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Review

The case of K.C.: contributions of a memory-impaired person to memory theory

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Abstract

K.C. has been investigated extensively over some 20 years since a motorcycle accident left him with widespread brain damage that includes large bilateral hippocampal lesions, which caused a remarkable case of memory impairment. On standard testing, K.C.'s anterograde amnesia is as severe as that of any other case reported in the literature, including H.M. However, his ability to make use of knowledge and experiences from the time before his accident shows a sharp dissociation between semantic and episodic memory. A good deal of his general knowledge of the world, including knowledge about himself, is preserved, but he is incapable of recollecting any personally experienced events. In displaying such "episodic amnesia," which encompasses an entire lifetime of personal experiences, K.C. differs from many other amnesic cases. Here, we document for the first time the full extent of K.C.'s brain damage using MRI-based quantitative measurements. We then review the many investigations with K.C. that have contributed to our understanding not only of episodic and semantic memory but also to the development of other aspects of memory theory. These include the distinction between implicit and explicit memory, the prospect of new learning in amnesia, and the fate of recent and remote memory for autobiographical and public events, people, and spatial locations.

Keywords: Episodic amnesia; Priming; Anterograde memory; Retrograde memory; Medial temporal lobes; Autobiographical memory; Neuroimaging; Case study

Contents

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1. Introduction

What we now may take for granted, the idea that memory comes in many kinds and varieties, was hardly acknowledged until a window was opened into the normal operations of the mind through the study of cognitive losses suffered by brain-damaged patients. The single case studies of Korsakoff (1889) were instrumental in laying the foundation for the tradition of using memory disorders as a means of studying mnemonic processes. Following in this tradition, Scoville and Milner (1957) introduced to the world the now famous case H.M. who graphically illustrated several fundamental distinctions in memory that had been psychologically contemplated at least as early as James (1890) but whose biological reality had remained in doubt. Work with H.M. produced clear distinctions between memory and other intellectual functions. First, it showed that severe anterograde amnesia for material encountered post-injury could occur despite relatively preserved intelligence, language, and reasoning ability. Second, it drew a sharp distinction between long-term and short-term memory: dense amnesia for ongoing happenings could occur despite normal ability to hold in mind and make use of information involved in ongoing activity. Third, it showed that not all expressions of long-term memory were impaired. H.M. was capable of learning skills and acquiring perceptual information, even in situations in which he was not aware that he had learned anything. This overall pattern of selective memory impairment was especially remarkable in that it occurred as a result of a relatively circumscribed lesion of the medial temporal lobes (MTL; Corkin, 1965, 1968, 2002; Corkin, Amaral, Gonzalez, Johnson, & Hyman, 1997; Milner, Corkin, & Teuber, 1968). Together with the observations reported by other experimentally minded neuropsychological students of memory disorders (Warrington & Weiskrantz, 1968), these findings helped pave the way to the widely accepted idea of multiple memory systems (Schacter & Tulving, 1994).

As a result of the intense study of, and behavioural/cognitive findings yielded by, the single case of H.M. with his extensive but precisely localized bilateral MTL lesions, many students of amnesia adopted a "single-memory, single-locus" concept of global amnesia. Amnesia came to be seen as a severe impairment of a single kind of memory ("declarative memory") attributable to the pathology of a single brain region (hippocampus or MTL). For the purposes of this paper, declarative memory was defined as long-term memory for facts and events; it excluded short-term (immediate) memory as well as non-declarative long-term memory (Squire, 1989). The tight coupling between amnesia, declarative memory,

and the MTL greatly simplified the problem of making sense of the otherwise complex phenomena.

The advantage of this scheme was three-fold. It facilitated the fit between data and theory, it allowed one to draw meaningful inferences even when some aspects of the total situation were unknown, and it kept difficulties in understanding amnesia at bay. Thus, for example, when an amnesic patient was identified for whom no neuroimaging data were available, it was possible to infer that he or she had suffered MTL damage. Similarly, when performance on a memory task was observed to be affected deleteriously by MTL damage, it was possible to classify the task as one of declarative memory; if it was not, it meant that the task was non-declarative. The scientific stratagem exemplified here is well known and widely used. For example, using similar logic, Tulving has claimed that the "encoding specificity principle," according to which any successful retrieval attempt requires an appropriate match between the encoded engram and the available retrieval cues, holds generally, and no exceptions to it exist (Tulving, 1983, p. 266).

The case of K.C. turned out to be one contributor to the eventual crumbling of the neat and tidy single-memory, single-locus model of amnesia. Today, there are as many puzzles surrounding memory impairment as there are surrounding "normal" memory. For instance, it is becoming increasingly clear that there is more than one type of declarative memory impairment much as there is more than one type of declarative memory system. As frequently happens, not only in life but also in science, the contribution that the case of K.C. made to such a shift from simplicity to complexity came about because of an accident.

It was in 1983 that Morris Moscovitch was told by a student in his Cognitive Neurology class at Erindale College of the University of Toronto, who was working part-time in a sheltered workshop, that in that setting he had met a man who had suffered traumatic brain injury in a traffic accident and now was "just like H.M." This person came to be known as K.C. Moscovitch agreed to test K.C. on standard neuropsychological measures and confirmed a pattern of severely impaired anterograde memory and relatively preserved retrograde memory. However, upon referral to the newly established Unit for Memory Disorders at the university, it was soon realized that K.C., though exhibiting severe anterograde amnesia, was not quite like H.M. in that he did not seem to recall any personal happenings from his own life. At that time, H.M. was thought to be able to remember some of his life experiences up to 5 years or so before his operation (Milner et al., 1968), though later this lucid period of personal recollections was shortened and estimated as comprising only the first 15 years of his life (Corkin, 1984; Sagar, Cohen, Corkin, & Growdon, 1985). More recent re-evaluation of H.M.'s case has thrown doubt on that figure, too, and raised the possibility that, with respect to what we now call episodic memory, H.M. is like K.C. in every way. Indeed, it has been suggested recently that H.M. cannot recollect any personal happenings involving his mother or father, from any period in his life (Corkin, 2002). If so, the cases of K.C. and H.M., seen as rather different through the eyes of the scientific community, are, in fact, much more similar in terms of psychopathological reality.

Clearly, the factors upon which any two cases vary are boundless, ranging from lesion variables, such as etiology and lesion site and extent, to age of onset, to pre-morbid personality. For example, unlike H.M.'s large, yet restricted, surgical excision of his MTL, K.C.'s closed head injury from a motorcycle accident resulted in brain damage that is multifocal and diffuse and therefore not readily mapped onto his behavioural/cognitive profile. However, independent of the nature and extent of his lesions, the behavioural regularities that he exhibits are real and reliable, allowing important theoretical and functional distinctions to be made and parallels drawn. K.C. has acted as a primary participant in over 20 published studies, many of which include multiple experiments, and has been tested as a member of a group of participants in many others. Given his special status and the wealth of data that he has provided, a general overview of his contributions is appropriate and timely.

It is the goal of this review to describe aspects of the mind of a remarkable single individual who has contributed greatly to our understanding of human memory and the brain, both by validating and extending what was already known from earlier studies and, more important, by helping to reveal at a biological level what had been earlier suspected at a theoretical level. Anecdotal findings are first presented within a case history format along with results from neurological, neuropsychological, and neuroimaging examinations. This is followed by a description of experimental findings provided by studies with K.C. across some 20 years of research. Wherever possible, we present and discuss K.C.'s data against a backdrop of other well-studied amnesic cases and prominent theoretical frameworks. In view of the comprehensive nature of this review, we have devoted a separate section to each major experimental theme, and each section may be read in isolation. Readers who prefer a brief overview of the range of K.C.'s spared and impaired functioning are referred to Table 1 for a summary.

2. Case history

K.C. is a right-handed man with 16 years of formal education. He was born prematurely in 1951 and raised within a supportive family of two parents and four younger siblings in a suburb of Toronto. Development was reported as normal and neurological history unremarkable until the summer of his 16th birthday when, while working at his aunt's Montreal-area farm, he lost consciousness when a bale of hay fell on his head. He was admitted to the Montreal Neurological Institute where he remained for 3 days for observation but no surgical intervention was performed. He was discharged on anticonvulsant medication that was discontinued upon his return to high school after a 1-year absence. After graduation,

Table 1
Summary of spared and impaired cognitive abilities in patient K.C. on experimental tasks

Performance cognitive domain	Intact	Partially intact	Impaired
Associative priming			
Word pairs (Section 6.1.1)	Lexical decision following one-trial learning via sentence generation (lasting 30 min)	Word-stem completion (no benefit in same context condition but overall priming intact)	
Familiar idioms (Section 6.1.1)	Free association		
Sentence puzzles (Section 6.1.1)	Generation of one-word solutions (lasting 1 week)		
Perceptual priming			
Word-fragment completion (Section 6.1.1)	Word-fragment completion	Cross-modal	
Three-word sentences (Section 6.1.3)	Word fragment completion (lasting 1 year)[a]		
Complex learning			
Computer-related vocabulary (Section 6.1.2)	Method of vanishing cues (lasting 6 weeks)		
Computer skills (Section 6.1.2)	Method of vanishing cues (lasting 7–9 months)		
Semantic learning			
Three-word sentences (Section 6.1.3)		Cued recall (two-word cue)	
Novel word definitions (Section 6.1.4)		Cued recall of amusing word definitions if interference minimal and stimuli repeated at study (lasting 30 months)	
Post-morbid knowledge of famous names and vocabulary terms (Section 6.1.4)	Recognition; reading speed and accuracy; familiarity ratings; guessing		Identification (categorization, matching); definitions
Remembering events			
Mnemonic precedence (Section 6.1.5)		Spatial location and identity of two hidden objects (only the first)	
Remote semantic memory			
Pre-morbid (>5 years pre-injury) knowledge of famous names and vocabulary terms (Section 6.2.1)	Recognition; reading speed and accuracy; familiarity ratings; identification (categorization, matching); definitions		
Autobiographical memory			
Personal episodic incidents (Sections 6.2.1, 6.4)			Family photographs Autobiographical interview (free recall, specific probing)
Personal semantics (Sections 6.1.4, 6.2.1)	Trait self-knowledge (self-descriptive adjective ratings) Family photographs		
Spatial memory			
Anterograde (Section 6.2.2)			Object-location memory Learning of spatial layouts Route learning
Retrograde (Section 6.2.2)	Localization of large geographical features on an outline map of the world		Localization of specific features on outline maps of Canada and Ontario
	Proximity judgments; distance judgments; landmark sequencing; blocked-route problem solving; vector mapping	Sketch mapping (accurate placement of streets but few landmarks included)	
	Landmark recognition and identification		House recognition
Visual imagery			
Object identity (Section 6.4)	Shape, size, colour		
Spatial relations (Section 6.4)	Angle of clock hands, route generation		
Image transformations (Section 6.4)	Letters, objects		

[a] Indicates better-than-normal performance.

K.C. enrolled in a 3-year business administration program at a community college, during which time he sustained a second blow to his head when his homemade dune buggy collided with a much larger vehicle, resulting in a fractured mandible but no loss of consciousness. Notably, there was no apparent change to K.C.'s cognitive functioning following either accident. He successfully completed his college degree at the age of 25 and became employed at an engineering and manufacturing plant at the age of 27, where he was responsible for delivery and pickup, and quality control of products.

In October of 1981, however, K.C.'s life took a dramatic turn. At the age of 30, he suffered his latest and most devastating head injury, leaving him densely amnesic, when he rode his motorcycle off an exit ramp on the stretch of highway from the plant to his nearby house. Upon arrival to a regional hospital, he was unconscious with dilated fixed pupils and was noted to have clonic seizures. Due to the severity of his neurological condition, he was soon transferred to a larger hospital where he underwent neurosurgery for the removal of a left-sided subdural hematoma that extended over the entire convexity and along the tentorium and the falx as revealed on CT. His return to consciousness at 72 h post-trauma took place in an intensive care unit where he was to remain for 1 month until stable enough to be transferred to a rehabilitation hospital for a 6-month stay. He remained stuperous over the next 5 days, responding only to simple commands. At around 7 days, he appeared to recognize his mother. A follow-up CT scan performed during week 3 showed a chronic bilateral frontal subdural hematoma, slightly enlarged ventricles and sulci, and left occipital lobe infarction presumed to be secondary to compression of the left posterior cerebral artery from increased intracranial pressure.

Upon his transfer to the rehabilitation hospital, K.C. was noted to be reading and conversing quite well and began to recognize friends but showed slowed mentation as well as hemiplegia and a homonymous hemianopia, both affecting the right side. A CT scan performed in May 1982 showed no remaining signs of the subdural hematoma and ventricles of normal size, except for a focal enlargement of the occipital horn of the left lateral ventricle. A well-defined area of decreased density was noted in the left occipital lobe together with prominent sulci over the convexity, particularly over the left frontal cortex.

K.C. was discharged home in July 1982. It was at this time that the severity of his inability to commit new information of any type to memory became more evident, forewarning what was to remain apparent on later MRI scans—namely severe injury to his medial temporal lobes, including almost complete hippocampal loss bilaterally. It also became increasingly clear, especially to those who knew K.C. from before his injury, that any details of personal happenings that they had shared with him, however meaningful at the time of occurrence, had ceased to exist in K.C.'s mind. Not even an intact corpus of mental faculties such as perception, language, and reasoning skills would enable K.C. to relive a personal episodic past or invent possible future events in which he might participate. In this sense, K.C. lacks 'autonoetic' consciousness, which refers to the subjective awareness of not only remembering the past but also thinking about the future. This differs fundamentally from 'noetic' consciousness, or simply knowing in the present of an episode that took place at an earlier time, which K.C. continues to possess (Tulving, 1985; Wheeler, Stuss, & Tulving, 1997).

The motorcycle accident had an equally profound impact on K.C.'s personality. Though he continues to be polite and easy-going, his once gregarious, thrill-seeking character changed into one that is soft-spoken and tranquil. The time in his life defined by hurrying to work without breakfast after sleeping in, socializing at bars and over card games, membership in a rock band, trips to Mardi Gras, and motorcycle rides remains familiar, but there is no trace of personal recollection of any episode. Whatever K.C. knows about his past is functionally in the same category as his knowledge of other people's past. Trait knowledge of his current, subdued self is similarly accurate in the absence of any 'remembering' of specific events involving this self (Tulving, 1993). K.C. has managed to acquire some personal gist-like knowledge over the years of his life since his injury, but this acquisition is attributable to a semantic learning mechanism that can operate without the luxury of rich episodic detail, an important point to which we shall return later.

K.C.'s new 'self' is readily apparent in his behaviour during testing sessions. He is always agreeable, courteous, and attentive, never complaining of fatigue and taking pleasure in the challenge posed by many of the tests. K.C.'s suitability as a research participant is further reinforced by the fact that he never confabulates. If anything, he is very conservative in his responses, saying 'yes' or 'no' to a question only when he feels absolutely sure of the answer. He therefore guesses that he has never met one of the authors (R.S.R.) who has, in fact, visited him at his home approximately eight times a year for the past 5 years, though there is a certain level of familiarity and comfort that he demonstrates, particularly in a greater willingness to initiate conversation and to ask questions.

Of relevance here is K.C.'s appropriate, albeit blunted, repertoire of emotional reactions. K.C.'s ability to comment on his current emotional state, together with his clear appreciation of humour and sarcasm, further suggests an intact "theory of mind," such that he is quite able to infer his own and others' thoughts, feelings, and intentions (for recent reviews of this topic, see Frith & Frith, 2003; Siegal & Varley, 2003). This is in sharp contrast to a complete personal disconnection from the emotional details of past experiences with personal and world tragedies that, under normal circumstances, would have been branded as a mental snapshot of the greatest vividness and intensity. Consider a few examples. K.C.'s younger brother from whom he was once inseparable met accidental death a few years prior to his own head injury. K.C. remembers nothing of the circumstances in which he had learned of this shocking news, including where he was at the time, who told him of the event, and how he reacted emotionally. Likewise, the events of a potentially lethal chemical spill from

a train derailment that forced him and his family to evacuate their home for over a week have been reduced to a dry fact of the world. The events surrounding a recent fall at his family's cottage that resulted in several operations to repair a shattered knee, a cast from waist to toe, and his residing in the main floor living room with crutches for over 6 months, are similarly as good as gone. Each time he is told of September 11, he expresses the same horror and disbelief as someone hearing of the news for the very first time.

Now 51 years old, details of personal occurrences continue to exist only in the present, vanishing from K.C.'s reality the moment his thoughts are directed elsewhere. He remains single and without children, and continues to live with his parents in the house in which they had lived since he was 9 years old. On most days, his mother wakes him between 7:30 h and 8:00 h in the morning for breakfast. After finishing his meal, a note on the microwave door tells him to return upstairs for his daily exercise routine on a treadmill and stationary bicycle. He then dresses and grooms himself in preparation for one of his scheduled half-day excursions, which alternate between volunteering at a local library and participating in such activities as playing pool, swimming, and bowling with a small group of other head-injured people whom he again sees on Friday nights for dinner and a movie. Weekends in the summer and autumn are spent at the family cottage, as they were before his injury, and in the winter and spring at home visiting with family and friends. When nothing specific is planned, K.C. will sit down to play the organ, but he most enjoys playing card games on the computer (particularly Bridge and Solitaire) with the television on in the background (his favourite shows include "Mash" reruns and "The Price is Right"). He then eats dinner with his family, watches television, and retires on his own at 11:00 p.m.

The seamless ease with which K.C. goes about daily activities might fool an uninformed observer into overlooking his complete loss of episodic memory function. As alluded to earlier, amnesia can also be defined by the kinds of memory that are commonly spared. Retention of the many skills and semantic facts learned in pre-accident years enables K.C. to locate without difficulty cereal and eating utensils in the kitchen, to know that the eight-ball is the last to sink in a game of pool, and to explain the difference between a strike and spare in bowling, and between the front crawl and breast stroke. He can describe the layout of his house and summer cottage, and the shortest route between them, without any recollection of a single event that occurred at either of these places. He expects a new 'trick' after four cards are placed in the centre of the Bridge table and anticipates Bob Barker on the "Price is Right" asking contestants to "spin the wheel," though he cannot foresee what he himself will do when the card game or television show is over. Like many individuals suffering from amnesia, he is also able to learn new information or skills normally, such as sorting books according to the Dewey decimal system in his library job, even though he is unable to recall explicitly the circumstances of this anterograde learning, indicating preserved implicit memory.

Taken together, anecdotal evidence suggests that K.C. is in many ways like any other healthy individual. His store of semantic facts about himself and the world, procedural skills that were acquired in the first 30 years of his life, and his effortless functioning in his everyday environment are comparable to most of his age mates. What makes him different, even from many amnesic cases, is his inability to recollect any specific event in which he himself participated or any happening that he himself witnessed. This overall profile has not changed much over the years, an observation consistent with the stability of results from extensive neurological and neuropsychological testing and with the pattern and extent of K.C.'s brain damage as revealed on MRI scans, to which we turn next. It also stands the test of more objective experimental measures that we will describe in later sections.

3. Neurological status

Based on three detailed neurological examinations performed approximately once per decade, it may be concluded that K.C.'s neurological status has remained largely stable since his 1981 accident. Similar to findings from his December 1986 exam (detailed in Tulving, Schacter, McLachlan, & Moscovitch, 1988), significant neurological signs described in October 1994 and March 2003 exams include bilateral anosmia, affecting both identification and discrimination of smells, and a right homonymous hemianopia, involving the upper field with lower quadrant and macular sparing. The additional presence of bilateral optic disk pallor relates to glaucoma that developed soon after K.C.'s 1981 accident and has been under treatment ever since. Corrected visual acuity as assessed most recently is 20/40 on the right and less than 20/400 on the left; with his left eye K.C. can identify large letters at 3 ft and see finger movement at 6 ft. This progressive visual loss in the left eye is due in large part to his glaucoma, but corrected vision in the right eye remains within normal limits. Eye movements are full in the horizontal and vertical planes, and there is no nystagmus. There is normal facial symmetry and strength. The remaining cranial nerves are intact as before. Somatosensory function is normal, though there may be a slight decrease in temperature perception on the right side. On motor examination, again as assessed most recently, strength, bulk, tone, and reflexes are within normal limits, except for decreased dexterity in the right hand and a right extensor plantar response. Cerebellar function is normal, but gait continues to be wide based and somewhat antalgic as a result of musculoskeletal problems (mostly osteoarthritis) from Ehler–Danlos syndrome.

