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Impairment of recollection but not familiarity in a case of developmental amnesia

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Abstract

In a re-examination of the recognition memory of Jon, a young adult with developmental amnesia due to perinatal hippocampal damage, we used a test procedure that provides estimates of the separate contributions to recognition of recollection and familiarity. Comparison between Jon and his controls revealed that, whereas he was unimpaired in the familiarity process, he showed abnormally low levels of recollection, supporting the view that the hippocampus mediates the latter process selectively.

Keywords

Developmental amnesia; Exclusion; Inclusion; Recollection; Familiarity

INTRODUCTION

An important distinction within recognition memory is that between recognition accompanied by memories of rich contextual details, referred to as recollection, and recognition that lacks this contextual memory and is based instead on a feeling of familiarity (Gardiner & Java, 1993; Jacoby, 1991; Tulving, 1983). A current issue in cognitive neuroscience research is whether or not this distinction between recollection and familiarity is rooted in differential contributions to recognition made by different components of the medial temporal lobe, specifically the hippocampus and parahippocampal region.

One view is that the hippocampus itself subserves both recognition processes as evidenced by findings that both processes are impaired in some patients with selective hippocampal damage (Knowlton & Squire, 1995; Manns, Hopkins, Reed, Kitchener, & Squire, 2003; Squire, Wixted, & Clark, 2007; Wais, Wixted, Hopkins, & Squire, 2006), or are impaired in some patients on some tests (Cipolotti et al., 2006). An opposing view is that the hippocampus mediates recollection selectively, as indicated by studies showing that other amnesic patients with selective hippocampal damage have normal levels of familiarity-

dependent recognition despite marked impairment in recollection (Aggleton et al., 2005; Holdstock et al., 2002; Mayes et al., 2004; Yonelinas, 2002). Additional support for this alternative position comes from a recent report of a patient who sustained damage to the left perirhinal cortex that spared the hippocampus and was found to have impaired familiarity-based recognition but normal recollection (Bowles et al., 2007); this finding provided the first direct evidence for the proposal that the familiarity process depends on cortex in the parahippocampal region (Aggleton & Brown, 1999; Aggleton et al., 2005).

The focus of the present research is on another patient, Jon, who sustained severe yet apparently selective bilateral hippocampal damage in early infancy as a result of hypoxia-ischemia (Vargha-Khadem et al., 1997). Jon was born prematurely at 26 weeks and suffered severe apnea, requiring intubation and positive pressure ventilation. MRI scans carried out in early adulthood revealed a 50% bilateral volume reduction in Jon's hippocampus but no visible damage on clinical radiological examination to the surrounding parahippocampal cortices or other brain regions (Vargha-Khadem et al., 1997).

On the issue of whether or not familiarity and recollection are functionally dissociable, Jon is thus an important test case. Because of the plasticity of the immature brain, greater functional compensation of the process of familiarity by spared components of the medial temporal lobe is more likely to follow early hippocampal injury than it is to follow the same injury sustained later in life. Consequently, failure by Jon to show selective preservation of familiarity-based recognition would pose a serious challenge to the view that the two recognition processes are dissociable. However, while the question has not previously been tested in Jon, many earlier findings regarding his memory ability point to the likelihood that the familiarity process is indeed preserved.

Formal testing of Jon's memory has revealed that he is markedly impaired on tests of episodic memory, yet has acquired a normal amount of semantic knowledge (Vargha-Khadem et al., 1997; Vargha-Khadem, Gadian, & Mishkin, 2001). In addition, whilst Jon's recall scores are consistently and significantly below those of matched controls (Baddeley, Vargha-Khadem, & Mishkin, 2001; Brandt, Gardiner, Vargha-Khadem, Baddeley, & Mishkin, 2006; Vargha-Khadem et al., 1997), he tends to demonstrate normal levels of performance on many tests of recognition for both verbal and non-verbal material (Baddeley et al., 2001; Gardiner, Brandt, Vargha-Khadem, Baddeley, & Mishkin, 2006; Vargha-Khadem et al., 1997). Of particular interest in connection with the debate on the role of the hippocampus in the two different recognition processes is the finding in an event-related potential (ERP) study that Jon shows the ERP signature that has been related to familiarity-based recognition but not the one that has been correlated with recollection (Düzel, Vargha-Khadem, Heinze, & Mishkin, 2001). Another study (Gardiner et al., 2006), which used the Remember/Know paradigm (Tulving, 1985), found that whereas matched controls correctly differentiated between remembering (or recollection) and knowing (or familiarity) on the basis of contextual details, Jon did not and, instead, differentiated between the two types of responses on the basis of confidence level, supporting previous work demonstrating Jon's idiosyncratic use of remember/know responses (Baddeley et al., 2001).

