($N = 23$); DA, patients with developmental amnesia ($N = 5$). Error bars, SEs.

Figure 4.

Mean percent novelty preference scores in (a) Experiment 1 and (b) Experiment 2. Despite the absolute difference in scores in the two experiments, the patterns of the scores are nearly identical: (i) Each of the four scores in Experiment 1 exceeds its matched score in Experiment 2 by about 10 percent; (ii) each of the four scores in the NC group exceeds its matched score in the DA group by about 7 percent; and each of the four scores for Fractals exceeds its matched score for Landscapes by about 3 percent. NC, normal control participants ($N = 23$ in both experiments; see text); DA, patients with developmental amnesia ($N = 5$). Error bars, SEs.

Table 1

Details of the patients with DA

DA	Sex	Age at injury (years:months)	Age at test (years)	Aetiology	HV Reduction in %		
					Left	Right	Mean
1	M	Perinatal	29	Birth asphyxia	56.6	40.7	48.7
5	F	Perinatal	18	Birth asphyxia	44.9	41.7	48.1
9	M	0 to 4:06	22	Seizures	21.2	30.7	26.0
10	F	9:01	33	Hypoxia-ischaemia	34.2	37.5	35.9
12	M	15:05	23	Hypoglycemia	53.5	42.7	43.3

The patients are listed by DA case number assigned when they were part of a larger group in earlier studies (Adlam et al., 2005; Adlam et al., 2009). The aetiology in case DA 10 was associated with acute seizures and respiratory arrest, and in DA 12, with diabetes. The reduction in each patient's hippocampal volume is the percent loss relative to the mean hippocampal volume of the control group in those earlier studies and is corrected for differences in intracranial volume; the volume reductions shown here for Case 5 were not available for inclusion in the 2005 report. Abbreviations: DA, developmental amnesia; F, female; M, male; HV, hippocampal volume.