On mental status screening tests administered in October 1994, K.C. received a score of 27/30 on the Mini Mental Status Examination. Retesting of mental status on the Dementia Rating Scale in March 2003 revealed a score of 125/144, which is above the cutoff for dementia, with most points lost on the memory subscale. A more elaborate assessment

of this and other mental capacities is discussed in the next section.

4. Neuropsychological profile

K.C. underwent a detailed neuropsychological examination across multiple sessions in 1996 and was re-examined in March 2003 on an abridged version of the test battery to ensure that earlier scores still reflect his current level of cognitive functioning. Comparison of the current test results with those from previous assessments conducted in the late 1980s (reported in Tulving et al., 1988; Tulving, Hayman, & Macdonald, 1991) indicates that K.C.'s cognitive status generally has remained stable over the years. We will comment on the few areas of function that do appear to have changed since the onset of his amnesia.

4.1. General intellectual and non-mnemonic cognitive function

As illustrated in Table 2, results from cognitive testing show that K.C.'s intellectual and cognitive function outside the domain of episodic memory are largely, although not completely, preserved. His verbal IQ on the revised version of the Wechsler Adult Intelligence Scale (WAIS-R; Wechsler, 1981), as administered in 1996, was in the normal range, and his performance IQ was in the lower normal range, which is slightly below expected based on a verbal estimate of premorbid intelligence derived from the National Adult Reading Test (Ryan & Paolo, 1992). Nonetheless, on the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999) administered in 2003, which produces IQ scores that are highly correlated with those from the full WAIS-R battery, he obtained Full-Scale, Performance, and Verbal IQ scores of 99. This indicates an improvement in the non-verbal Performance domain back to earlier levels, perhaps due to better management of his glaucoma in more recent years.

K.C.'s language functions are also generally well preserved. His spontaneous speech is sparse but well articulated. He shows no word-finding difficulties, paraphasic errors, or syntactic errors in daily conversation. In line with these informal observations, he shows no signs of aphasia on the Western Aphasia Battery (Kertesz, 1982) and has no difficulty in naming line drawings of objects on the Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 1983). Word generation to a category cue is in the average range, which is consistent with average performance on a vocabulary test of semantic memory (WASI Vocabulary subtest). However, he exhibits a markedly reduced fluency for spontaneous verbal output, including poor performance on the FAS phonemic fluency task (Spreen & Strauss, 1998). With respect to visuospatial function, K.C. performs well on tasks that require basic visual feature analysis such as matching lines of the same orientation on the Judgment of Line Orientation Test or matching simple forms on the Visual Form Discrimina-

Table 2
Neuropsychological profile of patient KC

	1996	2003
Mental status		
DRS (/144)[a]		125
Attention (/37)		37
Initiation/perseveration (/37)		34
Construction (/6)		6
Conceptualization (/39)		34
Memory (/25)		14
General intellectual function		
WAIS-R (standard score)		
FSIQ	88	99[b]
VIQ	96	99
PIQ	79	99
AM-NART (standard score)	102	
Language		
Western Aphasia Battery (/100)	98.2 (unimpaired)	
WAIS-R vocabulary (scaled score)	9	9[b]
Boston naming (/60)	57 (unimpaired)	
Semantic fluency[c] (scaled score)	10	
Anterograde memory		
WMS-R		
General memory (standard score)	61	
Verbal memory (standard score)	67	
Visual memory (standard score)	69	
Logical memory I (percentile)	5	< 5
Logical memory II (percentile)	<1	< 1
Visual reproduction I (percentile)	13	
Visual reproduction II (percentile)	<1	
WRMT (/50)		
Words	26	
Faces	25	
CVLT		
Acquisition (*T*-score)	12	
Short delay free (*Z*-score)	−5	
Long delay free (*Z*-score)	−5	
Recognition Discrimination (*Z*-score)	−5	
ROCF (/36)		
Immediate recall	4	
Delayed recall	0	
Retrograde memory		
AMI autobiographical (/9)		
Childhood	2	
Early adult life	3	
Recent life	1	
AMI personal semantics (/21)		
Childhood	16	
Early adult life	13.5	
Recent life	8	
Visuospatial function		
Judgement of line orientation (/30)	23[d] (unimpaired)	
Benton Visual Discrimination Test (percentile)	>95	
ROCF copy (/36)	36	
WAIS-R Block Design	6	9[b]
Hooper visual organization (*T*-score)	79[d]	
Benton Face Recognition Test (percentile)	1st	2–16
Executive function		
Letter fluency[e] (scaled score)	6	
WAIS-R Digit Span (scaled score)	12	
WASI similarities (scaled score)		11

Table 2 (*Continued*)

	1996	2003
WASI matrix reasoning (scaled score)		11
WCST		
Categories (/6)	6 (unimpaired)	
Perseveration response (*Z*-score)	−0.9	
Trail Making Test		
Part A	Raw score = 138 s	
Part B	Raw score = 291 s	
Concept Generation Test groupings	4 (unimpaired)	

Note: DRS, Dementia Rating Scale; WAIS-R, Wechsler Adult Intelligence Scale-revised; AM-NART, American National Adult Reading Test; WMS-R, Wechsler Memory Scale-revised; CVLT, California Verbal Learning Test; ROCF, Rey Osterrieth complex figure; AMI, autobiographical memory interview; WCST, Wisconsin Card Sorting Test.

[a] Normal cutoff = 123.

[b] Score on the Wechsler Abbreviated Scale of Intelligence (WASI).

[c] Score is based on the number of animal names produced in 1 min.

[d] Age-corrected score.

[e] Score is based on the total number of words produced for the letters F, A, and S when given 1 min for each.

tion Test (Benton, Hamsher, Varney, & Spreen, 1983). He is also unimpaired in visuospatial reproduction of the Rey Osterrieth Complex Figure (ROCF; Osterrieth, 1944), reconstruction of designs with blocks (WASI Block Design subtest), and in identifying objects on the basis of line drawings on the BNT (see above). Visual impairments are, however, apparent in colour perception on the City University Color Vision Test (classification: borderline tritan; Fletcher, 1980) and on the Farnsworth–Munsell 100-Hue Test (Farnsworth, 1957). Impairments were also present on a more complex face-matching task that requires the synthesis of multiple visual features (Facial Recognition Test; Benton et al.), but performance on this task improved to borderline-low average since the 1996 assessment.

With respect to tests of executive function, K.C. exhibits no deficits on the Wisconsin Card Sorting Test (WCST; Heaton et al., 1993). The number of categories obtained for 128 items as well as the number of perseverations to preceding categories is within the normal range. K.C. also has no difficulty performing the Concept Generation Test (Levine, Stuss, & Milberg, 1995). The number of correct groupings K.C. generated for the items of the test is comparable to the number achieved by healthy control subjects of similar age. Moreover, he does not perseverate on any of the self-generated responses. K.C.'s completion times for the two parts of the Trail Making Test (Army Individual Test and Battery, 1944), another test of executive function, clearly falls outside of the normal range of performance, but this could in part be attributed to his decreased right limb dexterity and osteoarthritic changes in his hands. It has been suggested that the ratio between the completion times for Trails A and B provides a measure of executive functioning that is independent of motor speed. The ratio for K.C. (0.47) is comparable to the ratio of means reported by Stuss, Stethem, and Poirier (1987) for healthy control subjects of equivalent age (0.43). Finally, working memory performance, as assessed in 2003, is within normal limits on both forward and backward digit span tests of the WAIS-R.

4.2. Anterograde memory function

K.C.'s performance on the Wechsler Memory Scale-Revised (WMS-R; Wechsler, 1987), California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987), Warrington Recognition Memory Test for words and faces (WRMT; Warrington, 1984), and recall of the ROCF confirmed his severe anterograde memory impairment. This is true whether the material is verbal (CVLT; WRMT for words; WMS-R logical memory) or non-verbal (WRMT for faces; WMS-R visual reproduction; ROCF immediate and delayed conditions) and whether the test format is free recall (CVLT; WMS-R logical memory; WMS-R visual reproduction), cued recall (CVLT), yes–no recognition (CVLT), or forced-choice recognition (WRMT). Of note, although K.C. is able, at times, to recall a limited amount of information immediately after learning (logical memory I; visual reproduction I; CVLT List A trials 1–5), he is unable to retain any information over delays as short as 20 or 30 min on the same tasks (CVLT long-delay recall; logical memory II; visual reproduction II). Moreover, he performs at chance on the WRMT for faces and words, even immediately after exposure to the target material; in the most recent examination, he obtained a scaled score of 4 (<5 percentile) for the immediate recall condition and a scaled score of 1 (<1 percentile) for the delayed condition of the WMS-III logical memory subtest.

Given that K.C. is impaired in the perceptual matching of faces, his severe deficits on the forced-choice recognition memory test for faces (WRMT) likely reflect a mixture of perceptual-discrimination and memory impairments. To obtain a purer measure of K.C.'s anterograde memory abilities for non-verbal information, he has also been tested on Smith and Milner's memory task for the spatial location of visually presented common objects (Smith & Milner, 1981; Smith, 1988). This task taps non-verbal memory processes by probing memory for the location of 16 easily identifiable objects in an array. K.C.'s mean displacement score, which reflects the Euclidian distance between target and remembered locations, was 23.0 cm. This score is comparable to the one reported by Smith (1988) for the densely amnesic patient H.M. (26.5 cm), whose performance is severely impaired relative to normal control subjects (mean = 7.4 cm).

4.3. Retrograde memory function

To document the extent of K.C.'s retrograde memory impairments, he was administered the Autobiographical Memory Inventory (AMI; Kopelman, Wilson, & Baddeley, 1989, 1990) and the Galton–Crovitz word–cue technique in 1996 (Crovitz & Schiffman, 1974). The AMI samples autobiographical incidents (unique episodes) and personal semantic information (facts pertaining to the person's past) from

childhood to recent years. In K.C.'s case, the scores for 'recent years' reflect a measure of anterograde memory functioning. According to available norms, K.C.'s scores on the autobiographical subsections fall within the 'definitely abnormal' range and are lower than the average for the two groups of amnesic patients presented in the manual. During testing, K.C. could not produce a single episode from his past that was distinct in time and place. Performance on the personal semantics subsections was comparable to that reported by Kopelman et al. for other amnesic patients, with the childhood period classified as 'acceptable' according to AMI norms. K.C. showed a similar pattern of deficit on the Galton–Crovitz task for autobiographical information, which was administered in the version developed by Moscovitch and Melo (1997). His performance improved only minimally when he was provided with additional prompts aimed at facilitating recall. When no prompts were presented, K.C. did not produce any confabulations. In response to prompts, he provided two details that were classified as confabulations. In comparison, the confabulating amnesic patients tested by Moscovitch and Melo produced on average 16 confabulations when no prompts were given and 38 confabulations in response to prompts.

5. Magnetic resonance imaging of brain pathology

Structural MRI of K.C.'s brain was first performed in 1990, the results of which are detailed in the paper by Tulving et al. (1991). K.C. underwent MRI scanning again in 1996 and in 2002. Visual inspection of the resulting images across the different examinations reveals no apparent changes. In the following, we will first provide a general, primarily qualitative description of K.C.'s MRI results. We then will present the quantitative results obtained from a volumetric analysis of medial temporal lobe and related limbic structures, which was based on the 1996 examination obtained with a MRI protocol that was optimized for this purpose (Callen, Black, Gao, Caldwell, & Szalai, 2001; see also Köhler et al., 1998). Images shown in Figs. 1–3 are from the most recent MRI in 2002.

5.1. Brain regions other than limbic structures

Overall, T1-weighted images show evidence of mild diffuse cortical atrophy. This atrophy reflects thinning of the cortical rims and underlying white matter in all lobes and coincides with bilateral ventricular enlargement. Throughout the brain, the left hemisphere is affected to a greater extent than the right hemisphere. Focal signal abnormalities are also observed predominantly in the left hemisphere. They include a posterior lesion in occipital–temporal cortex and an anterior lesion in frontal–parietal cortex and underlying white matter.

The left-sided posterior hypointensity on the MR images reflects a lesion that appears to be occipital–temporal infarction probably resulting from posterior cerebral artery compression secondary to the increased intracranial pressure caused by the head trauma in K.C.'s motorcycle accident. A contiguous volume of encephalomalacia (softening of the brain tissue) is seen in the lingual gyrus, fusiform gyrus,

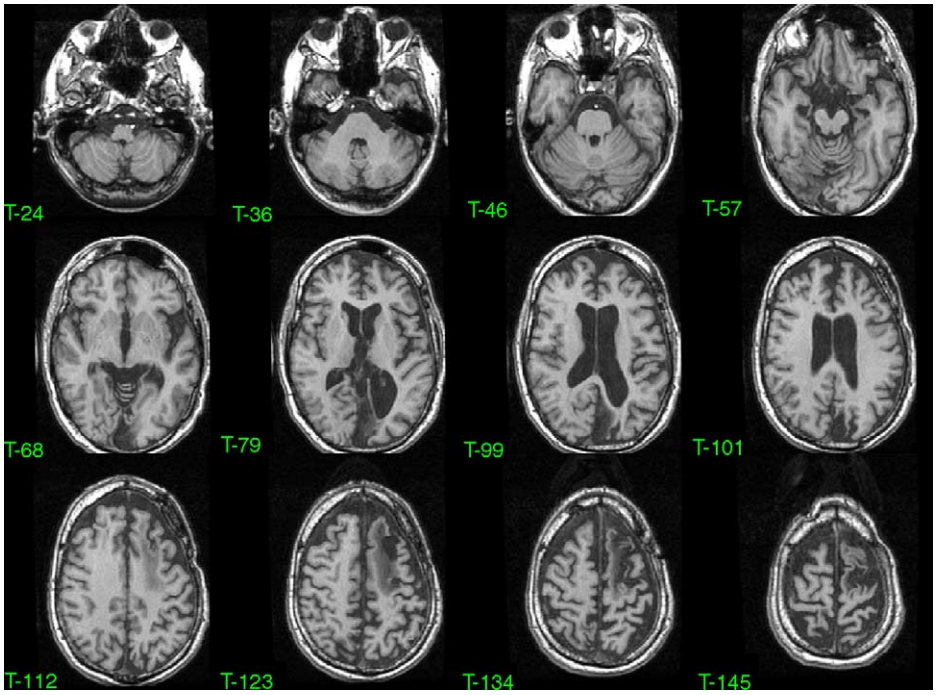

Fig. 1. T1-weighted axial images of K.C.'s brain arranged from inferior to superior. Images are 0.86 mm thick and are spaced 9.46 mm apart. Dark signal indicates damaged tissue. The right hemisphere is shown on the left side of the images.

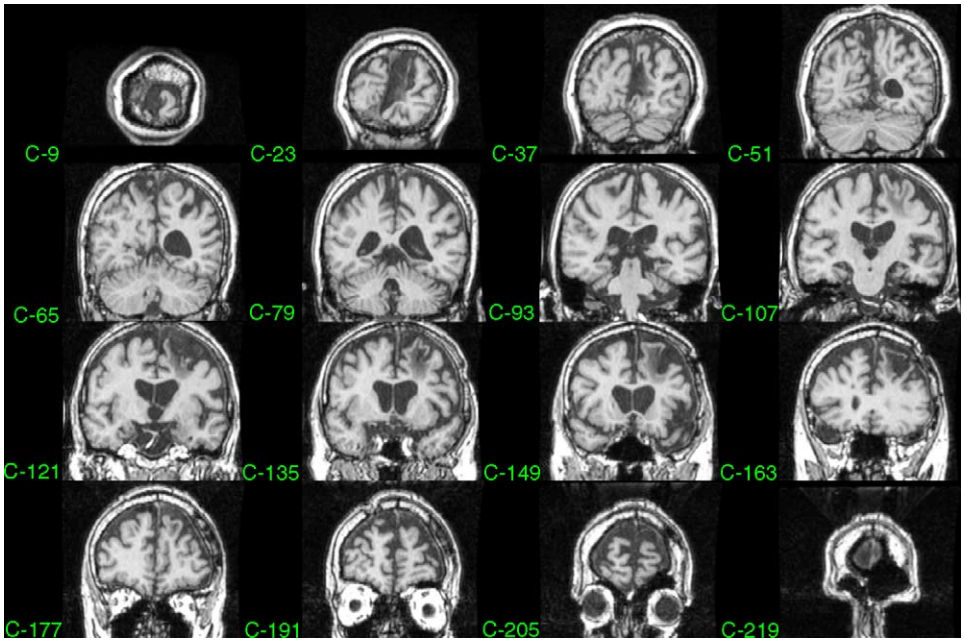

Fig. 2. T1-weighted coronal images of K.C.'s brain arranged from anterior to posterior. Images are spaced 12.04 mm apart. Dark signal indicates damaged tissue. The right hemisphere is shown on the left side of the images.

cuneus, precuneus, and parts of superior, middle, and inferior occipital gyri (lesion volume = 21,094 mm^3). Rostrally, medial aspects of the lesion extend into retrosplenial cortex. Whereas the cuneus and lingual gyrus, including calcarine cortex, are quite necrotic, the superior, middle, and inferior occipital gyri show substantial sparing. Large portions of the fusiform gyrus are also spared. Approximate visual matching of the MR images with the template of Brodmann's areas (BA) provided by Talairach and Tournoux (1988) suggests that the posterior lesion affects BA 17–19, 31, 30, and 23.

The left anterior hypointensity (lesion volume = 27,909 mm^3) may reflect sequelae of the subdural hematoma that was diagnosed and removed in hospital immediately following K.C.'s head trauma. Encephalomalacia is observable primarily in the white matter superior to the lateral ventricles, undercutting adjacent gray matter. Caudally, it begins approximately at the level of the posterior commissure, undercutting

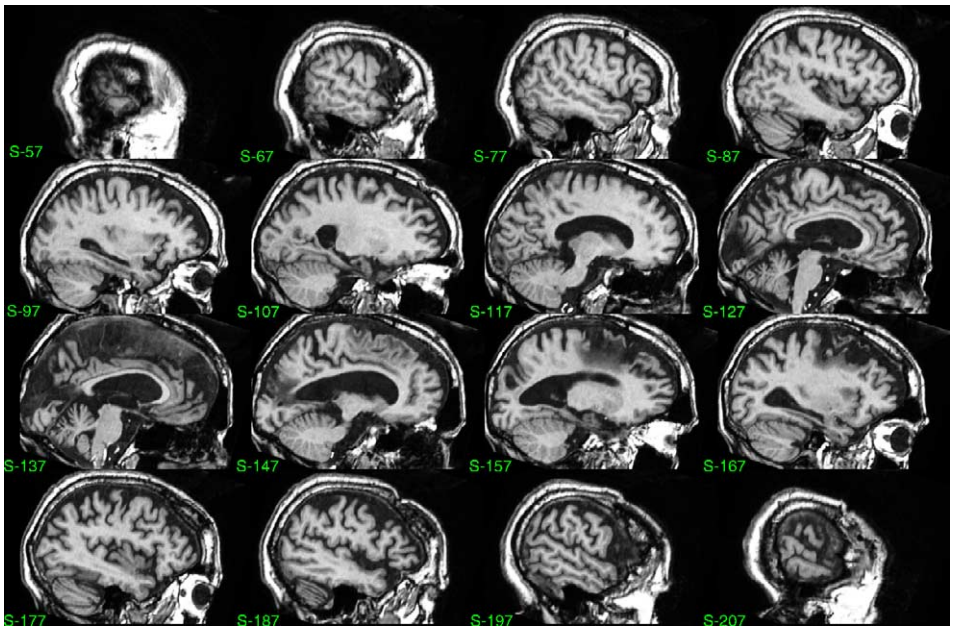

Fig. 3. T1-weighted sagittal images of K.C.'s brain arranged from right to left. Images are spaced 8.6 mm apart. Dark signal indicates damaged tissue. Images proceed from right to left.

the left post-central gyrus. From there, it extends into the white matter that underlies the superior pre-central gyrus, affecting large portions of the pyramidal tract. Further rostrally, the lesion undercuts superior pre-motor cortex and large aspects of the middle and superior frontal gyri (dorsolateral prefrontal cortex), extending to a level approximately 1.5 cm anterior to the genu of the corpus callosum. Anterior gray matter signal abnormalities appear to be limited to premotor cortex, suggestive of cystic alterations. Ventrolateral pre-frontal cortex and underlying white matter are spared in their complete extent. Approximate visual matching of the MR images with the Talairach and Tournoux atlas (1988) suggests that the anterior lesion affects white matter underlying BA 1–4, 6, 8, and 9. White matter underlying BA 44–46 and 10 seems to be spared.