Given Jon's idiosyncratic use of these two response categories, we addressed the issue of hippocampal contributions to recognition in another way, by employing the Process Dissociation Procedure (PDP; Jacoby, 1991). The PDP paradigm estimates the separate quantitative contributions to recognition made by recollection and familiarity, which are deemed to be independent of each other, as follows:

Participants are asked to recall, for example, words presented at study in either a male or a female voice. An inclusion condition, i.e., an instruction to recall all words, is presumed to

assess recollection and familiarity working in conjunction. By contrast, an exclusion condition, e.g., an instruction to recall only those words presented in a male voice, thereby requiring rejection of words spoken in a female voice, is presumed to assess recollection operating alone, with failure to correctly reject the latter words reflecting familiarity operating alone. Given this assumption that the two processes are independent, the contribution of recollection [R] can be estimated by subtracting the probability of exclusion [$p(e)$] from the probability of inclusion [$p(i)$] using hits minus false alarms [$R = p(i) - p(e)$], and the contribution of familiarity [F] can be estimated by calculating the probability of exclusion divided by 1 minus the probability of recollection [$F = p(e)/(1 - R)$].

Previous research with this paradigm conducted on amnesic patients with relatively selective hippocampal damage sustained in adulthood found that while recollection was severely impaired, the process of familiarity was preserved (Bastin et al., 2004; Turriziani, Serra, Fadda, Caltagirone, & Carlesimo, 2008). Here we asked whether or not Jon, a patient with early-onset, or developmental, amnesia, would show the same pattern of results. For the reason stated earlier, a positive outcome is important if we are to be confident that the two different recognition processes are indeed functionally dissociable.

METHOD

Jon's performance was compared to a group of eight male controls, matched on age (Jon vs. mean of controls: 25 vs. 23), and on intelligence assessed with the WAIS-R (full-scale IQ, 114 vs. 112; verbal IQ, 120 vs. 115; and performance IQ, 108 vs. 110). Jon was tested at the Developmental Cognitive Neuroscience Unit, University College London Institute of Child Health, University College London. Participants in the control group were recruited and tested at the University of Sussex. The study was approved by the Ethics Committees of both institutions and all participants gave their informed consent prior to their inclusion in the experiment.

The present design, which was based on a previous study that used the PDP paradigm (Wilding & Rugg, 1997), consisted of three conditions, one inclusion and two exclusion, with each test phase following the relevant study condition. In each condition, participants heard 40 words for 2 s each, half of which were spoken in a male voice and the other half in a female voice. For each word, participants were required to judge the gender of the voice as well as how pleasant the word was using a 3-point Likert scale. The words consisted of two-syllable high-frequency English nouns taken from the MRC psycholinguistic database. Each word was recorded twice, once by a male and once by a female voice. The items were digitally recorded at a 44.1-kHz, 8-bits sampling rate, using Cubase VST sound engineering software, and were then normalised for volume and amplitude levels, and finally transferred to a CD. The word and gender of voice uttering the word were the same for Jon and for all the controls in each condition.

For each of the three test conditions, following a 10-min retention interval during which the participants played computer games, they were given an old/new visual recognition test in which they saw the 40 study and an additional 40 distracter words. The distracter items were also taken from the MRC psycholinguistic database and matched to the targets for word frequency and length. In the inclusion condition, participants were instructed to say 'old' to all words presented in the study phase regardless of the voice in which the word was presented. In the first exclusion condition, participants were asked to say 'old' only to words that were presented in the study phase in a male voice. In the second exclusion condition, participants were asked to say 'old' only to words presented in the study phase in a female voice.

RESULTS

Inclusion and exclusion scores

Treatment means are shown in Table 1. As Jon's false alarm rates were generally higher than those of the controls, all analyses were based on correct proportion of hits minus false alarms. Results from the inclusion condition revealed that the controls scored significantly higher than Jon ($t(7) = 3.15, p < .02$).

Proportions of correct recognition (hits minus false alarms) for the controls in the exclusion condition were submitted to paired samples t -tests. Ability to correctly exclude in the exclusion test is demonstrated by a higher score for words to-be-included than for words to-be-excluded. The controls demonstrated successful exclusion ($t(7) = 5.46, p < .01$); however, Jon was only marginally successful ($t(7) = 1.79, p < .06$). This reflected the finding that although Jon and his controls did not differ significantly for words to be included (in the exclusion condition; $t(7) = <1, ns$), Jon's scores were lower for words to be excluded (i.e., $t(7) = 1.79, p < .06$).

Recollection and familiarity estimates

Treatment means are shown in Table 2. Analyses indicated no difference between Jon and the controls in estimates of familiarity ($t(7) <2, ns$), but Jon scored significantly lower than controls on estimates of recollection ($t(7) = 3.81, p < .01$). Moreover, Jon's scores yielded familiarity estimates that were five times greater than those of recollection, whereas the familiarity estimates in the controls were only slightly higher than those for recollection.