Signal hypointensity in the right hemisphere can be seen in the right precuneus and in the white matter underlying the medial frontal sulcus and the head of the caudate nucleus, both reflecting sequelae from surgical shunting.

5.2. Medial temporal lobes: qualitative examination

Visual inspection of the T1-weighted MR images reveals pronounced bilateral signal abnormalities in the hippocampal formation and notable atrophy in neighbouring parahippocampal gyrus. These structures appear severely affected along the entire rostrocaudal extent (i.e., longitudinal axis) of the hippocampus (see Fig. 4). Lateral temporal cortex appears to have been spared from focal damage.

More fine-grained analysis of the MR images suggests that the hippocampal formation is in large parts necrotic in both hemispheres, and any remnants of non-necrotic tissue appear severely atrophic. Tissue loss in neighbouring medial temporal cortices seems to be less severe but substantial nonetheless. Signal abnormalities suggestive of necrosis can be observed in entorhinal cortex, and there is evidence of pronounced atrophy in perirhinal and parahippocampal cortices (see Amaral & Insausti, 1990 for a definition of these structures in humans). The collateral sulcus, which is lined in anterior portions by perirhinal cortex and more posteriorly by the parahippocampal cortex, is visible along its entire rostrocaudal extent in both hemispheres, indicating that tissue loss in these cortices is only partial.

5.3. Medial temporal lobes and related limbic structures: volumetric analyses

The extent of tissue loss in medial-temporal and related limbic areas was quantified using a volumetric protocol developed in our laboratory in conjunction with a study on Alzheimer's disease (Callen et al., 2001). To do this, comparisons were made with the MR images of five age-matched participants who had served as healthy controls in the Callen et al. study (three males, two females; mean age = 52.8 years, S.D. = 8.1). The structures measured included the hippocampus, amygdala, adjacent cortices in the parahippocampal gyrus (i.e., a combined estimate of entorhinal, perirhinal, and parahippocampal cortex), mammillary bodies, the septal area, basal forebrain, hypothalamus, anterior and posterior thalamus, caudate nucleus, different portions of the cingulate cortex, and orbitofrontal cortex.

A factor that complicates the interpretation of volumetric reductions in the structures assessed in K.C. is the presence of generalized cortical atrophy that was described above. To determine which structures in the medial temporal lobes and other parts of the limbic system show a disproportionate volume loss that extends beyond the expected reduction associated with generalized cortical atrophy, we computed an

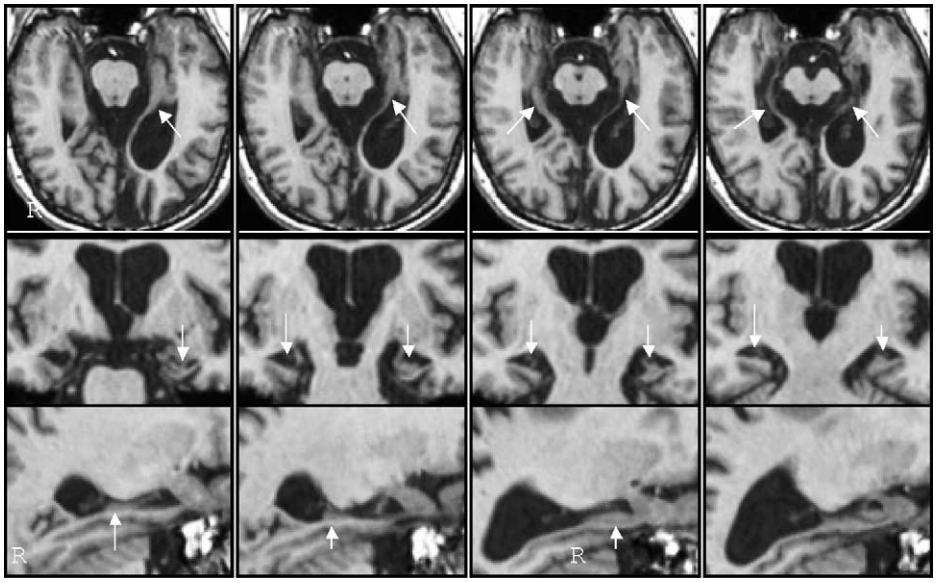

Fig. 4. T1-weighted images in axial (top), coronal (middle), and sagittal (bottom) views indicating the extent of damage in K.C.'s medial temporal lobe (dark signal areas).

Table 3
Comparison of volumes for medial temporal lobe and related limbic structures in K.C. and control participants

Brain structure	Controls volume (mm^3) (S.D.)		K.C. volume (mm^3) (*Z*-score)	
	Left	Right	Left	Right
Hippocampus	3974.01 (413.13)	4020.28 (356.94)	**749**.12 (**−7.8**)	**533**.55 (**−9.8**)
Parahippocampal gyrus	1871.68 (73.05)	2009.95 (241.86)	**476**.40 (**−19.1**)	**857**.48 (**−4.8**)
Amygdala	1564.09 (309.97)	1326.81 (396.13)	**512**.46 (**−3.4**)	452.29 (−2.2)
Mammillary bodies	49.19 (9.33)	50.67 (10.01)	**15**.03 (**−3.7**)	25.55 (−2.5)
Septal area	351.63 (76.18)	339.14 (69.73)	**68**.67 (**−3.7**)	**59**.65 (**−4.0**)
Basal forebrain	199.19 (94.60)	206.38 (88.96)	69.22 (−1.4)	81.25 (−1.4)
Hypothalamus	295.81 (82.54)	304.22 (107.26)	116.85 (−2.2)	172.46 (−1.2)
Anterior thalamus	991.56 (118.29)	1072.87 (144.93)	**252**.68 (**−6.2**)	617.78 (−3.1)
Posterior thalamus	4864.96 (327.17)	4794.41 (302.44)	**2619**.51 (**−6.9**)	**2876**.23 (**−6.3**)
Caudate nucleus	1901.14 (70.40)	1830.32 (96.65)	**1424**.07 (**−6.8**)	**1191**.41 (**−6.6**)
Anterior cingulate cortex	4827.40 (1831.43)	4288.69 (1550.68)	4415.09 (−0.2)	4061.62 (−0.1)
Middle cingulate cortex	2509.00 (593.56)	2455.43 (421.35)	2324.19 (−0.3)	1925.48 (−1.3)
Posterior cingulate cortex	3834.90 (793.29)	3524.72 (568.19)	2617.50 (−1.5)	2389.30 (−2.0)
Orbitofrontal cortex	14133.63 (3793.92)	14658.61 (3608.29)	9143.69 (−1.3)	9371.85 (−1.5)

Note: *Z*-scores shown in bold typeface reflect disproportionate volume loss in K.C. (see text for details). Volumes were corrected for variations in head size.

additional estimate of K.C.'s global atrophy based on ventricular enlargement. This measure was obtained after segmenting the T2-weighted and proton-density MR images into the various tissue components. K.C.'s estimate for ventricular CSF was then compared with that of the controls after correcting for differences in head size, and special care was taken to exclude any lesion areas filled with CSF from this estimate. Using this approach, we found K.C.'s ventricles to be enlarged by 3.38 standard deviations as compared to the mean value in the controls. Accordingly, we chose to consider differences in volume greater than $Z = 3.38$ to reflect a disproportionate tissue loss.

The results of the volumetric analyses for all structures examined are displayed in Table 3. All estimates were corrected for inter-individual differences in head size using the procedure described by Callen et al. (2001). Taking global atrophy into account, the most prominent volume reductions were observed bilaterally in K.C.'s hippocampus and parahippocampal gyrus. Disproportionate tissue loss was also found to extend into other limbic structures that are neuroanatomically connected to the hippocampus and that have been suggested to play a role in memory, including the septal area bilaterally, mammillary bodies and amygdala on the left, caudate nuclei, and anterior and posterior portions of the thalamus. The observation that not all structures examined showed a volume loss greater than the critical score of $Z = 3.38$ provides direct support for our interpretation that the described volume reductions in the medial temporal lobes and in a few related limbic structures are indeed disproportionate and cannot be accounted for by generalized brain atrophy.

5.4. Summary of neuroanatomical damage and its relation to performance on standard neuropsychological tests

The pattern of damaged and spared tissue in K.C. may help account for some of his neuropsychological test profile. Damage to occipitotemporal structures, largely in the left hemisphere, from cuneus and through lingual and parahippocampal gyri, is consistent with difficulties in perception of colour and face matching under degraded conditions. Importantly, other aspects of his perception and recognition are preserved, including tasks requiring basic visual feature analysis such as line orientation and form discrimination, as well as more complex processes such as reading and recognition of objects and familiar faces. It is possible that damage to posterior neocortical areas contributed to K.C.'s autobiographical episodic memory loss by affecting his visual imagery (Rubin & Greenberg, 1998), a hypothesis that we tested and report later in the paper.

Damage to regions of frontal cortex is limited to dorsolateral and pre-motor areas. As a result, performance on tests of phonemic, but not semantic, fluency is impaired. No other deficits were observed on tests of executive function, including WCST, the ratio of Trails B to A, working memory, and tests of abstract reasoning. Nonetheless, because frontal functions contribute to strategic retrieval on tests of recent and remote memory, we tested the possibility that frontal deficits may be related to loss of autobiographical memory and report the results below.

The extent of damage to K.C.'s medial temporal lobes, particularly to his hippocampus and parahippocampus, and associated diencephalic and basal forebrain structures, is in line with his profound impairment on all explicit tests of new learning and memory. There is some uncertainty as to whether this pattern of neurological damage also accounts for his severe remote autobiographical memory loss while sparing his remote spatial memory. These issues are discussed at length in later sections. Additional damage to K.C.'s amygdala may account for his blunted affect and personality changes, contributing, in turn, to his remote autobiographical memory loss, but it remains for future research to investigate these possibilities more fully. Sparing of lateral temporal cortex and occipital structures accounts for his preserved semantic

memory and performance on implicit tests of learning, which we review next.

6. Experimental investigations

6.1. Studies of new learning

The detailed analysis of K.C.'s lesion and related deficit profiles presented in the last section accentuates the fact that, unlike H.M., K.C.'s story is more complicated on several counts: aspects of both anterograde and retrograde memory were affected by his closed head injury, consistent with the multiple loci of damage amply demonstrated by his MRI scans. The diffuse nature of K.C.'s brain pathology becomes especially problematic when one wishes to attribute any particular deficit to a single lesion site. However, as will become increasingly apparent in the following sections, it is his deficits against a background of preserved function that makes him remarkable to study. K.C. first participated in memory experiments during the early-to-mid-1980s at the Unit for Memory Disorders at the University of Toronto. Most of the early studies can be divided into two broad categories: priming and new semantic learning. K.C. also participated in a study of memory for object location and identity that described a phenomenon called mnemonic precedence, which relates to acquisition of episodic information. These experiments, along with others on retrograde memory described later on, pioneered a number of conceptual traditions for which our Toronto group became known and that (for better or for worse) continue to influence the field at large to this day.

6.1.1. Priming

Priming refers to an improvement or change in the identification or production of an item as a consequence of a prior encounter with the item (e.g., Tulving & Schacter, 1990). Priming is a form of non-conscious or implicit memory in the sense that it can occur in the absence of explicit or conscious recollection of a prior encounter with a primed item (Schacter, 1987; Schacter & Curran, 2000). In the early-to-mid-1980s, when K.C. began to participate in experiments at the Unit for Memory Disorders, priming was a new and hot topic in memory research. Building on the seminal findings of Warrington and Weiskrantz (1974) and of Rozin and Diamond (Diamond & Rozin, 1984; Rozin, 1976) that revealed surprising preservation of memory in amnesic patients when they were cued with word beginnings for recently studied words, new data showed that priming could occur at normal levels in amnesic patients (e.g., Graf, Squire, & Mandler, 1984) and that priming could be dissociated from explicit recollection in healthy young adults (e.g., Graf et al.; Jacoby & Dallas, 1981; Tulving, Schacter, & Stark, 1982).

During the mid-1980s, a fundamental theoretical question concerned whether priming is based on the activation of pre-existing items or associations, or whether priming reflects the establishment of novel representations that are newly created during a specific study episode (Rozin, 1976). K.C. participated in several studies that addressed this issue. Graf and Schacter (1985) tested the hypothesis that priming depends on the activation of pre-existing representations by presenting amnesic patients and normal subjects with unrelated word pairs to study (e.g., window–reason, jail–strange). On a subsequent word-stem completion test, subjects were instructed to write down the first word that came to mind in response to a three-letter word beginning, paired either with the identical word from the study list (e.g., window–rea__; *same context condition*) or another list word (e.g., jail–rea__; *different context condition*). Amnesic patients and controls showed greater priming in the same, than in the different context condition, thereby indicating that novel associations between the unrelated words, formed during the study trial, influence the magnitude of priming (see also Moscovitch, Winocur, & McLachlan, 1986, in which K.C. participated).

Subsequent analyses of these data indicated that priming of new associations was observed mainly in patients with relatively mild memory disorders. Schacter and Graf (1986) followed up on this observation by using a variant of their original paradigm to compare the performance of four "severely amnesic" patients (including K.C.) with that of four "mildly amnesic" patients, where severity of amnesia was based on the difference between Wechsler IQ and MQ scores. To increase the reliability of data from individual patients, each patient participated in four separate study-test sessions; each study-test session used different word lists. Mildly amnesic patients showed more priming in the same, than in the different context condition, whereas severely amnesic patients did not. K.C. showed no hint of associative priming. Across four lists, he actually completed fewer stems with previously studied words in the same context condition (0.38) than in the different context condition (0.46). Note, however, that K.C. did exhibit a powerful overall priming effect compared with the baseline completion rate for non-primed items (approximately 0.10).

K.C. also participated in a study by Schacter (1985) that examined priming of old and new associations using a different approach. Schacter compared priming of familiar idioms (e.g., *sour grapes*, *small potatoes*) with novel phrases that were generated by repairing components of familiar idioms (e.g., *sour potatoes*, *small grapes*). Priming was assessed with a free association task in which the first word from the pair was presented and subjects wrote down the first word that came to mind. Amnesic patients showed priming following study of familiar idioms (0.27) as did control subjects (0.23), but did not show any priming after studying the re-paired items. However, even control subjects failed to show priming of the re-paired items (0.02).

The idea that association-specific, relational learning is simply not possible, even at an implicit level, and that only item-specific, non-relational priming can be observed in amnesia held prominence for many years after the initial studies with K.C. (e.g., Cohen, Poldrack, & Eichenbaum, 1997).

Although other groups had been successful at demonstrating intact implicit associative learning in amnesic patients (Gabrieli, Keane, Zarella, & Poldrack, 1997; Moscovitch et al., 1986), the possibility that these effects were due to a motor skill-learning mechanism was not ruled out. The validity of the relational-deficit theory was finally overturned in a very recent investigation of single-trial learning in a group of amnesic patients that again included K.C. (Goshen-Gottstein, Moscovitch, & Melo, 2000). Word pairs from sentences generated by participants at study (intact pairs) were presented along with re-arranged pairs of studied words and pairs of unstudied words intermixed with non-words for a lexical decision to be made at test as to whether both items in each pair are legal English words. K.C., along with the other patients, was able to recover implicitly these new associations for as long as 30 min after they were formed, indicated by faster decisions to intact pairs (1434 ms) compared to rearranged pairs (1528 ms) or pairs of new words (1641 ms). Importantly, he failed to recollect the same items on explicit testing. Moreover, the use of sentence generation for studying the word pairs within a one-trial learning episode prevented a stimulus–response or skill-learning explanation of the results that would have been viable had an identical response to stimuli at study and at test been made. The results of studies of associative priming, therefore, indicate that binding of unrelated materials, which some consider to be hippocampally dependent, can occur in the absence of this structure. Further research is needed to determine the nature and limits of this extra-hippocampal binding process, in particular, whether it is domain-specific or whether it can bind material across domains as is possible in hippocampally mediated learning.

Yet another priming study from earlier years examined an issue that assumed theoretical importance during the 1980s: the longevity of priming effects. An early study with college students showed that the priming effects on a word fragment completion task—enhanced facility of identifying words in which some letters were deleted, for example, AS--SS- - for ASSASSIN—could persist for a week (Tulving et al., 1982). However, research with both amnesic patients and healthy subjects using another kind of priming task—stem completion—suggested that priming is a far more transient phenomenon, disappearing completely after only a 2-h interval between study and test (Graf et al., 1984; Rozin, 1976). These findings raised the possibility that long-lasting priming effects are attributable to explicit recollection of previously encountered words, the so-called 'explicit contamination' hypothesis. McAndrews, Glisky, and Schacter (1987) included K.C. in a study to test this idea. Amnesics and controls were given sentence puzzles that are difficult to comprehend in the absence of a critical solution word. For example, the sentence "The haystack was important because the cloth ripped" seems to make little sense—until the key word "parachute" is presented (Auble, Franks, & Soraci, 1979). Participants were presented with a series of such sentences and were provided with solution words when they could not generate solutions of their own. The sentences for which solution words had been provided by the experimenter were presented again after delays ranging from 1 min to 1 week, and subjects again attempted to generate a solution word.

The critical data came from the two patients in this study who were classified as "severely amnesic:" K.C. and a patient with amnesia attributable to a ruptured aneurysm of the anterior communicating artery. They showed robust priming following a single study exposure at all delays (approximately 50% correct solutions to previously unsolved sentence puzzles), the magnitude of priming did not change between the 1 min and 1 week delays, and the number of study repetitions (varied from one to five) had no systematic effect on the magnitude of priming. This learning and its retention over time, shown by both K.C. and the aneurysm patient, contrasted starkly with the finding of the two patients' explicit memory for once-presented sentences at any delay: they responded "new" on an old/new recognition test to all once-presented sentences, and both showed negligible levels of recognition even after five study repetitions. These observations showed clearly that priming could persist for up to 1 week, in the absence of possibility of 'explicit contamination.' Thus, because K.C. exhibits no hint of any explicit, conscious, or episodic recollection of having encountered the materials, these findings indicate that long-lasting priming can occur entirely on the basis of processes associated with implicit memory.

Köhler et al. (1997) capitalized on K.C.'s resistance to explicit influences in an additional experiment on perceptual priming. Perceptual implicit memory involves the indirect cueing of a previously studied stimulus by one that is structurally similar. By definition then, transfer from one perceptual modality to another should disrupt this effect such that words studied in the visual modality should produce less priming when the test cue is auditory than when it is also visual. However, significant priming in healthy individuals has been observed in cross-modal conditions (Craik, Moscovitch, & McDowd, 1994). One possibility is that cross-modal implicit memory reflects semantic or lexical priming rather than perceptual priming (Bassili, Smith, & MacLeod, 1989). Another possibility, however, is that this priming is ascribed to contamination from explicit memory processes that normally rely on the hippocampus (Jacoby, Yonelinas, & Jennings, 1996). If so, amnesic patients with damage to this structure should benefit from prior exposure to a stimulus only if it was presented within the same modality at test as it was at study.

To test whether perceptual priming effects are 'pure' and therefore modality-specific, Köhler et al. (1997) asked K.C. to make semantic living–non-living judgments either in the same (visual) or different (auditory) modality as visual fragment completion on which he was later tested. K.C. showed normal within-modal priming (0.58), but deficits in cross-modal priming (0.32) and in explicit memory of the same fragments (0.28), indicating that explicit contamination may indeed contribute to cross-modal priming in the healthy brain (but see Verfaellie, Keane, & Cook, 2001).

6.1.2. Complex learning: implications for rehabilitation

Studies of priming clearly indicated that K.C. retains some types of recently studied information over relatively long time periods. However, the form of learning demonstrated in priming experiments is relatively simple, and leaves open the question of whether a severely amnesic patient such as K.C. could acquire more complex forms of knowledge. Further, this issue also has potentially important practical implications: if amnesic patients can acquire information and retain it over time, such learning might help them in their day-to-day lives. A parallel line of study at the Unit for Memory Disorders in earlier years explored this possibility with K.C. and other patients.

The first of several studies on complex learning examined whether K.C. and other amnesics could acquire new vocabulary related to the operation of a desktop computer, and examined a novel method to enhance knowledge acquisition (Glisky, Schacter, & Tulving, 1986a). K.C. and three other patients with memory disorders were repeatedly shown definitions of computer-related words, such as *the blinking symbol on the screen that marks typing location* or *a list of choices presented by a program*. Two methods of learning were compared. The first was a standard anticipation condition in which patients saw the definition and were given 10 s to generate the correct word; if they failed to do so, the word appeared on the computer screen. The second method, called "the method of vanishing cues," resembles a technique devised by Terrace (1963) and was adopted because of the finding that K.C. and many other amnesics show priming when presented with word beginnings. The definition was exposed for 10 s, and if the patient failed to produce the word, the first letter appeared. If the patient still failed to produce the target word after 10 more seconds had elapsed, an additional letter was provided, and so on until the word was produced correctly. The computer recorded the number of letters needed to generate the word, providing one less letter on the subsequent trial. This procedure continued across eight trials, with the cue gradually "vanishing" as one less letter than required on the prior trial for successful production of the word was presented on each successive trial. Patients returned to the laboratory every 2–3 days for a total of eight sessions. A delayed test was given 6 weeks after the final learning-test trial.

K.C. and the other amnesic patients showed higher levels of learning in the vanishing cues condition than in the standard anticipation condition, perhaps reflecting the contribution of preserved priming processes to performance in the vanishing cues condition (control subjects showed no such advantage, possibly because they did not rely as much on priming). Across a 6-week delay, K.C. showed no forgetting in the vanishing cues condition and only a small (7%) loss in the anticipation condition. This robust retention occurred despite the fact that, as expected, he had no recollection that he had ever learned any words and definitions on a computer (nor did K.C. ever show any such recollection from session-to-session during the initial learning phase).

Building on these observations, Glisky, Schacter, and Tulving (1986b) examined whether K.C. and other patients could acquire and retain even more complex forms of knowledge involved in the actual operation and programming of a microcomputer. Using the vanishing cues procedure, K.C. and three additional patients were taught to execute commands such as *save*, *print*, *load*, *run*, *list*, and *lock*, and to use them to write simple programs. Patients were trained during three lessons of increasing complexity. The third lesson, for instance, required patients to master 73 separate keyboard operations. Despite the formidable nature of the learning necessary to master these operations, K.C., like other amnesics, gradually learned to perform the tasks without any letter hints (as usual, he expressed no recollection of having worked on a computer before). In a follow-up study, Glisky and Schacter (1988) reported that K.C. and other amnesics showed excellent retention of the computer-related knowledge after delays of 7–9 months following initial training. K.C. required only a few more hints to perform the computer operations after the long delay than at the conclusion of the initial training. As with work on long-lasting priming, such findings in K.C. highlight that long-lasting complex learning can be manifest as "pure" implicit memory.

Glisky et al. (1986b) noted one way in which the learning attained by K.C. and other patients differed dramatically from that of controls: it was extremely rigid or "hyperspecific." When asked general or open-ended questions about what he had learned, K.C. was unable to provide any answers; when the wording of commands was slightly altered, K.C. could no longer execute them. Such open-ended questions and changes in wording posed no difficulties for control subjects. Glisky et al. suggested that the knowledge acquired by K.C. and other amnesics consists of "simple" stimulus–response connections, whereas healthy controls develop more richly interconnected knowledge structures.

These experiments on complex learning made the important point that dense anterograde amnesia does not prevent people from acquiring new symbolically represented knowledge, the kind of knowledge that extends beyond procedural memory and perceptual priming. Scattered reports of such acquisition were available in the literature at that time (e.g., Kovner, Mattis, & Goldmeier, 1983; Mattis & Kovner, 1984; Wood, Ebert, & Kinsbourne, 1982), but they had not had much influence on theoretical thinking about amnesia. Two further experiments that we describe next provided additional relevant evidence. The first (Tulving et al., 1991) explored the longevity of, and the relation between, primed word-fragment completion and learning of semantic information, and the second (Hayman, Macdonald, & Tulving, 1993) was designed to study the effects of several independent variables on new semantic learning.

Semantic learning in these experiments referred to the learning of new meaningful relations among otherwise familiar words. Thus, in one experiment (Tulving et al., 1991), K.C. saw "stripped down" three-word sentences, such as TRAIN FRIGHTENED KANGAROO and MEDICINE

CURED HICCUP, and later was asked to complete each sentence by producing its last word when its first two words were presented as cues. In the other experiment, K.C. was shown a collection of humorous definitions of words, such as A DIGITAL TERMINATOR—FINGERNAIL, and BALD, OR GOLDEN, BUT ALWAYS YOUNG—EAGLET, and was later tested for his knowledge of the target word when its newly learned definition was given. The central question posed in these studies was whether the kind of semantic learning that these tasks entail is possible in the absence of episodic memory, and if so, what are some of its characteristics. We discuss these two studies next.

6.1.3. The "case experiment" on semantic learning and perceptual priming

Earlier studies with K.C. (Tulving, 1985; Tulving et al., 1988) suggested a rather sharp dissociation between his largely absent or dysfunctional episodic memory and his relatively preserved semantic memory. This idea was based on the observation that K.C. seemed incapable of remembering any personally experienced events from the years preceding his accident while having obviously retained a great deal of semantic knowledge. This pattern is consistent with the suggestion of a dissociation between different memory systems (e.g., Moscovitch, 1982; Schacter & Tulving, 1994; Tulving, 1972, 1983; Tulving & Schacter, 1990). But other interpretations of the pattern are also possible, including some that are more parsimonious than the episodic/semantic distinction, and that, at the time, fit better into the then current views on amnesia. Namely, the apparent dissociation between an inability to remember personally experienced events, on the one hand, and the general knowledge derived from these events, on the other hand, may reflect nothing more than the fact that people think about and use general semantic knowledge more, and hence, the contents of semantic memory are more rehearsed and better practiced than is the information about single or infrequent episodic happenings. In other words, what appears to be a dissociation between two systems may have come about as a result of a simple confound between the two kinds of information and the amount of learning and practice (e.g., Baddeley, Vargha-Khadem, & Mishkin, 2001).

In the "case experiment," this alternative interpretation of the episodic–semantic dissociation was put to the test (Tulving et al., 1991). The idea was this: suppose K.C. is brought repeatedly to the laboratory for an extended period of time and taught small pieces of new factual knowledge, each of which appears only for a few seconds, and which he cannot rehearse outside of the experiment. If he acquires the briefly presented factual material, but does not remember the much more extended, repeated visits to the laboratory (as was expected), the "differential practice" hypothesis would be weakened, or even rejected. We were also interested in the relation between learning of factual knowledge and perceptual priming, and we designed the experiment accordingly.

The experiment comprised a series of 22 learning and test sessions held once or twice a week, plus a final test session conducted 12 months after the 22nd session to test long-term retention. In these sessions, K.C. was exposed to and tested on skeletal three-word sentences that were meaningful but that he had never seen or heard before (e.g., *VACATIONER ATTRACTED MOSQUITO*; *MEDICINE CURED HICCUP*). At the time of study, each sentence was accompanied by a coloured picture that could be seen as (remotely) related to the meaning of the sentence, but that could not have been used to generate any part of the sentence in the absence of exposure. For example, the sentence *VACATIONER ATTRACTED MOSQUITO* was shown next to a picture of a lone fisherman in a boat on a lake; the sentence *MEDICINE CURED HICCUP* was shown next to a picture of a man in a hospital setting with his forehead covered with electrodes.

During the first 6 of the 22 sessions, K.C. was shown and tested on a list of 64 such sentence–picture pairs. In the study phase of each session, sentence–picture complexes ("pairs") were presented in a sequence, one pair at a time, and K.C. was asked to make a binary judgment about how well the picture fit the sentence—"fits" or "does not fit." In each of these six sessions, the study phase was followed by a test phase with different cues. Different kinds of test cues were used, varied between sessions. In each of these first six sessions, the study phase was followed by a test phase with different cues. In the first session, four different sets of cues were used, each targeting one quarter of the learned material: (1) picture + (two-word sentence frame) + fragment of the target word, (2) picture plus fragment, (3) sentence frame + fragment, and (4) fragment alone. In Sessions 5 and 6, K.C. was tested with fragments alone for all the words.

In the following 16 sessions, K.C. was no longer shown the original study materials, and was tested for what he had learned and retained in the course of the experiment. Different kinds of test cues were used, varied between sessions. The cues within a particular session were always of the same type. Some cues were designed to assess semantic learning. The first two words of a studied sentence were presented and K.C. was asked to come up with a word that would complete the sentence. In other tests, graphemic fragments of the target word, the third word of a sentence, were presented, and K.C. was asked to complete the fragment to make a word. Thus, he would see -O-Q- -TO and would attempt to produce "MOSQUITO," or see R- -U-EM and attempt to produce "REQUIEM" (each fragment had only one possible completion). In a third type of test, the presence or absence of the pictures that had been shown with the sentences at study was also systematically manipulated at test. Each test session also included 32 sentence–picture pairs that K.C. had never seen. These served to provide a non-studied baseline for both semantic learning and word-fragment priming. K.C. was tested again for the retention of both fragment completion and sentence knowledge 12 months later. In the meantime, he had no experience with or access to any of the materials.

The experiment produced three major results. First, K.C. showed a high degree of priming in fragment completion—higher than what was produced by control subjects—that

remained largely unchanged after 12 months. In the very first session, his fragment completion performance was 0.13 for non-primed words and 0.56 for primed words, for a net difference of 0.43. Twelve months later, the corresponding figures were 0.28 and 0.69, for a net difference of 0.41. This finding confirmed earlier findings with K.C. and was also very much in line with the generally accepted fact that amnesia usually leaves perceptual priming intact.

Second, K.C. learned to produce the target word to the two-word cue for a number of the studied sentences, though not for all. Starting with essentially zero-level performance, he reached the level of 0.50 for visually presented cues and 0.55 for auditorily presented cues at the end of the experiment. Twelve months later, he could still respond correctly to 0.39 of the visually presented cues. These levels of performance, of course, were not spectacular when compared with the performance of healthy controls, but they were noteworthy in light of the then widely accepted assumption that dense anterograde amnesic patients are incapable of any new "declarative-memory" acquisition. Sensory modality of these cues (visual or auditory) did not matter, ruling out the possibility that what we think of as semantic learning was nothing more than perceptual priming manifesting itself at the level of words of a sentence. Perceptual priming, in contrast, is always less effective across than within modalities (e.g., Köhler et al., 1997).

The third major result had to do with the relation between primed fragment completion and semantic learning as revealed by a contingency analysis conducted at the level of individual subject items (Kahana, 2000). This kind of analysis had, in an earlier experiment with university students, yielded 'stochastic independence' between episodic recognition of words and primed fragment completion of the same words (Tulving et al., 1982). 'Stochastic independence' means that the product of the simple probabilities of two events is identical with their joint probability. That is, knowing the value of one variable does not allow one to predict the value of the other variable at better than chance accuracy. The stochastic independence in Tulving et al. experiment meant that whether or not a subject recognized a given item provided no useful information about whether or not the subject could complete the fragment of that item and, conversely, whether or not a subject could complete a word fragment provided no useful information as to whether the subject could recognize that item as a member of the studied list. The finding was interesting, because such a stochastic independence between any two measures of memory had never before been reported in the literature on learning and memory (a similar finding was reported by Jacoby & Witherspoon, also in 1982).

In Tulving et al. (1991) experiment, the relation between these two measures of memory was measured for nine separate sets of data in terms of Yule's *Q*, which can vary from −1.0 (perfect negative association between the two tests) through 0 (no association, that is, stochastic independence) to +1.0 (perfect positive association; for a recent application, see Rizzuto & Kahana, 2000). The mean *Q* yielded by nine separate "replications" of this assessment turned out to be −0.03, or essentially zero, indicating stochastic independence between semantic learning and perceptual priming (the data are shown in the first 10 rows in Table 8 in Tulving et al., 1991).

The theoretical importance of this finding lies in the fact that it provides for an exact parallel to stochastic independence between fragment-completion priming and (episodic) recognition, and it does so in a setting in which episodic memory could not affect either measure. Thus, in terms of these measures, priming is independent of episodic memory, and, independently of this fact, priming is also independent of semantic memory. In this respect then, episodic and semantic memory behave identically. The immediate practical importance of the finding of stochastic independence lies in the fact that it rules out a simple but uninteresting explanation of K.C.'s learning. This is the idea that he managed to learn those words that were especially significant to him, or especially 'easy' for some other reason, idiosyncratic or otherwise. In light of the obtained results, K.C.'s better-than-normal fragment-completion priming cannot be accounted for in terms of any residual episodic memory capability any more than it can be accounted for in terms of a residual semantic memory capability.

6.1.4. The nature and limits of new semantic learning in amnesia

A companion study to the "case experiment" was conducted at about the same time but reported 2 years later (Hayman et al., 1993). In the course of eight study sessions distributed over 4 weeks, we taught K.C. novel, amusing definitions of 96 target words (e.g., *a talkative featherbrain—PARAKEET* or *a servant in name only—BRIDESMAID*). K.C.'s task was to produce the target word when cued with the definition. For different subsets of materials, we varied systematically (i) the degree of pre-experimental associative interference between the cue phrase and the target word (presence or absence of a pre-existing response to the "definition"), (ii) presentation frequency per session (once or twice), and (iii) the type of training ("study-and-test" or "study only"). The last variable was manipulated in order to produce different levels of intra-experimental associative interference.

The results of the experiment were most orderly. They showed that K.C. can (i) learn new semantic knowledge and (ii) retain it over a period as long as 30 months indistinguishably from control subjects. In this respect, they fully corroborated the results of Tulving et al. (1991) "case experiment." More important, they add the fact that all three independent variables manipulated in the study were highly influential in determining the efficacy of K.C.'s learning. Table 4 shows the results quantitatively. The main conclusion derived from these results was that evidence of new semantic learning in amnesia depends critically on the conditions under which the learning occurs. Therefore, generalizations of the kind that are sometimes found in the literature (e.g., "amnesic patients

Table 4
Proportion of correct target words produced by K.C. in response to amusing definitions as a function of retention interval, associative interference (intra-experimental and pre-experimental), and presentation frequency

	Intra-experimental interference								Mean
	Study + test				Study only				
	2x[a]		1x[a]		2x		1x		
	High[b]	Low[b]	High[b]	Low[b]	High	Low	High	Low	
Immediate (mean of days 3 and 7)	0.46	0.71	0.12	0.38	0.75	0.92	0.67	0.75	0.59
14-month delay	0.17	0.33	0.17	0.33	0.17	0.42	0.33	0.50	0.30
30-month delay	0.08	0.38	0.00	0.17	0.13	0.29	0.08	0.29	0.18

[a] Presentation frequency.
[b] Pre-experimental interference.

cannot learn new factual information") are invalid. Whether or not they can learn depends not only on the amnesic individual, but also on the conditions under which the learning occurs. Even in the single case of K.C., the probability of successful performance on the task, as a result of eight exposures to the material, varied from a low of 0.12 to a high of 0.92! A critical determinant seems to be the extent of pre-experimental and on-line associative interference engendered by the processing of the to-be-learned materials: the less the interference, the more effective the learning, very much along the lines that hold for healthy subjects as well.

The frequency of exposure and the quality of the learning environment thus emerge as experimental variables to explain at least in part the earlier-reported failures to find evidence of new semantic learning in (at least) some amnesic patients (e.g., Gabrieli, Cohen, & Corkin, 1988; Rozin, 1976; Verfaellie, Reiss, & Roth, 1995; but see Bayley & Squire, 2002). It is quite possible that the conditions of learning in some of these earlier experiments were non-optimal. However, individual differences among amnesic patients, such as etiology and site of lesion, are also clearly involved, as demonstrated by follow-up work conducted by others (Hamann & Squire, 1995; Rajaram & Coslett, 2000a, 2000b).

Among the problems left open by the new semantic learning studies with K.C. was the extent to which post-morbidly encountered semantic information becomes integrated into pre-existing knowledge structures (Hamann & Squire, 1995). To gain relevant evidence, Westmacott and Moscovitch (2001) tested K.C.'s knowledge of famous people and vocabulary words that achieved popularity in the four 5-year time periods since his head injury. K.C. identified explicitly and with confidence real famous names (e.g., Monica Lewinsky) and vocabulary terms (e.g., internet) that supplemented the implicit memory he showed in reading speed and accuracy, familiarity judgments, and correct guesses of items deemed as unfamiliar (summarized in Table 5). Evidence of better performance in K.C. for names and words made famous closer to the time of his injury suggests a benefit of repeated exposure. However, K.C.'s relative inability to ascribe meaning to these labels on more elaborate measures of semantic processing, such as categorizing famous names according to occupation, emphasizes the inflexible, rudimentary nature of his post-morbid non-relational semantic learning.

Presumably, it is this capacity for semantic acquisition, in the relative absence of associative interference, that has allowed K.C. to update his trait self-knowledge, although this knowledge appears to be without the full experiential flavour of self-identity. In a formal investigation of self-descriptiveness judgments, Tulving (1993) asked K.C. to rate the extent to which a number of trait adjectives describe K.C.'s own personality. Not only were his ratings consistent across two separate testing sessions (78% agreement), but they also corresponded to his mother's perception of his personality on the same dimensions (73% agreement). This finding received strong support in a subsequent case study of a head injury patient, W.J., who experienced transient retrograde amnesia for episodic information but whose trait self-knowledge ratings were the same whether they were made after or during the patient's amnesic state (i.e., with or without access to personal episodic memory; Klein, Loftus, & Kihlstrom, 1996). In contrast, a recent study reported that individuals with Alzheimer's disease have an impoverished sense of identity (Addis & Tippett, 2004), which may relate to deficient autobiographical memory together with loss of personal semantic memory (record of personal facts) as a result of atrophy to hippocampal and temporal neocortical regions.

Table 5
Post-morbid semantic acquisition of famous names and vocabulary terms

Task	K.C. (with guessing)	Controls (S.D.)
Famous names		
Reading speed (s)	3.435	6.75 (0.5)
Reading accuracy (%)	81.67	100 (0.0)
Recognition (%)	83.3 (88.0)	98.9 (4.7)
Familiarity rating (/7)	4.6	6.7 (1.1)
Categorization (%)	5.0 (55.0)	98.9 (4.9)
First–last name matching (%)	25.0 (75.0)	97.3 (7.3)
Television and movie actor matching (%)	55.0 (77.0)	98.7 (5.1)
Vocabulary terms		
Reading speed (s)	6.862	17.35 (0.7)
Reading accuracy (%)	81.67	100 (0.0)
Recognition (%)	82 (91.7)	99.1 (2.6)
Definition: recall (%)	25.0	94.3 (3.9)
Definition: recognition (%)	43.3 (73.3)	

K.C.'s overall profile in post-morbid semantic learning is remarkably similar to that of the patient R.S., who is close to K.C. both in chronological age and the age at which he became densely amnesic (Kitchener, Hodges, & McCarthy, 1998). Despite differences in etiology and brain pathology, R.S.'s encephalitis resulted in a complete obliteration of autobiographical memories that, however, has not prevented the acquisition of new semantic information relating to public figures and events and vocabulary.