DISCUSSION

In the inclusion condition, the controls obtained significantly higher scores than Jon did, indicating that on this particular test Jon showed an overall impairment in word recognition. An impairment in Jon's recognition of studied words was also found by Düzel et al. (2001) and by Gardiner et al. (2006). In all three experiments, the instructions at study encouraged deep encoding of one or more contextual details – the gender of the voice and the word's pleasantness in the present experiment, a living/nonliving category judgment in the Düzel experiment, and pleasantness or imaging ratings in the Gardiner experiment – instructions that presumably enhanced recollection-dependent recognition in the controls. By contrast, Jon usually shows no impairment on tests in which participants are instructed simply to remember the words (Baddeley et al., 2001; Vargha-Khadem et al., 1997) or to perform shallow word encoding, e.g., by counting their syllables (Gardiner et al., 2006), instructions that presumably do not enhance recollection in controls. This interpretation of the difference between those tests of recognition that do and those that do not reveal an impairment in Jon is strongly supported not only by the ERP finding of Düzel et al. (2001) indicating Jon's lack of the ERP correlate of recollection, but also by the present results demonstrating his recollection impairment.

The quantitative estimates of the two processes that contribute to recognition memory indicate that whereas Jon did not differ from the controls in estimates of familiarity, he fell significantly below them in levels of recollection. The selectivity of Jon's impairment is consistent with those recognition memory studies of adult-onset amnesic patients with selective hippocampal damage that have shown normal familiarity in the presence of impaired recollection (Aggleton et al., 2005; Holdstock et al., 2002; Mayes et al., 2004; Yonelinas, 2002), including, in particular, the ones that used the Process Dissociation Procedure (Bastin et al., 2004; Turriziani et al., 2008). The results on Jon thus appear to support the proposal that the hippocampus primarily subserves recollection and that the process of familiarity is mainly reliant on the subjacent parahippocampal region (Aggleton

& Brown, 1999; Bowles et al., 2007; Mayes et al., 2004; Yonelinas, 2002). At the same time, the results on Jon are inconsistent with those of other studies on adult-onset amnesic patients whose lesions were likewise described as being relatively restricted to the hippocampus (Knowlton & Squire, 1995; Manns et al., 2003; Squire et al., 2007; Wais et al., 2006). How are these differences to be reconciled?

Because the differences in results are present within the category of adult-onset amnesia, with some of these older patients showing the dissociation while others do not, age-at-onset is not the relevant variable. Indeed, the similarity of outcome in Jon and in several of the patients with amnesia incurred in adulthood weigh in favour of an earlier proposal (Vargha-Khadem et al., 2003) that the effects of selective hippocampal damage might well prove to be independent of age at injury. That proposal was predicated on the finding of little or no difference in long-term memory functions between children with perinatal onset of pathology and those with onset later in childhood (ages 6–14). Since then, other similarities have been found between these two groups of patients with developmental amnesia and some patients with amnesia sustained later in life, such as a significantly greater deficit in recall than in recognition (Adlam, Malloy, Mishkin, & Vargha-Khadem, in press). Again, however, other adult-onset cases do not show this disparity, indicating once more that differences in mnemonic results are present within the category of adult-onset amnesia, and that age-at-onset can be excluded as the critical factor.

One possibility that cannot yet be excluded is that the differences in outcome are due to differences in the neuropathology. For example, neural tissue such as the parahippocampal cortices can appear to be intact based on structural imaging of grey matter, yet show abnormality when white matter is examined with diffusion tensor imaging (e.g., Papanicolaou, Hasan, Boake, Elovathingal, & Kramer, 2007) or show reduced activity when the functional integrity of the tissue is assessed with fMRI (e.g., Nestor, Fryer, Smielewski, & Hodges, 2003). Perhaps only when these and other more comprehensive and more refined neuroimaging techniques are used will an explanation be found for the differences in mnemonic outcome among patients with ‘hippocampal’ amnesia, whatever the age at onset.

CONCLUSION

The findings presented here on Jon are consistent with the view that despite severe bilateral damage to the hippocampus, the familiarity process in memory can remain normal, whereas the recollection process in memory cannot.

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TABLE 1

Memory performance as a function of condition and criteria in the inclusion and exclusion tests

Participants	Inclusion	Exclusion	
	Include word	Include word	Exclude word
<i>Hits-False alarms</i>			
Control group	0.65 (0.20)	0.54 (0.21)	0.25 (0.13)
Jon	0.43	0.48	0.33
Hits			
Control group	0.73 (0.17)	0.57 (0.20)	0.28 (0.13)
Jon	0.70	0.61	0.46
False alarms			
Control group	0.08	0.06	
Jon	0.28	0.26	

Standard deviations in parentheses, here and Table 2.

TABLE 2

Estimates of recollection and familiarity

Participants	Estimates	
	Recollection	Familiarity
Control group	0.41 (0.23)	0.47 (0.20)
Jon	0.10	0.50