Both patient profiles (K.C. and R.S.) fit well with what is perhaps the most compelling evidence to date of disproportionately affected episodic encoding relative to semantic encoding, namely findings in amnesia of developmental origin (Vargha-Khadem et al., 1997; Vargha-Khadem, Gadian, & Mishkin, 2001). In this line of research, hypoxic-ischemic injury to the hippocampus, whether sustained perinatally or during childhood, was found to result in a profound memory impairment for everyday events such as conversations, placement of belongings, appointments, and spatial routes. Despite their severe impairment of episodic memory, these developmentally amnesic individuals have been successful in their school studies well beyond what could be expected given their anterograde amnesia, and have managed to build a sizeable store of facts about the world. These observations again suggest that semantic learning does not require episodic memory (Tulving & Markowitsch, 1998; see Squire & Zola, 1998; Baddeley et al., 2001, for alternative explanations).

6.1.5. Mnemonic precedence

K.C.'s performance in studies of priming and new learning reveals a stark contrast between his ability to exhibit robust implicit and semantic memory and an apparently complete absence of explicit, episodic recollection of a recent experience. Does K.C. possess any type of episodic memory at all? A study that examined K.C.'s memory for the location and identity of recently hidden objects suggests that he might (Schacter, Moscovitch, Tulving, McLachlan, & Freedman, 1986). Schacter et al.'s experiment was motivated in part by an observation of infant behaviour originally described by Piaget (1954), and later by many others. When 8–10-month-old infants are required to search for objects hidden at two successive locations, they typically find it after it has been hidden at the first location (A). But when the object is hidden at a second location (B), many infants of this age continue to look for it at location A. This phenomenon is known as the $A\overline{B}$ (pronounced "A not B") error (e.g., Diamond, 1988).

To examine whether poor memory plays a role in the kind of behaviour revealed by the AB error, Schacter et al. constructed two adult analogs of the infant AB error task. In the *room search* task, amnesic patients and controls watched an experimenter hide an object at a nearby location (A) in the testing room. After a 2.5-min delay, participants searched for the object. There were two further trials at location A (different objects were used on each trial), and then the experimenter hid a different object at a new location (B). There were two additional trials at location A followed by a trial at a novel location (C). In the *container search* task, a similar sequence of events unfolded, except that participants searched for small objects in different drawers of a small container (locations A, B, or C).

The key finding in both tasks was that K.C. and most other amnesics could find the object when it was hidden at location A, but failed to find it at locations B and C. On the B and C trials, K.C. and other patients instead continued to search at location A, suggesting that this location took precedence in memory over the other locations (hence the term "mnemonic precedence," which Schacter et al. used to describe this phenomenon and distinguish it from the $A\overline{B}$ error in infants). Similarly, K.C. and other patients remembered the identity of the object accurately on the first trial of the room and container search tasks, but showed less recall on subsequent trials. Taken together, the findings suggest that K.C. possesses some limited or rudimentary type of memory for the location and identity of objects that he recently encountered. However, such memory is subject to an extreme form of proactive interference in which encoding, storage, and/or retrieval beyond the first trial is highly limited. Studies with non-human primates indicate that the $A\overline{B}$ error is associated with frontal, rather than medial-temporal, lesions (Diamond & Goldman-Rakic, 1989), which might explain K.C.'s performance, but does not account for that of the other amnesic patients who do not share his frontal pathology. Moreover, the protocol used with amnesic patients differed from that used with infants and with primates. Although it is unclear whether mnemonic precedence in amnesic patients shares mechanisms with the AB error in infants (see Diamond, 1988), it remains an intriguing and unexplained feature of memory in K.C. and in other amnesic individuals.

6.2. Studies of retrograde memory

Investigations of K.C. conducted in the last decade have placed greater focus on semantic and episodic memory in the retrograde domain, in which the distinction is even more pronounced. Its application to remote spatial memory has also been of recent interest in our work with K.C. in the context of evaluating classic theories of hippocampal function.

6.2.1. Retrograde amnesia: further evidence that episodic and semantic systems are dissociable

The fate of memories in the brain has intrigued cognitive neuroscientists for over a century, from at least as early as Ribot's (1881) and Burnham's (1903) attempts to account for observations in amnesic humans of spared remote memories relative to those that were acquired more recently. This phenomenon of temporally graded retrograde amnesia was finally linked to MTL function in Scoville and Milner's hallmark investigation of patient H.M. (Scoville & Milner, 1957; see also Corkin, 1984, 2002; Corkin et al., 1997; Milner et al., 1968). Though H.M. was profoundly amnesic for information acquired in the few years before surgery, his older memories seemed to be largely spared, a pattern that has since

been corroborated in a host of other amnesic patients with hippocampal damage of various etiologies using an assortment of memory measures (e.g., Bayley, Hopkins, & Squire, 2003; Beatty, Salmon, Berstein, & Butters, 1997; Beatty, Salmon, Butters, Heindel, Granholm, 1988; Penfield & Mathieson, 1974; Penfield & Milner, 1958; Reed & Squire, 1998; Squire, Slater, & Chace, 1975; Zola-Morgan, Squire, & Amaral, 1986). These findings have been interpreted as evidence that memories depend on the hippocampus only until the physiological process of consolidation is complete, whereby memories are fully integrated with pre-existing neocortical representations and the hippocampus is no longer needed for their maintenance and retrieval, whether semantic or episodic (e.g., Squire, 1992; Squire & Alvarez, 1995).

Despite the widely held view that retrograde amnesia is relatively brief and temporally graded, not all evidence is consistent with this pattern (for reviews, see Fujii, Moscovitch, & Nadel, 2001; Kapur, 1999; Nadel & Moscovitch, 1997, 2001). K.C., too, has remote memory loss that is minimal in duration, but only for factual information; his memory loss for personal episodes encompasses his entire past. Across several detailed investigations, he has consistently demonstrated a severe impairment of autobiographical memory that covers his whole life, whether in response to actual visits to houses that he had lived in and schools that he had attended (Tulving et al., 1988) or to family photographs of past and more recent events (Westmacott, Leach, Freedman, & Moscovitch, 2001). There was no sign that the locations or photographs triggered any feeling of re-experiencing, so that any narratives that he managed to produce lacked the subjective re-evoking of the emotional and contextual details that define a personal from a non-personal episodic experience. Westmacott et al. made particular note of the observation that K.C. was not able to convey any sequence of events, nor could he relate any of the photographs to other life experiences. With hesitation, he relied on his intact reasoning skills and personal semantics to reconstruct what seemed most plausible. Otherwise, he was unable to elaborate beyond his immediate percept of the photograph, as though encountering for the first time the events being portrayed (see Fig. 5).

Westmacott et al.'s (2001) investigation also revealed that K.C.'s recollections were, in fact, limited for the most part to identifying people in each photograph, with those encountered in his childhood, adolescence, and early adulthood recognized with much greater ease than those he had met for the first time in the years after his 1981 accident. Similar to this pattern of personal semantic retrieval, a temporal gradient in remote memory for general semantics has also been demonstrated; he showed worse performance for famous names and vocabulary terms that came into popular use in the 5-year time period predating his injury relative to those that became popular in earlier years (Westmacott & Moscovitch, 2002). This held true whether K.C.'s memory was tested with speeded reading, pronunciation, or three-alternative forced-choice recognition, among other experimental measures. Interestingly, however, this temporal gradient was found to be

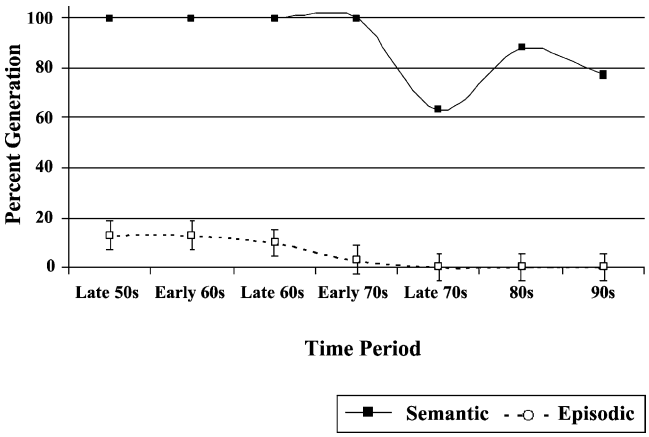

Fig. 5. Percent generation of semantic and episodic details for successive 5-year periods on the family photograph task.

attenuated on implicit testing. For example, when asked to guess the familiarity of names and words from 5 years pre-injury, his performance improved substantially as compared to explicit recognition, though he still performed worse than for more remote time periods. Likewise, in Tulving et al.'s (1988) earlier experiment, repeated visual exposure of knowledge unique to the job that K.C. held during the 3 years before his accident allowed for the progressive improvement of such expert knowledge. This knowledge included the names of co-workers as well as familiarity with work-related technical terms and equipment presented in photographs. For example, by the final session, K.C. was able to provide an accurate description of the very same film die that he had handled frequently before his accident. He was, however, unable to comment on his own personal experience with the die, despite having viewed a photograph of himself with it. That this facilitation did not extend to the domain of personal episodic information further strengthens the claim that these two forms of memory are fundamentally separate, at least with respect to their accessibility (Tulving, 1972, 1983).

K.C. is not alone in the severity and extent of his autobiographical memory loss. Amnesics like him have been reported in the literature, some even before K.C.'s deficit was made known. The post-encephalitic patients S.S. (Cermak & O'Connor, 1983) and Boswell (Damasio, Eslinger, Damasio, Van Hoesen, & Cornell, 1985), for example, developed a virtually complete loss of retrograde memory for personal incidents without similar disruption of personal facts. A similar dissociation was reported for D.B., a case of amnesia due to hypoxia (Klein, Loftus, & Kihlstrom, 2002). Other cases have been described in more recent publications (Barr, Goldberg, Wasserstein, & Novelly, 1990; Calabrese et al., 1996; Cipolotti et al., 2001; Della Sala, Laiacona, Spinnler, & Trivelli, 1993; Kitchener et al., 1998; Kopelman, Stanhope, & Kingsley, 1999; Levine et al., 1998; Markowitsch et al., 1993; McCarthy & Warrington, 1992; Rousseaux, Godfrey, Cabaret, Bernati, & Pruvo, 1997; Viskontas, McAndrews, & Moscovitch, 2000; Wilson, Baddeley, & Kapur, 1995),

though the asymmetry is not always as striking as that which characterizes K.C.'s amnesia.

6.2.2. Retrograde spatial memory: representations of environments learned long ago

In a separate line of research, we investigated whether well-rehearsed spatial information learned by K.C. in the remote past is impaired like episodic memory or spared like semantic memory. The classic cognitive map theory predicted that amnesic patients with damage to the hippocampus would be impaired on tests of allocentric spatial memory, whether anterograde or retrograde (O'Keefe & Nadel, 1978). In line with this theory, a wealth of data had indicated that amnesic patients are unable to form new spatial representations (e.g., Holdstock et al., 2000; Maguire, Frackowiak, & Frith, 1996; Morris, Garrud, Rawlins, & O'Keefe, 1982; O'Keefe & Dostrovsky, 1971; Olton, Becker, & Handelman, 1979; Smith & Milner, 1981). However, cursory observations in several amnesic patients had suggested that spatial memories acquired long ago might not be affected by hippocampal damage (Beatty et al., 1987; Milner et al., 1968; Zola-Morgan et al., 1986). Tulving made a similar anecdotal observation in K.C., noting that he could easily negotiate his way in a neighbourhood familiar from youth (TV Ontario, 1988).

Rosenbaum et al. (2000) pursued this question in a more systematic way by assessing K.C.'s memory for many different kinds of spatial relationships contained within the neighbourhood in which he lived since long before his injury and where he continues to live to this day. The measures were adopted from the field of environmental psychology to simulate the many demands on memory posed by environmental circumstances in the natural world. K.C.'s performance was compared with that of four controls, two of whom continue to live in his neighbourhood as he does, and two who moved away at the time that he sustained his brain damage. As expected, K.C. performed normally on more structured mental navigation tests of his neighbourhood, such as estimation of direction (Fig. 6) and selecting the most direct route between locations while avoiding an obstructed street, tests similar to those performed well by the amnesic patient E.P. in a separate study (Teng & Squire, 1999). Additional spatial tests on which K.C. performed normally included accurate placement of streets in relation to one another in a sketch map (Fig. 7), recognition and identification of neighbourhood landmarks, estimating absolute and relative distances between landmarks, sequencing randomly ordered landmarks along a route, and locating gross geographical features on outline maps of the world. These findings contrast with K.C.'s dramatic inability to acquire spatial information in a new environment. He failed to recall the spatial locations of common objects on a board following a short delay (Smith & Milner, 1981), a floor plan of a library in which he has worked since 1997, and a simple route after receiving extensive training. Unlike the semantic fragments that K.C. has accumulated since his accident, this information is more complex and associative in nature, requiring the hippocampus for integration. The distinction between impaired recent spatial memory but spared remote spatial memory following extensive loss of hippocampal tissue is not taken into account by any spatial theories of hippocampal function. Our findings encourage a re-examination of these theories to determine whether other processes, representations, and structures outside the hippocampus are implicated depending on the age of the memory, extensive experience with the environment, or both.

However, even remote spatial memory did not appear to be completely intact (Rosenbaum et al., 2000). This was first suggested by K.C.'s impoverished sketch map with respect to landmark inclusions and his difficulty in identifying specific features on outline maps of Canada and Ontario. More extensive examination of his ability to identify detailed aspects of his neighbourhood revealed that he was unable to distinguish photographs of houses that he had visited often in the past from those of foil houses, whether the foils were similar in appearance or not. K.C.'s loss of memory for topographical details and environmental features resembles loss of contextually rich and detailed memories of autobiographical episodes. By contrast, the bare, schematic representation

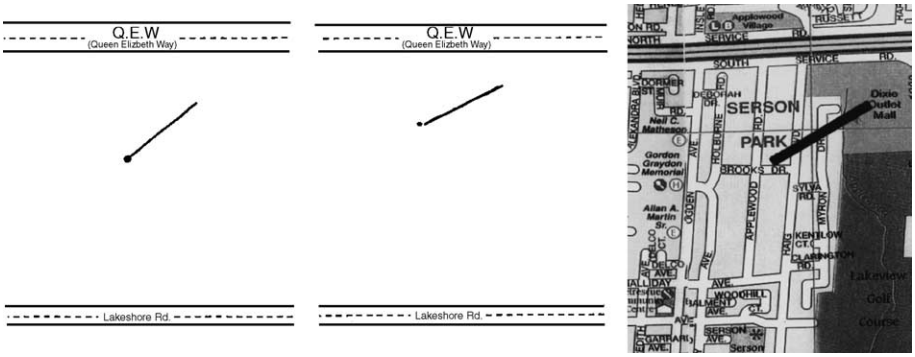

Fig. 6. Vector maps produced in the first trial by K.C. (left) and by a friend (middle) who moved away from the neighbourhood at the time of K.C.'s brain injury. The arrow on each map represents the judged direction and distance from K.C.'s house to a specified landmark. The actual map of K.C.'s neighbourhood (right). The superimposed line indicates the correct direction and distance from K.C.'s house to the landmark for comparison with the vector maps produced by participants.

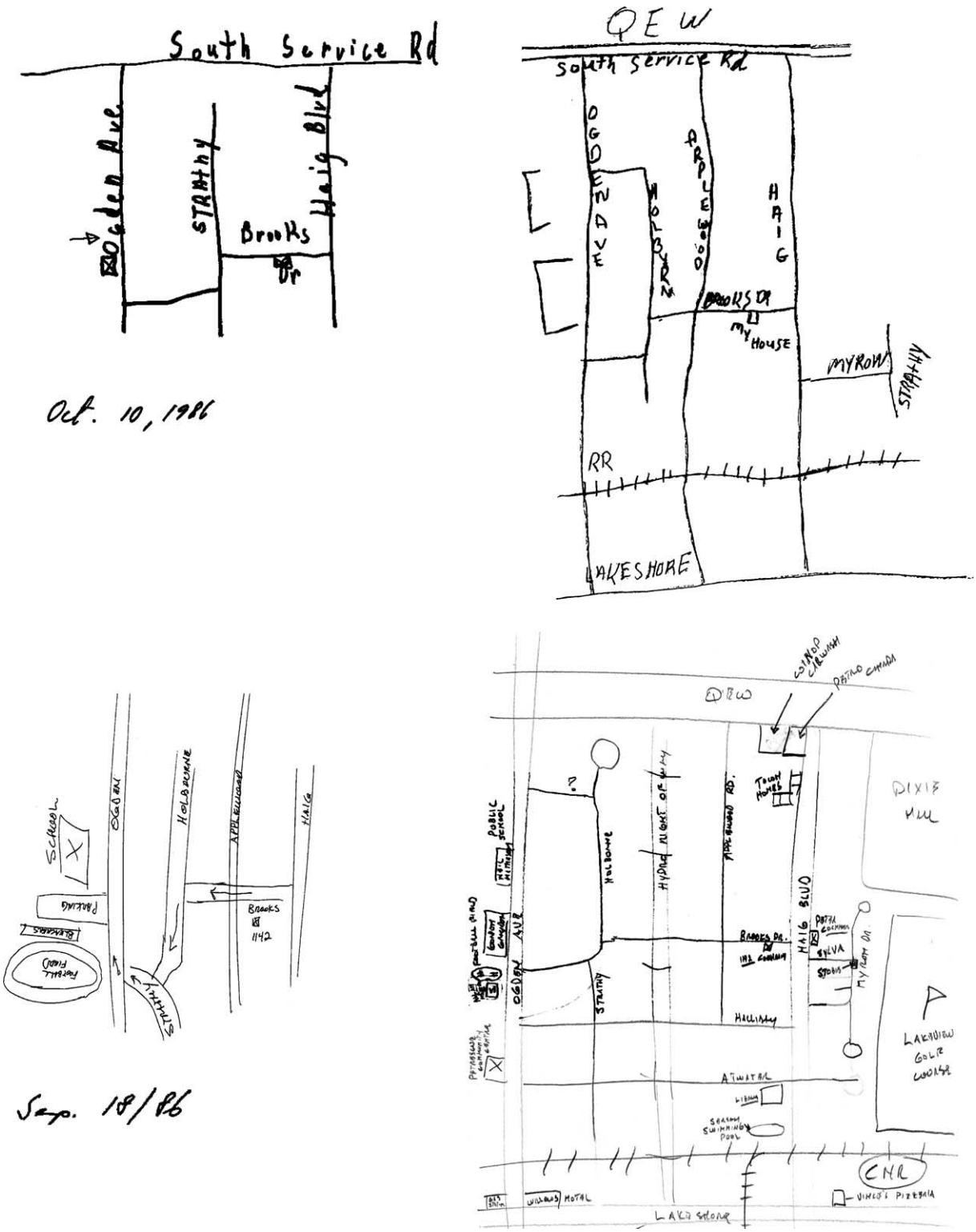

Fig. 7. Sketch maps of a neighbourhood learned long ago drawn in 1986 and 1999 by K.C. (top row) and by a friend who moved away at the time of K.C.'s brain injury (bottom row).

of an environment learned long ago that K.C. did remember resembles the gist of personal experiences or context-independent semantic information that is typically spared in retrograde amnesia. In a striking illustration of this correspondence, viewing of familiar houses elicited in controls a rush of personal experiences with visiting the houses or with the families who occupied them, whereas familiar landmarks did not evoke such extended networks of associative information.

6.3. What parts of K.C.'s brain support spared memory? A combined lesion–fMRI investigation

For a long time, clinical cases of brain damage provided the only kind of evidence relevant to "localization of function." By this method, the normal function of a brain region is equated with what is lost following selective damage to that region. Although the neuropsychological approach was undoubtedly useful and successful, its shortcomings were also known from the outset. One of the major criticisms, advanced by Jackson (1931–1932), was that localizing a lesion was not really the same as localizing a behavioural or mental ability. That is, it is not what is destroyed, but the differences between what is destroyed and tissues remaining after destruction that account for the differences between pathological and healthy functions (Oppenheimer, 1956). Investigations of K.C.'s memory for an "old" neighbourhood where he continues to live raised the possibility that, at least under some circumstances, his hippocampus is not needed for supporting remote spatial memories and that a normal or compensatory network of structures outside of the hippocampus is sufficient. An alternative interpretation, however, is that as long as some portion of the hippocampus is viable it can support memory of old, highly familiar environments. What little remains of K.C.'s hippocampus may be functional and enough to support mental representations of landmark appearance and location along routes, as well as distance and direction computations if this information was well established pre-morbidly. The feasibility of such a result is indicated by the recent finding that activation of a small amount of remaining hippocampal tissue in the developmental amnesic patient Jon was associated with retrieval of episodic memories (Maguire, Vargha-Khadem, & Mishkin, 2001).

To address these issues, K.C.'s brain was scanned with functional magnetic resonance imaging (fMRI) as he performed neighbourhood tasks similar to the ones administered in the behavioural study described above (Rosenbaum, Winocur, et al., 2004). Previous lesion and neuroimaging studies in healthy young adults show that each of these tasks engages to a different degree a host of brain structures specialized in representing and processing particular aspects of a spatial layout (Aguirre & D'Esposito, 1999; Rosenbaum, Ziegler, Winocur, Grady, & Moscovitch, 2004). Recruitment of parahippocampal gyrus has been associated with recognition of landmarks, posterior parietal regions with egocentric processing of landmarks in relation to the self during route tasks, retrosplenial cortex with allocentric processing of landmarks in relation to each other when judging heading vectors, and a sector of inferior temporal cortex (posterior parahippocampal–anterior lingual gyrus) with landmark perception.

Overall, the results from this investigation indicated that these extra-hippocampal structures were engaged in all participants, including K.C., in a way that is consistent with the pre-eminent processing demands of each task, on the right in K.C. and bilaterally in control participants (displayed in Fig. 8). Nevertheless, recruitment of additional left-hemisphere regions only by the controls raises the possibility that this activation pattern is optional, or that activation of either right or left regions can lead to successful performance. By contrast, additional regions in posterior cingulate and posterior parietal cortex were consistently and uniquely active in K.C. when he imagined movement along routes and judged the direction of vectors between landmarks. Activation of these regions, together with the left cuneus and additional sectors of superior and medial frontal cortex, is suggestive of functional compensation for structural damage elsewhere in K.C.'s brain. Like controls, however, no hippocampal activity was evident in K.C. on tasks that he performs successfully, though he has part of his hippocampus still remaining. The latter finding corroborates the lesion evidence that, contrary to cognitive map theory, allocentric spatial representations of familiar environments are not dependent on the hippocampus.

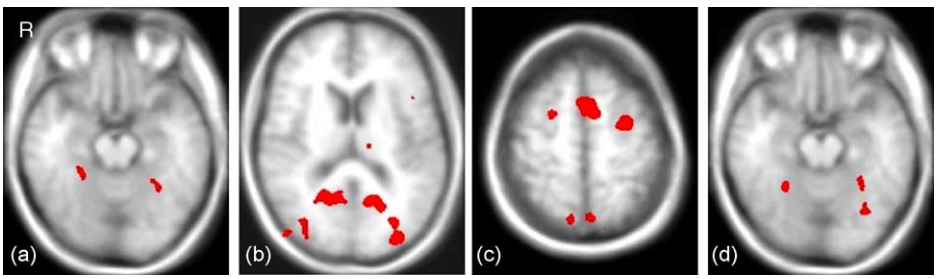

Fig. 8. Areas of activation associated with the remote spatial memory tasks. The functional maps are overlaid on the averaged anatomical scans from all participants in axial views. Images were thresholded at $p < 0.01$, corrected. The right hemisphere is shown on the left side of the images.

6.4. Neocortical accounts of K.C.'s impaired remote memory for personal and spatial details

Given the many ways in which retrograde amnesia can emerge, it is always a danger to draw inferences about the extent of a certain region's involvement, especially when etiology leads to widespread neuropathological consequences (see Bayley & Squire, 2002). Non-experimental lesions are seldom limited to the hippocampus and often invade functionally heterogenous neocortex, as in the case of K.C. Accordingly, K.C.'s profound deficits in autobiographical memory and house recognition could be symptomatic of a more general impairment in constructing details in visual imagery due to visual cortex damage (e.g., Ogden, 1993; Rubin & Greenberg, 1998) or in strategic retrieval of details due to pre-frontal cortex damage (e.g., Della Sala et al., 1993; Levine et al., 1998), rather than loss of memory relating to hippocampal lesions.

We (Rosenbaum, McKinnon, Levine, & Moscovitch, 2004) tested and ruled out the first possibility using an extensive battery of visual imagery measures. K.C. showed preserved imagery for the shapes of letters and animal body parts, the relative size of objects, and the colour of objects (Farah, Hammond, Levine, & Calvanio, 1988), which is particularly notable given his perceptual deficit in colour vision. Also intact was his imagery for the spatial relations of hands on a clock (Paivio, 1978) and of a supposed route along the perimeter of block letters (Brooks, 1968), which corroborates findings of intact imagery on real-world topographical tasks. These results were complemented by performance on a sentence verification task requiring imagery (Eddy & Glass, 1981). It is highly doubtful that K.C. achieved solutions to each task through verbal representations, as the visual features that were probed (e.g., *What colour is the inside of a cantaloupe*?) are not high semantic associates, as would be the case for other items (e.g., *What colour is the sky*?), which were excluded from the test. In any case, even more convincing than K.C.'s ability to judge in his mind's eye a single visual property of a previously encoded object is his ability to apply a series of transformations to those objects in imagery to create new ones (Behrmann, Moscovitch, & Winocur, 1994; Finke, Pinker, & Farah, 1989).

Having found that K.C.'s autobiographical memory deficit did not seem to relate to impaired visual imagery, we proceeded to test the possibility that it might relate to deficits in strategic retrieval associated with frontal lobe damage. To do so, we used a formal autobiographical interview requiring generation of personal events from different life periods under varying levels of retrieval support (Levine, Svoboda, Hay, Winocur, & Moscovitch, 2002). Similar to results from earlier testing of free recall (Tulving et al., 1988; Westmacott et al., 2001), K.C. was unable to produce a single personal story from any time in his life, however remote the episode. Importantly, with supplementary retrieval support in the form of specific cueing, K.C.'s performance continued to remain well below control levels (see Fig. 9), which contrasts with that of patients with frontal lesions who benefit significantly from cueing (e.g., Svoboda et al., 2002). Even those events that K.C. was able to generate with fairly rigorous verbal prompting were without the richness in episodic detail typical of the personal incidents recalled by control participants. Moreover, it is unlikely that any discrepancy in K.C.'s performance between uncued and cued performance reflects a problem of strategic retrieval, as he improved only on memory for events that are known to be highly over-rehearsed. For these latter memories, consistent, repeated exposure of meaningful material within varied contexts may have allowed for the restructuring of autobiographical information into a more personal semantic form or verbal script, making it less vulnerable to hippocampal damage (Cermak, 1984; Neisser, 1981; Weiskranz, 1985). This resembles the phenomenon of progressive priming that helped to restore some of K.C.'s remote personal semantic memories in Tulving et al.'s (1988) initial investigations (see also Cermak & O'Connor, 1983;

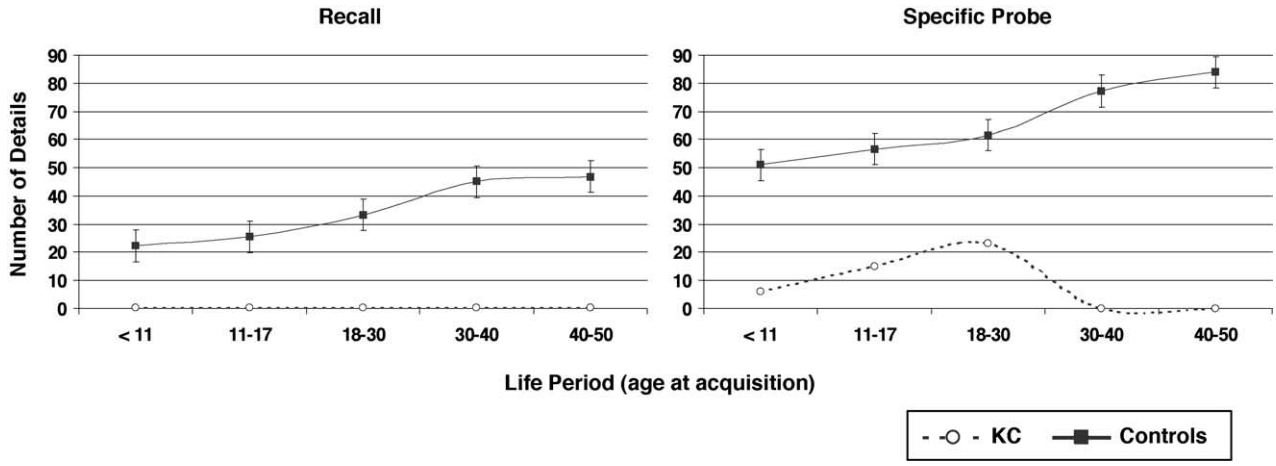

Fig. 9. Total number of episodic details given by K.C. and demographically matched control participants for all life events during recall (left) and after specific probing (right).

Lhermitte & Serdaru, 1993). That is, rather than a reduction in the organization of effortful retrieval processes, this pattern may reflect a transformation of the long-standing contents of autobiographical memory into a semantic structure that, itself, is more amenable to being retrieved.

We also devised and administered a test analogous to the autobiographical interview in structure, but which instead requires the imagining of fictional events that were not experienced personally. Though providing fewer details than controls, K.C. did manage to invent a logical sequence of events in response to most topics. Importantly, his fictional stories were more detailed than his memories for personally experienced events (Rosenbaum, McKinnon, Levine, & Moscovitch, 2003). In informal testing, his ability to generate plausible events related to his own personal future appeared to be as compromised as his ability to describe personal events from his past, though we have not yet tested this systematically. This inference is supported by the case D.B. described by Klein et al. (2002), mentioned earlier, who was tested systematically. D.B.'s ability to describe past and future public events and issues was quite good, whereas his ability to do so with respect to personal events was clearly impaired.

Overall, studies with K.C. help to discount impaired visual imagery and deficits in effortful, organizational retrieval as explanations for his impaired remote autobiographical memory. Nevertheless, there is evidence that autobiographical memory relies on a more extensive network of brain regions, including the amygdala and parahippocampal gyrus, which are structurally compromised in K.C. (Maguire et al., 2001). It remains for future research to determine the functional status of these regions.

7. Discussion

We have presented as complete an account as possible of the case of K.C. and showed that work with him has refined and broadened our understanding of memory and its many components at a functional level. We have summarized the relevant findings in Table 1. For researchers in Toronto, his case served as a touchstone for many of the theories that were developed, from issues of priming to those relating to new semantic learning and the organizational structure of remote memory. K.C. has played a critical role in the evolution and development of concepts and ideas such as episodic memory, multiple memory systems, autonoetic and noetic consciousness, the "remember/know" paradigm, the SPI model of the relations between episodic and semantic memory, and chronesthesia, an individual's conscious awareness of subjective time (Tulving, 1985, 2004).

K.C.'s contribution to our understanding of human memory has been especially beneficial because, unlike other amnesic persons who usually stay hidden from the public eye, K.C. and his family have chosen to participate openly in the study of his case, thereby helping to demystify this otherwise difficult-to-understand concept of amnesia (see Fig. 10). They have done so without any expectation that the study will improve K.C.'s lot, but realizing that it will help the whole world better understand the complexities of the human mind. Because of the privileged access that they allowed us, we were able to put many ideas to the test and generate new ones based on casual and systematic observation. Though we, ourselves, have always been excited about what we have discovered from working with K.C., we never quite realized how much of an impact this work would have on the scientific community at large. We also did not dare to expect that K.C. would be recognized by many as a psychological marvel, which he has now turned out to be. Even when these subjective assessments are disregarded, the sheer number of studies published on K.C. and the citations that they continue to receive attest to his influence on the field.

More controversial is whether we can learn much about the neural basis of human memory from a person like K.C., whose widely and unevenly distributed brain damage from a closed-head injury prompted Bayley and Squire (2002) to assert that he is "unlikely to illuminate the function of the hippocampus or other medial temporal lobe structures." Certainly, from a strictly neurological or purist perspective, K.C. is far from an ideal case to study. Even with a strong psychological framework to guide research, it has often been difficult to convince colleagues that examining brain–behaviour relationships in K.C. is a worthwhile empirical endeavour. In spite of this skepticism, K.C. has inspired new ways of thinking about memory and the brain, just as he has inspired thinking about the organization of memory at a strictly functional level. In fact, the same patients described by Korsakoff who we credited in Section 1 with encouraging the case-based approach to probing memory are at least as complicated or 'messy' as K.C. Their characteristic psychosis, lack of insight, apathy, and tendency to confabulate coheres with the neuropathological consequences of thiamine depletion, often affecting multiple brain structures, including the mammillary bodies, dorsomedial nucleus of the thalamus, and frontal circuitry (Kopelman, 1995; Reed et al., 2003). Yet, no one would deny the valuable knowledge imparted by the patients' primary inability to retain recent experiences as well as temporal aspects of past events, which may be the very fabric of episodic recollection (Tulving, 1983, 2002).

In the case of K.C. (and other patients with extensive neuropathology), there is a difference in the types of inferences that one can draw based on observations of impaired and preserved abilities. When K.C. exhibits impaired performance, it is indeed difficult to draw any firm conclusions about specific damaged regions that may be responsible for the impairment. By contrast, when K.C. exhibits preserved memory on a particular task or class of tasks, as in a number of studies reviewed earlier, then it is plausible to infer that none of his damaged regions are necessary for performance of that task or tasks. Thus, preservation of memory in K.C. is likely to be more informative from a neurobiological perspective than impairment of memory.

Fig. 10. Photograph of K.C.'s family taken in 1979, 2 years before his accident, on the occasion of his brother's wedding. K.C. recognizes the individuals in the photograph but has no recollection of the event that is depicted or why he has curly hair (he surprised his family the evening before with a new perm).

Some of the hypotheses formulated on the basis of K.C.'s performance are still in their infancy but, at the very least, they encourage researchers to revise, and in some cases abandon, old views of memory. Theories of neural involvement in both spared and impaired abilities can then be tested in other patients with more focal brain lesions and with neuroimaging, so that it is only a matter of time before discrepancies are resolved and specific brain–behaviour relationships verified. In the meantime, investigations with K.C. continue to bring us closer to solving the following questions and ultimately provide a framework for dealing with other neurologically complex cases.

7.1. What can be accomplished without a hippocampus?

Though we are unable to say with certainty much, if anything, about the normal functioning of damaged parts of K.C.'s brain when a deficit is found, as noted above, we can draw conclusions about what those parts *do not* contribute to when performance is normal. For example, because of K.C., we know that even without a functional hippocampus, priming can occur for pre-existing and self-generated novel word associates, is modality-specific, can last on the order of 30 min in some cases and up to 1 year in others, and is possible following a single study exposure. Findings such as these have been followed up with complementary lesion studies of other patients and neuroimaging studies that show the existence of dissociable left pre-frontal and extrastriate occipital memory systems dedicated to conceptual and perceptual priming, respectively, through a reduction of their activity in response to a repeated event (for reviews, see Henson, 2003; Buckner & Koutstaal, 1998; Schacter & Buckner, 1998).

Studies with K.C. have also demonstrated considerable procedural or complex learning, again in the absence of hippocampal support, such as the acquisition of computer-related knowledge through the "method of vanishing cues." This finding alone prompted rehabilitation efforts that are still in practice today (e.g., Kapur, Glisky, & Wilson, 2002). Also notable is evidence of learning of semantic facts relating to the self (trait self-knowledge, familiarity with family and friends) and the world (famous people, vocabulary terms) and a very limited amount of information that may be regarded as episodic (i.e., mnemonic precedence). However, for the most part, such learning depends heavily on repeated exposure of meaningful study material under conditions in which associative interference is kept to a minimum, and

the contents of learning are almost always inflexible, inaccessible in novel situations, or impoverished in some way. The same applies to semantic facts from the 5-year time period just prior to injury, whereas personal and general knowledge predating that period can be accessed without difficulty. Other hippocampal amnesics with more circumscribed lesions show savings of similar quality (e.g., Corkin, 2002; Kitchener et al., 1998; Shimamura & Squire, 1987; Vargha-Khadem et al., 1997; Verfaillie, Koseff, & Alexander, 2000; but see Bayley & Squire, 2002; Gabrieli et al., 1988; Verfaellie et al., 1995), whereas studies of individuals with temporal neocortical pathology indicate that this region is a necessary component of a semantic memory network (e.g., De Renzi, Liotti, & Nichelli, 1987; Graham & Hodges, 1997; Snowden, Griffiths, & Neary, 1996; Westmacott et al., 2001).

It is now reasonably clear from K.C. and from cases like him (Teng & Squire, 1999; see also Beatty et al., 1987; Milner et al., 1968; Zola-Morgan et al., 1986) that at least some types of spatial memory, including representing allocentric cognitive maps, can become independent of the hippocampus over time. Subsequent functional neuroimaging of K.C.'s brain not only confirmed this finding, but also further demonstrated that the same extra-hippocampal regions implicated in various dissociable aspects of spatial memory on the basis of earlier case studies (e.g., Aguirre & D'Esposito, 1999) are engaged by K.C. and healthy controls.

7.2. Are K.C.'s areas of impairment due to hippocampal damage?

Despite intact priming and partially intact new learning, K.C. has no episodic memory whatsoever for autobiographical details, whether experienced long ago or in more recent times. The severity of K.C.'s autobiographical memory deficit is emphasized by the fact that his remote semantic and spatial memory are virtually normal, as is his visual imagery, and that his deficit remains unaltered even when given retrieval support through specific cueing. Though K.C. has figured prominently in our own thinking and has guided autobiographical memory research in general, he may not be such an unusual case after all. Coincidentally, more sensitive testing is beginning to reveal that H.M.'s amnesia for autobiographical experiences does not adhere to Ribot's law of temporally graded remote memory as was once believed and instead affects his autobiographical episodic memory for events that took place as far back as childhood (Corkin, 2002). We do not know to what this loss is attributed, and we do not want to imply that the same neural mechanisms are at work in both cases. However, if it were not for K.C., we and others might not have followed up on these incongruities by revisiting other cases, which shaped a novel theory of hippocampal function (see Nadel & Moscovitch, 1997, 2001) that was later tested in neuroimaging experiments (e.g., Gilboa, Winocur, Grady, Hevenor, & Moscovitch, 2004; Ryan et al., 2001).

7.3. Lessons on the fractionation of memory and amnesia

Two more general lessons may be drawn from K.C.'s areas of spared and impaired performance. The first is the notion that there are multiple forms of amnesia, much as there are multiple forms of memory (see also Warrington, 1996). While this concept may seem obvious to many investigators, there is a tendency in the literature to focus on the 'amnesic syndrome' as if it is a unitary entity. In fact, for many years, the standard view was that there are individual differences across amnesic patients, but that these differences may be reduced to unidimensional concepts of severity (i.e., magnitude of memory deficit) and purity (i.e., whether faculties other than memory are impaired). However, as research with K.C. has clearly demonstrated, it is not necessarily the case that episodic and semantic memory follow the same trajectory of impairment and preservation. Indeed, K.C.'s amnesia may be classified as affecting at least two dimensions of memory, the first relating to the quality or type of to-be-remembered information as just mentioned and the second to the way in which information is processed in memory. Like H.M., K.C. has serious difficulties in learning and retaining any consciously apprehended information encountered *after* the onset of his brain damage. Any new learning of facts about the world and of himself that has occurred over the years was accomplished under incidental or highly constrained learning conditions, with the resulting representations fragmentary and detached from existing knowledge. For all practical purposes, then, K.C. may be said to have *global anterograde amnesia* that coincides with *retrograde episodic amnesia*.

K.C. has played an important role in sensitizing the research community to the idea that amnesia is not a unitary condition, but his case is not the only one that speaks to this issue. Other patients have been described with isolated retrograde amnesia of varying types, including a profile opposite to that exhibited by K.C. of intact episodic memory at the relative expense of semantic memory (e.g., De Renzi et al., 1987; Grossi, Trojano, Grasso, & Orsini, 1988; Yasuda, Watanabe, & Ono, 1997). Comprehensive assessments of retrograde amnesia by Warrington (1996) and by Kapur (1999) spurred a recent revival of the topic, which may be traced to Goldberg and colleagues in the early 1980s (Goldberg, Hughes, Mattis, & Antin, 1981). Warrington opens her commentary with the observation that "retrograde impairments like anterograde impairments are not global but fractionate (p. 13,523)." Kapur is of similar opinion, arguing forthrightly: "Retrograde amnesia is a functionally heterogeneous rather than a unitary phenomenon. Discontinuities and dissociations found in published studies point to the potential fractionation of retrograde amnesia into component disorders, each with its own neural profile (p. 800)." If correct, it is unlikely that we will ever encounter another case exactly like K.C.

A second lesson addresses the way in which we think about spatial memory. If the hippocampus is fundamentally involved in spatial processing, as cognitive map theory

would predict, anterograde and retrograde memory for spatial information should be affected equally. However, evidence from behavioural and neuroimaging experiments with K.C. suggests that this is not always the case. On the other hand, in departure from traditional models of consolidation, not all types of memory are characterized by temporally graded memory loss—context-dependent topographical and personal episodic details always seem to rely on the hippocampus no matter how old the memory is. This raises the issue as to whether there are different types of spatial memory or whether spatial memory, itself, is a subtype of memory much as verbal memory is viewed. Perhaps it is more accurate to speak of achievements in memory that relate to space rather than of 'spatial memory' per se, a proposal that was endorsed by O'Keefe and Nadel (1978) and by Tolman (1948) and Hebb (1949) before them.

Therefore, it may be further instructive to consider spatial memory within the more general structure of semantic and episodic, or context-free and context-dependent representations. One possibility is that these two forms of memory are complementary systems that differ in terms of their underlying cognitive mechanics and neural circuitry and that apply equally to spatial and non-spatial domains. Initially, a spatial layout may be attached to other, non-spatial elements that define an event as unique, so that recovery of either the layout or of any other element might lead to the recovery of remaining aspects of the episode. However, with multiple and varied encounters, a spatial layout has the capacity to shed itself of other episodic elements and to survive within a highly interconnected array of neocortical structures. Though the relational nature of spatial memory would not be denied, it would take on a different form—one that captures only the core elements of a layout and that may be conjured up in memory at once. In this way, the transformation of spatial representations into deep-rooted 'maps' may be thought of as a forgetting process and access to them as relatively automatic. This differs from the voluntary and laborious reconstruction process that takes place during episodic memory, which may be likened to what occurs during spatial learning (for a related perspective, see Burgess & Shallice, 1996). Though still in its infancy and frankly speculative, it is important to put forth an alternative theoretical perspective within which to characterize the contributions of various brain structures to remote and recent spatial memory, if only to call attention to the need for re-evaluation of existing models (for a more detailed discussion, see Rosenbaum, Winocur, and Moscovitch, 2001).

8. Concluding thoughts and future prospects

We will always be fascinated by the rather 'clean' dissociations in memory observed in an otherwise 'messy' patient. Perhaps even more remarkable than the fractionations of implicit and explicit memory, semantic and episodic memory, and remote and recent spatial memory that K.C. exhibits is the fact that, despite his extensive brain damage, his cognitive abilities are generally as well preserved as they are. This fact reminds us of the importance of keeping in mind the relations between undamaged parts of the brain and intact mental functions in all neuropsychological cases. However, too often, patients with multiple lesions, such as K.C., are dismissed, and the pure cases are held up as the gold standard against which all other patients are measured. Given the rarity (or even existence) of pure cases in the human literature, a better approach than appealing to them and relegating all others to the sidelines or worse, is to treat all interesting material as gold ore, needing only different amounts of effort to extract the nugget. As we emphasized earlier, different types of inferences can be made on the basis of cases in which lesions are highly restricted and those like K.C. with more extensive damage. But the evidence reviewed in this paper suggests that both types of cases can be useful in advancing the cognitive neuroscience enterprise. We hope that the remarkable contributions made by this single memory-impaired person to memory theory will encourage future investigators to mine brain–behaviour relationships more carefully, even in ostensibly pure cases. In the meantime, K.C.'s generous offer to participate in future studies assures us that we might continue to extract new ideas about memory and refine the lessons that have already been extracted.

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References

Addis, D. R., & Tippett, L. J. (2004). Memory of myself: Autobiographical memory and identity in Alzheimer's disease. *Memory, 12*, 56–74.

Aguirre, G. K., & D'Esposito, M. (1999). Topographical disorientation: A synthesis and taxonomy. *Brain, 122*, 1613–1628.

Army Individual Test Battery. (1944). *Manual of directions and scoring*. Washington, DC: War Department, Adjutant General's Office.

Auble, P. M., Franks, J. J., & Soraci, S. A. (1979). Effort toward comprehension: Elaboration or AHA. *Memory and Cognition, 7*, 426–434.

Baddeley, A., Vargha-Khadem, F., & Mishkin, M. (2001). Preserved recognition in a case of developmental amnesia: Implications for the acquisition of semantic memory? *Journal of Cognitive Neuroscience, 13*, 357–369.

Barr, W. B., Goldberg, E., Wasserstein, J., & Novelly, R. A. (1990). Retrograde amnesia following unilateral temporal lobectomy. *Neuropsychologia*, *20*, 243–255.

Bassili, J. N., Smith, M. C., & MacLeod, C. M. (1989). Auditory and visual word-stem completion: Separating data-driven and conceptually driven processes. *Quarterly Journal of Experimental Psychology*, *41*, 439–453.

Bayley, P. J., Hopkins, R. O., & Squire, L. R. (2003). Successful recollection of remote autobiographical memories by amnesic patients with medial temporal lobe lesions. *Neuron*, *38*, 135–144.

Bayley, P. J., & Squire, L. R. (2002). Medial temporal lobe amnesia: Gradual acquisition of factual information by nondeclarative memory. *Journal of Neuroscience*, *22*, 5741–5748.

Beatty, W. W., Salmon, D. P., Berstein, N., & Butters, N. (1987). Remote memory in a patient with amnesia due to hypoxia. *Psychological Medicine*, *17*, 657–665.

Beatty, W. W., Salmon, D. P., Butters, N., Heindel, W. C., & Granholm, E. A. (1988). Retrograde amnesia in patients with Alzheimer's disease or Huntington's disease. *Neurobiology of Aging*, *9*, 181–186.

Behrmann, M., Moscovitch, M., & Winocur, G. (1994). Intact visual imagery and impaired visual perception in a patient with visual agnosia. *Journal of Experimental Psychology: Human Perception and Performance*, *20*, 1068–1087.

Benton, A. L., Hamsher, K. deS., Varney, N. R., & Spreen, O. (1983). *Contributions to neuropsychological assessment*. New York: Oxford University Press.

Brooks, L. R. (1968). Spatial and verbal components in the act of recall. *Canadian Journal of Psychology*, *22*, 349–368.

Buckner, R. L., & Koutstaal, W. (1998). Functional neuroimaging studies of encoding, priming, and explicit memory retrieval. *Proceedings of the National Academy of Sciences, U.S.A.*, *95*, 891–898.

Burgess, P. W., & Shallice, T. (1996). Confabulation and the control of recollection. *Memory*, *4*, 359–411.

Burnham, W. H. (1903). Retrograde amnesia: Illustrative cases and a tentative explanation. *American Journal of Psychology*, *14*, 382–396.

Calabrese, P., Markowitsch, H. J., Durwen, H. F., Widlitzek, H., Haupts, M., Holinka, B., et al. (1996). Right temporofrontal cortex as critical locus for the ecphory of old episodic memories. *Journal of Neurology, Neurosurgery, and Psychiatry*, *61*, 304–310.

Callen, D. J. A., Black, S. E., Gao, F., Caldwell, C. B., & Szalai, J. P. (2001). Beyond the hippocampus: MRI volumetry confirms widespread limbic atrophy in AD. *Neurology*, *57*, 1669–1674.

Cermak, L. S. (1984). The episodic–semantic distinction in amnesia. In L. R. Squire & N. Butters (Eds.), *The neuropsychology of memory* (pp. 55–62). New York: Guilford Press.

Cermak, L. S., & O'Connor, M. (1983). The anterograde and retrograde retrieval ability of a patient with amnesia due to encephalitis. *Neuropsychologia*, *2*, 213–234.

Cipolotti, L., Shallice, T., Chan, D., Fox, N., Scahill, R., Harrison, G., et al. (2001). Long-term retrograde amnesia. . .the crucial role of the hippocampus. *Neuropsychologia*, *39*, 151–172.

Cohen, N. J., Poldrack, R. A., & Eichenbaum, H. (1997). Memory for items and memory for relations in the procedural/declarative memory framework. *Memory*, *5*, 131–178.

Corkin, S. (1965). Tactually-guided maze learning in man: Effects of unilateral cortical excisions and bilateral hippocampal lesions. *Neuropsychologia*, *3*, 339–351.

Corkin, S. (1968). Acquisition of motor skill after bilateral medial temporal-lobe excision. *Neuropsychologia*, *6*, 225–264.

Corkin, S. (1984). Lasting consequences of bilateral medial temporal lobectomy: Clinical course and experimental findings in H.M. *Seminars in Neurology*, *4*, 249–259.

Corkin, S. (2002). What's new with the amnesic patient H.M.? *Nature Reviews Neuroscience*, *3*, 153–160.

Corkin, S., Amaral, D. G., Gonzalez, R. G., Johnson, K. A., & Hyman, B. T. (1997). H.M.'s medial temporal lobe lesion: Findings from magnetic resonance imaging. *Journal of Neuroscience*, *17*, 3964–3979.

Craik, F. I. M., Moscovitch, M., & McDowd, J. M. (1994). Contribution of surface and conceptual information to performance on implicit and explicit memory tests. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *20*, 864–875.

Crovitz, H. F., & Schiffman, H. (1974). Frequency of episodic memories as a function of their age. *Bulletin of the Psychonomic Society*, *4*, 519–521.

Damasio, A. R., Eslinger, P. J., Damasio, H., Van Hoesen, G. W., & Cornell, S. (1985). Multimodal amnesic syndrome following bilateral temporal and basal forebrain damage. *Archives of Neurology*, *42*, 252–259.

De Renzi, E., Liotti, M., & Nichelli, P. (1987). Semantic amnesia with preservation of autobiographic memory. A case report. *Cortex*, *23*, 575–597.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (1987). *California Verbal Learning Test: Adult Version Manual*. San Antonio, TX: The Psychological Corporation.

Della Sala, S., Laiacona, M., Spinnler, H., & Trivelli, C. (1993). Autobiographical recollection and frontal damage. *Neuropsychologia*, *31*, 823–839.

Diamond, A. (1988). Abilities and neural mechanisms underlying AB performance. *Child Development*, *59*, 523–527.

Diamond, A., & Goldman-Rakic, P. S. (1989). Comparison of human infants and rhesus monkeys on Piaget's AB task: Evidence for dependence on dorsolateral prefrontal cortex. *Experimental Brain Research*, *74*, 24–40.

Diamond, R. J., & Rozin, P. (1984). Activation of existing memories in anterograde amnesia. *Journal of Abnormal Psychology*, *93*, 98–105.

Eddy, J. K., & Glass, A. L. (1981). Reading and listening to high and low imagery sentences. *Journal of Verbal Learning and Verbal Behavior*, *20*, 333–345.

Farah, M. J., Hammond, K. M., Levine, D. N., & Calvanio, R. (1988). Visual and spatial mental imagery: Dissociable systems of representation. *Cognitive Psychology*, *20*, 439–462.

Farnsworth, D. (1957). *The Farnsworth–Munsell 100-Hue Test for the examination of color discrimination*. Maryland: Munsell Color Company, Inc.

Finke, R. D., Pinker, S., & Farah, M. J. (1998). Reinterpreting visual patterns in mental imagery. *Cognitive Science*, *13*, 51–78.

Fletcher, R. (1980). *The City University Color Vision Test* (2nd ed.). London: Keeler.

Frith, U., & Frith, C. D. (2003). Development and neurophysiology of mentalizing. *Philosophical Transactions of the Royal Society of London, B, Biological Sciences*, *358*, 459–473.

Fujii, T., Moscovitch, M., & Nadel, L. (2001). Consolidation, retrograde amnesia, and the temporal lobe. In F. Boller & J. Grafman (Eds.), *The handbook of neuropsychology: Vol. 4*. Amsterdam: Elsevier.

Gabrieli, J. D. E., Cohen, N. J., & Corkin, S. (1988). The impaired learning of semantic knowledge following bilateral medial temporal-lobe resection. *Brain and Cognition*, *7*, 157–177.

Gabrieli, J. D. E., Keane, M. M., Zarella, M. M., & Poldrack, R. A. (1997). Preservation of implicit memory for new associations in global amnesia. *Psychological Science*, *8*, 326–329.

Gilboa, A., Winocur, G., Grady, C. L., Hevenor, S. J., & Moscovitch, M. (2004). Remembering our past: Functional neuroanatomy of recollection of recent and very remote personal events. *Cerebral Cortex*, *14*, 1214–1225.

Glisky, E. L., & Schacter, D. L. (1988). Long-term retention of computer learning by patients with memory disorders. *Neuropsychologia*, *26*, 173–178.

Glisky, E. L., Schacter, D. L., & Tulving, E. (1986a). Learning and retention of computer related vocabulary in memory-impaired patients: Method of vanishing cues. *Journal of Clinical and Experimental Neuropsychology*, *8*, 292–312.

Glisky, E. L., Schacter, D. L., & Tulving, E. (1986b). Computer learning by memory-impaired patients: Acquisition and retention of complex knowledge. *Neuropsychologia*, *24*, 313–328.

Goldberg, E., Hughes, J. E., Mattis, S., & Antin, S. P. (1981). Isolated retrograde amnesia: Different etiologies, same mechanisms? *Cortex, 18*, 459–462.

Goshen-Gottstein, Y., Moscovitch, M., & Melo, B. (2000). Intact implicit memory for newly formed verbal associations in amnesic patients following single study trials. *Neuropsychology, 14*, 570–578.

Graf, P., & Schacter, D. L. (1985). Implicit and explicit memory for new associations in normal and amnesic subjects. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 11*, 501–518.

Graf, P., Squire, L. R., & Mandler, G. (1984). The information that amnesic patients do not forget. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 10*, 164–178.

Graham, K. S., & Hodges, J. R. (1997). Differentiating the roles of the hippocampal complex and the neocortex in long-term memory storage: Evidence from the study of semantic dementia and Alzheimer's disease. *Neuropsychology, 11*, 77–89.

Grossi, D., Trojano, L., Grasso, A., & Orsini, A. (1988). Selective "semantic amnesia" after closed-head injury. A case report. *Cortex, 24*, 457–464.

Hamann, S. B., & Squire, L. R. (1995). On the acquisition of new declarative knowledge in amnesia. *Behavioural Neuroscience, 109*, 1027–1044.

Hayman, C. A. G., Macdonald, C. A., & Tulving, E. (1993). The role of repetition and associative interference in new semantic learning in amnesia—a case experiment. *Journal of Cognitive Neuroscience, 5*, 375–389.

Heaton, R. K., Chelune, G. J., Talley, J. L., Kay, G. G., & Curtis, G. (1993). *Wisconsin Card Sorting Test (WCST) manual revised and expanded*. Odessa, FL: Psychological Assessment Resources.

Hebb, D. O. (1949). *The organization of behaviour*. New York: Wiley.

Henson, R. N. A. (2003). Neuroimaging studies of priming. *Progress in Neurobiology, 70*, 53–81.

Holdstock, J. S., Mayes, A. R., Cezayirli, E., Isaac, C. L., Aggleton, J. P., & Roberts, N. (2000). A comparison of egocentric and allocentric spatial memory in a patient with selective hippocampal damage. *Neuropsychologia, 38*, 410–425.

Jackson, J. H. (1931–1932). *Selected writings of John Hughlings Jackson*. London: Hodder & Stoughton.

Jacoby, L. L., & Dallas, M. (1981). On the relationship between autobiographical memory and perceptual learning. *Journal of Experimental Psychology: General, 110*, 306–340.

Jacoby, L. L., & Witherspoon, D. (1982). Remembering without awareness. *Canadian Journal of Psychology, 32*, 300–324.

Jacoby, L. L., Yonelinas, A. P., & Jennings, J. M. (1996). The relation between conscious and unconscious (automatic) influences: A declaration of independence. In J. Cohen & J. W. Schooler (Eds.), *Scientific approaches to the questions of consciousness* (pp. 13–37). Mahwah, NJ: Erlbaum.

James, W. (1890). *The principles of psychology*. New York: Holt, Rinehart and Winston.

Kahana, M. J. (2000). Contingency analyses of memory. In E. Tulving & F. I. M. Craik (Eds.), *The Oxford handbook of memory* (pp. 59–69). Oxford University Press.

Kaplan, E. F., Goodglass, H., & Weintraub, S. (1983). *The Boston Naming Test*. Philadelphia: Lea & Febiger.

Kapur, N. (1999). Syndromes of retrograde amnesia: A conceptual and empirical synthesis. *Psychological Bulletin, 125*, 800–825.

Kapur, N., Glisky, E. L., & Wilson, B. A. (2002). External memory aids and computers in memory rehabilitation. In A. D. Baddeley, M. D. Kopelman, & B. A. Wilson (Eds.), *The handbook of memory disorders* (2nd ed., pp. 757–783).

Kertesz, A. (1982). *Western Aphasia Battery*. San Antonio, TX: The Psychological Corporation.

Kitchener, E. G., Hodges, J. R., & McCarthy, R. (1998). Acquisition of post-morbid vocabulary and semantic facts in the absence of episodic memory. *Brain, 121*, 1313–1327.

Klein, S. B., Loftus, J., & Kihlstrom, J. F. (1996). Self-knowledge of an amnesic patient: Toward a neuropsychology of personality and social psychology. *Journal of Experimental Psychology: General, 125*, 250–260.

Klein, S. B., Loftus, J., & Kihlstrom, J. F. (2002). Memory and temporal experience: The effects of episodic memory loss on an amnesic patient's ability to remember the past and imagine the future. *Social Cognition, 20*, 353–379.

Köhler, S., Habib, R., Black, S. E., Szekely, C., Sinden, M., & Tulving, E. (1997). Cross-modal priming in the densely amnesic subject K.C. *Brain and Cognition, 35*, 420–423.

Köhler, S., Black, S. E., Sinden, M., Szekely, C., Kidron, D., Parker, J. L., et al. (1998). Memory impairments associated with hippocampal versus parahippocampal–gyrus atrophy: An MR volumetry study in Alzheimer's disease. *Neuropsychologia, 36*, 901–914.

Kopelman, M. D. (1995). The Korsakoff syndrome. *British Journal of Psychiatry, 166*, 154–173.

Kopelman, M. D., Stanhope, N., & Kingsley, D. (1999). Retrograde amnesia in patients with diencephalic, temporal lobe, or frontal lesions. *Neuropsychologia, 37*, 939–958.

Kopelman, M. D., Wilson, B. A., & Baddeley, A. D. (1989). The autobiographical memory interview: A new assessment of autobiographical and personal semantic memory in amnesic patients. *Journal of Clinical and Experimental Neuropsychology, 5*, 724–744.

Kopelman, M. D., Wilson, B. A., & Baddeley, A. D. (1990). *The autobiographical memory interview*. Suffolk, England: Thames Valley Test Company.

Korsakoff, S. S. (1889). Etude mèdico-psychologique sur une forme des maladies de la mémoire. *Rèvue Philosophique, 28*, 501–530.

Kovner, R., Mattis, S., & Goldmeier, E. (1983). A technique for promoting robust free recall in chronic organic amnesia. *Journal of Clinical Neuropsychololgy, 5*, 65–71.

Levine, B., Black, S. E., Cabeza, R., Sinden, M., Mcintosh, A. R., Toth, J. P., et al. (1998). Episodic memory and the self in a case of isolated retrograde amnesia. *Brain, 121*, 1951–1973.

Levine, B., Stuss, D. T., & Milberg, W. P. (1995). Concept generation: Validation of a test of executive functioning in a normal aging population. *Journal of Clinical and Experimental Neuropsychology, 17*, 740–758.

Levine, B., Svoboda, E., Hay, J. F., Winocur, G., & Moscovitch, M. (2002). Aging and autobiographical memory: Dissociating episodic from semantic retrieval. *Psychology and Aging, 17*, 677–689.

Lhermitte, F., & Serdaru, M. (1993). Unconscious processing in memory recall: A study of three amnesic patients. *Cortex, 29*, 25–43.

Maguire, E. A., Frackowiak, R. S. J., & Frith, C. D. (1996). Learning to find your way: A role for the human hippocampal formation. *Proceedings of the Royal Society of London B Biological Sciences, 263*, 1745–1750.

Maguire, E. A., Vargha-Khadem, F., & Mishkin, M. (2001). The effects of bilateral hippocampal damage on fMRI regional activations and interactions during memory retrieval. *Brain, 124*, 1156–1170.

Markowitsch, H. J., Calabrese, P., Liess, J., Haupts, M., Durwen, H. F., & Gehlen, W. (1993). Retrograde amnesia after traumatic injury of the frontotemporal cortex. *Journal of Neurology, Neurosurgery, and Psychiatry, 56*, 988–992.

Mattis, S., & Kovner, R. (1984). Amnesia is as amnesia does: Toward another definition of the anterograde amnesias. In L. R. Squire & N. Butters (Eds.), *Neuropsychology of memory* (pp. 115–121). New York: Guilford Press.

McAndrews, M. P., Glisky, E. L., & Schacter, D. L. (1987). When priming persists: Long-lasting implicit memory for a single episode in amnesic patients. *Neuropsychologia, 25*, 497–506.

McCarthy, R. A., & Warrington, E. K. (1992). Actors but not scripts: The dissociation of people and events in retrograde amnesia. *Neuropsychologia, 30*, 633–644.

Milner, B., Corkin, S., & Teuber, H. L. (1968). Further analysis of the hippocampal amnesic syndrome: 14-year follow-up of H.M. *Neuropsychologia*, *6*, 215–234.

Morris, R. G. M., Garrud, P., Rawlins, J. N. P., & O'Keefe, J. (1982). Place navigation impaired in rats with hippocampal lesions. *Nature*, *297*, 681–683.

Moscovitch, M. (1982). Multiple dissociations of function in amnesia. In L. S. Cermak (Ed.), *Human memory and amnesia* (pp. 337–370). Hillsdale: Erlbaum.

Moscovitch, M., & Melo, B. (1997). Strategic retrieval and the frontal lobes: Evidence from confabulation and amnesia. *Neuropsychologia*, *35*, 1017–1034.

Moscovitch, M., Winocur, G., & McLachlan, D. (1986). Memory as assessed by recognition and reading time in normal and memory-impaired people with Alzheimer's disease and other neurological disorders. *Journal of Experimental Psychology: General*, *5*, 331–347.

Nadel, L., & Moscovitch, M. (1997). Memory consolidation, retrograde amnesia and the hippocampal complex. *Current Opinion in Neurobiology*, *7*, 217–227.

Nadel, L., & Moscovitch, M. (2001). The hippocampal complex and long-term memory revisited. *Trends in Cognitive Sciences*, *5*, 228–230.

Neisser, U. (1981). John Dean's memory: A case study. *Cognition*, *9*, 1–22.

Ogden, J. A. (1993). Visual object agnosia, prosopagnosia, achromatopsia, loss of visual imagery, and autobiographical amnesia following recovery from cortical blindness: Case M.H. *Neuropsychologia*, *31*, 571–589.

O'Keefe, J., & Dostrovsky, J. (1971). The hippocampus as a spatial map: Preliminary evidence from unit activity in the freely-moving rat. *Brain Research*, *34*, 171–175.

O'Keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map*. Oxford: Clarendon Press.

Olton, D. S., Becker, J. T., & Handelman, G. H. (1979). Hippocampus, space and memory. *Behavioural Brain Sciences*, *2*, 313–365.

Oppenheimer, J. M. (1956). Some problems of nervous function. In H. Helson (Ed.), *Theoretical foundations of psychology* (pp. 47–113). New York: Van Nostrand.

Osterrieth, P. A. (1944). Le test de copie d'une figure complexe: Contribution a l'étude de la perception et de la memoire [a test of copying a complex figure: A contribution to the study of perceptionand memory]. *Archives de Psychologie, Geneva*, *30*, 205–220.

Paivio, A. (1978). Comparisons of mental clocks. *Journal of Experimental Psychology*, *4*, 61–71.

Penfield, W., & Mathieson, G. (1974). Memory: Autopsy findings and comments on the role of the hippocampus in experiential recall. *Archives of Neurology*, *31*, 145–154.

Penfield, W., & Milner, B. (1958). Memory deficit produced by bilateral lesions in the hippocampal zone. *Archives of Neurology and Psychiatry*, *79*, 475–497.

Piaget, J. (1954). *The construction of reality in the child*. New York: Basic Books.

Rajaram, S., & Coslett, H. B. (2000a). New conceptual associative learning in amnesia: A case study. *Journal of Memory and Language*, *43*, 291–315.

Rajaram, S., & Coslett, H. B. (2000b). Acquisition and transfer of new verbal information in amnesia: Retrieval and neuroanatomical constraints. *Neuropsychology*, *14*, 427–455.

Reed, J. M., & Squire, L. R. (1998). Retrograde amnesia for facts and events: Findings from four new cases. *Journal of Neuroscience*, *18*, 3943–3954.

Reed, L. J., Lasserson, D., Marsden, P., Stanhope, N., Stevens, T., Bello, F., et al. (2003). FDG–PET findings in the Wernicke–Korsakoff syndrome. *Cortex*, *39*, 1027–1045.

Ribot, T. (1881). *Diseases of memory*. Appleton: New York.

Rizzuto, D. S., & Kahana, M. J. (2000). Associative symmetry vs. independent associations. *Neurocomputing*, *32–33*, 973–978.

Rosenbaum, R. S., Winocur, G., & Moscovitch, M. (2001). New views on old memories: Re-evaluating the role of the hippocampal complex. *Behavioural Brain Research*, *127*, 183–197.

Rosenbaum, R. S., McKinnon, M., Levine, B., & Moscovitch, M. (2003). Visual imagery or strategic retrieval: Disentangling the nature of patient KC's autobiographical memory deficit. *Cognitive Neuroscience Society Abstracts*, *10*, 36.

Rosenbaum, R. S., McKinnon, M., Levine, B., & Moscovitch, M. (2004). Visual imagery deficits, impaired strategic retrieval, or memory loss: Disentangling the nature of an amnesic person's autobiographical memory deficit. *Neuropsychologia*, *42*, 1619–1635.

Rosenbaum, R. S., Priselac, S., Kohler, S., Black, S. E., Gao, F., Nadel, L., et al. (2000). Remote spatial memory in an amnesic person with extensive bilateral hippocampal lesions. *Nature Neuroscience*, *3*, 1044–1048.

Rosenbaum, R. S., Winocur, G., Ziegler, M., Hevenor, S. J., Grady, C. L., & Moscovitch, M. (2004). fMRI studies of remote spatial memory in an amnesic person. *Brain and Cognition*, *54*, 170–172.

Rosenbaum, R. S., Ziegler, M., Wincour, G., Grady, C. L., & Moscovitch, M. (2004). "I have often walked down this street before:" fMRI studies on the hippocampus and other structures during mental navigation of an old environment. *Hippocampus*, *14*, 826–835.

Rousseaux, M., Godfrey, O., Cabaret, M., Bernati, T., & Pruvo, J. P. (1997). Retrograde memory after rupture of aneurysms of the anterior communicating artery. *Revue de Neurologie*, *153*, 659–668.

Rozin, M. (1976). The psychobiological approach to human memory. In M. R. Rosenzweig & E. L. Bennett (Eds.), *Neural mechanisms of learning and memory* (pp. 3–46). Cambridge, MA: MIT Press.

Rubin, D. C., & Greenberg, D. L. (1998). Visual memory-deficit amnesia: A distinct amnesia presentation and etiology. *Proceedings of the National Academy of Sciences, U.S.A.*, *95*, 5413–5416.

Ryan, J. J., & Paolo, A. M. (1992). A screening procedure for estimating premorbid intelligence in the elderly. *The Clinical Neuropsychologist*, *6*, 53–62.

Ryan, L., Nadel, L., Keil, K., Putnam, K., Schnyer, D., Trouard, T., et al. (2001). Hippocampal complex and retrieval of recent and very remote autobiographical memories: Evidence from functional magnetic resonance imaging in neurologically intact people. *Hippocampus*, *11*, 707–714.

Sagar, H. J., Cohen, N. J., Corkin, S., & Growdon, J. H. (1985). Dissociations among processes in remote memory. *Annals of the New York Academy of Sciences*, *444*, 533–535.

Schacter, D. L. (1985). Priming of old and new knowledge in amnesic patients and normal subjects. *Annals of the New York Academy of Sciences*, *444*, 41–53.

Schacter, D. L. (1987). Implicit memory: History and current status. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *13*, 501–518.

Schacter, D. L., & Buckner, R. L. (1998). Priming and the brain. *Neuron*, *20*, 185–195.

Schacter, D. L., & Curran, T. (2000). Memory without remembering and remembering without memory: Implicit and false memories. In M. S. Gazzaniga (Ed.), *The cognitive neurosciences* (2nd ed., pp. 829–840). Cambridge: MIT Press.

Schacter, D. L., & Graf, P. (1986). Preserved learning in amnesic patients: Perspectives from research on direct priming. *Journal of Clinical and Experimental Neuropsychology*, *8*, 727–743.

Schacter, D. L., & Tulving, E. (1994). What are the memory systems of 1994? In D. L. Schacter & E. Tulving (Eds.), *Memory systems* (pp. 1–38). Cambridge, MA: MIT Press.

Schacter, D. L., Moscovitch, M., Tulving, E., McLachlan, D. R., & Freedman, M. (1986). Mnemonic precedence in amnesic patients: An analogue of the AB error in infants? *Child Development*, *57*, 816–823.

Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery, and Psychiatry*, *20*, 11–21.

Shimamura, A. P., & Squire, L. R. (1987). A neuropsychological study of fact memory and source amnesia. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *13*, 464–473.

Siegal, M., & Varley, R. (2003). Neural systems involved in "theory of mind". *Nature Reviews Neuroscience*, *3*, 463–471.

Smith, M. L. (1988). Recall of spatial location by the amnesic patient H.M. *Brain and Cognition*, *7*, 178–183.

Smith, M. L., & Milner, B. (1981). The role of the right hippocampus in the recall of spatial location. *Neuropsychologia*, *19*, 781–793.

Snowden, J. S., Griffiths, H. L., & Neary, D. (1996). Semantic–episodic memory interactions in semantic dementia: Implications for retrograde memory function. *Cognitive Neuropsychology*, *13*, 1101–1137.

Spreen, O., & Strauss, E. (1998). *A compendium of neuropsychological tests* (2nd ed.). New York: Oxford University Press.

Squire, L. R. (1989). On the course of forgetting in very long-term memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *15*, 241–245.

Squire, L. R. (1992). Memory and the hippocampus: A synthesis from findings with rats, monkeys and humans. *Psychological Review*, *99*, 195–231.

Squire, L. R., & Alvarez, P. (1995). Retrograde amnesia and memory consolidation: A neurobiological perspective. *Current Opinion in Neurobiology*, *5*, 169–177.

Squire, L. R., Slater, P. C., & Chace, P. M. (1975). Retrograde amnesia: Temporal gradient in very long-term memory following electroconvulsive therapy. *Science*, *187*, 77–79.

Squire, L. R., & Zola, S. M. (1998). Episodic memory, semantic memory, and amnesia. *Hippocampus*, *8*, 205–211.

Stuss, D. T., Stethem, L. L., & Poirier, C. A. (1987). Comparison of three tests of attention and rapid information processing across six age groups. *The Clinical Neuropsychologist*, *1*, 139–152.

Svoboda, E., Hynes, C. A., Campbell, A. F., Dade, L. A., Moscovitch, M., & Levine, B. (2002). The frontal lobes and autobiographical memory: Differential effects of dorsolateral and ventrolateral prefrontal damage. *Journal of the International Neuropsychological Society*, *8*, 275.

Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. New York: Thieme Medical Publishers.

Teng, E., & Squire, L. R. (1999). Memory for places learned long ago is intact after hippocampal damage. *Nature*, *400*, 675–677.

Terrace, H. S. (1963). Discrimination learning with and without "errors". *Journal of Experimental Analysis of Behaviour*, *6*, 1–27.

Tolman, E. C. (1948). Cognitive maps in rats and man. *Psychological Review*, *55*, 189–208.

Tulving, E. (1972). Episodic and semantic memory. In E. Tulving & W. Donaldson (Eds.), *Organization of memory* (pp. 381–403). New York: Academic Press.

Tulving, E. (1983). *Elements of episodic memory*. Oxford: Clarendon.

Tulving, E. (1985). Memory and consciousness. *Canadian Psychologist*, *25*, 1–12.

Tulving, E. (1993). Self-knowledge of an amnesic individual is represented abstractly. In T. K. Sdrull & R. S. Wyer Jr. (Eds.), *The mental representation of trait and autobiographical knowledge about the self* (pp. 147–156). Hillsdale, NJ: Lawrence Erlbaum Associates.

Tulving, E. (2002). Episodic memory: From mind to brain. *Annual Review of Psychology*, *53*, 1–25.

Tulving, E. (2004). Episodic memory and autonoesis: Uniquely human? In H. Terrace & J. Metcalfe (Eds.), *The missing link in cognition: Evolution of self-knowing consciousness* (pp. 3–56). New York, NY: Oxford University Press.

Tulving, E., Hayman, C. A., & Macdonald, C. A. (1991). Long-lasting perceptual priming and semantic learning in amnesia: A case experiment. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *17*, 595–617.

Tulving, E., & Schacter, D. L. (1990). Priming and human memory systems. *Science*, *247*, 301–306.

Tulving, E., & Markowitsch, H. J. (1998). Episodic and declarative memory: Role of the hippocampus. *Hippocampus*, *8*, 198–204.

Tulving, E., Schacter, D. L., McLachlan, D. R., & Moscovitch, M. (1988). Priming of semantic autobiographical knowledge: A case study of retrograde amnesia. *Brain and Cognition*, *8*, 3–20.

Tulving, E., Schacter, D. L., & Stark, H. A. (1982). Priming effects in word-fragment completion are independent of recognition memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *8*, 336–342.

Vargha-Khadem, F., Gadian, D. G., & Mishkin, M. (2001). Dissociations in cognitive memory: The syndrome of developmental amnesia. *Philosophical Transactions of the Royal Society of London, B, Biological Sciences*, *356*, 1435–1440.

Vargha-Khadem, F., Gadian, D. G., Watkins, K. E., Connelly, A., Van Paesschen, W., & Mishkin, M. (1997). Differential effects of early hippocampal pathology on episodic and semantic memory. *Science*, *277*, 376–380.

Verfaellie, M., Keane, M. M., & Cook, S. P. (2001). The role of explicit memory processes in cross-modal priming: An investigation of stem completion priming in amnesia. *Cognitive, Affective, and Behavioral Neuroscience*, *1*, 222–228.

Verfaellie, M., Koseff, P., & Alexander, M. P. (2000). Acquisition of novel semantic information in amnesia: Effects of lesion location. *Neuropsychologia*, *38*, 484–492.

Verfaellie, M., Reiss, L., & Roth, H. L. (1995). Knowledge of new English vocabulary in amnesia: An examination of premorbidly acquired semantic memory. *Journal of the International Neuropsychological Society*, *1*, 443–453.

Viskontas, I. V., McAndrews, M. P., & Moscovitch, M. (2000). Remote episodic memory deficits in patients with unilateral temporal lobe epilepsy and excisions. *Journal of Neuroscience*, *20*, 5853–5857.

Warrington, E. K. (1984). *Recognition Memory Test*. Windsor, England: NFER-Nelson.

Warrington, E. K. (1996). Studies of retrograde memory: A long-term view. *Proceedings of the National Academy of Sciences, U.S.A.*, *93*, 13523–13526.

Warrington, E. K., & Weiskrantz, L. (1968). New method of testing long-term retention with special reference to amnesic patients. *Nature*, *217*, 972–974.

Warrington, E. K., & Weiskrantz, L. (1974). The effect of prior learning on subsequent retention in amnesic patients. *Neuropsychologia*, *12*, 419–428.

Wechsler, D. (1981). *The Wechsler Adult Intelligence Scale-Revised*. New York: The Psychological Corporation.

Wechsler, D. (1987). *Wechsler Memory Scale-Revised*. San Antonio, TX: Psychological Corporation.

Wechsler, D. (1999). *The Wechsler Abbreviated Scale of Intelligence*. New York: The Psychological Corporation.

Weiskranz, L. (1985). On issues and theories of the human amnesia syndrome. In N. M. Weinberger, J. L. McGaugh, & G. Lynch (Eds.), *Memory systems and the brain* (pp. 380–418). New York: Guilford Press.

Westmacott, R., Leach, L., Freedman, M., & Moscovitch, M. (2001). Different patterns of autobiographical memory loss in semantic dementia and medial temporal lobe amnesia: A challenge to consolidation theory. *Neurocase*, *7*, 37–55.

Westmacott, R., & Moscovitch, M. (2001). Names and words without meaning: Incidental postmorbid semantic learning in a person with extensive bilateral medial temporal damage. *Neuropsychology*, *15*, 586–596.

Westmacott, R., & Moscovitch, M. (2002). Temporally-graded retrograde memory loss for famous names and vocabulary terms in amnesia and semantic dementia: Further evidence for opposite gradients using implicit memory tasks. *Cognitive Neuropsychology*, *19*, 135–163.

Wheeler, M., Stuss, D. T., & Tulving, E. (1997). Toward a theory of episodic memory: The frontal lobes and autonoetic consciousness. *Psychological Bulletin*, *121*, 331–354.

Wilson, B. A., Baddeley, A. D., & Kapur, N. (1995). Dense amnesia in a professional musician following herpes simplex encephalitis.

Journal of Clinical and Experimental Neuropsychology, *17*, 668–681.

Wood, F., Ebert, V., & Kinsbourne, M. (1982). The episodic–semantic memory distinction in memory and amnesia: Clinical and experimental observations. In L. S. Cermak (Ed.), *Human memory and amnesia* (pp. 167–194). Hillsdale, NJ: Erlbaum.

Yasuda, K., Watanabe, O., & Ono, Y. (1997). Dissociation between semantic and autobiographic memory: A case report. *Cortex*, *33*, 623–638.

Zola-Morgan, S., Squire, L. R., & Amaral, D. G. (1986). Human amnesia and the medial temporal region: Enduring memory impairment following a bilateral lesion limited to field CA1 of the hippocampus. *Journal of Neuroscience*, *6*, 2950–2967.