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The scope of preserved procedural memory in amnesia

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Summary

The finding that patients with amnesia retain the ability to learn certain procedural skills has provided compelling evidence of multiple memory systems in the human brain, but the scope, defining features and ecological significance of the preserved mnemonic abilities have not yet been explored. Here, we tested the hypothesis that subjects with amnesia would be able to learn and retain a broad range of procedural skills, by examining their acquisition and retention performance on five novel experimental tasks. The tasks are based on real-world activities and encompass a broad range of perceptual–motor demands: (i) the weaving task involves weaving pieces of fabric from woollen strings, using a manual weaver's loom; (ii) the geometric figures task consists of tracing geometric figures with a stylus as they move horizontally across a touch screen monitor; (iii) the control stick task involves tracking a sequence of visual target locations using a joystick control; (iv) the pouring task consists of pouring 200 ml of water from a watering can into a series of graduated cylinders, from a point 20 cm above the cylinders; and (v) the spatial sequence task involves learning an ordered sequence of pushing five spatially distributed buttons without visual guidance. Ten chronic and stable amnesic subjects (nine with bilateral medial temporal lobe damage due to herpes simplex encephalitis or anoxia, and one with thalamic stroke) and 25 matching normal comparison subjects were tested on three occasions: initial learning at time 1; retention at time 2 (24 h later); and retention at time 3 (2 months later). Despite impaired declarative memory for the tasks, the amnesic subjects demonstrated acquisition and retention of the five skills; their learning slopes over repeated trials were comparable with those of comparison subjects. These findings indicate that preserved learning of complex perceptual–motor skills in patients with amnesia is a robust phenomenon, and that it can be demonstrated across a variety of conditions and perceptual–motor demands. The comparability of the tasks employed in this study with real-world activities highlights the potential application of this memory dissociation in the rehabilitation of patients with amnesia.

Keywords: procedural memory; medial temporal lobes; amnesia; motor skill

Abbreviations: DFT = distance from target; HSE = herpes simplex encephalitis; ROI = region of interest

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Introduction

Severe anterograde amnesia for declarative information can result from damage to medial temporal lobe structures (Scoville and Milner, 1957), medial diencephalic nuclei (Graff-Radford *et al*., 1990) or basal forebrain nuclei (Damasio *et al*., 1985*b*). Amnesia in such patients is not complete, however, but rather leaves preserved the ability to learn and retain some perceptual–motor skills at normal or near normal levels. Amnesics have shown the ability to learn and retain the skill to trace a figure reflected in the mirror—'mirror tracing' (Milner, 1962; Damasio *et al.*, 1985*a*; Nichelli *et al*., 1988; Gabrieli *et al*., 1993; Tranel *et al*., 1994); the skill to maintain contact between a hand-held stylus and a target metal disk, on a revolving turntable—'rotor pursuit' (Brooks and Baddeley, 1976; Tranel *et al*., 1994); and the skill to press an imbedded sequence of keys—'serial reaction time' (Nissen and Bullemer, 1987).

There is much evidence to suggest that at least some perceptual–motor skill learning depends on anatomical systems distinct from those involved in declarative memory.

Studies involving subjects with focal lesions (Pascual-Leone *et al*., 1993, 1995; Doyon *et al*., 1997; Gomez Beldarrain *et al*., 1999; Vakil *et al*., 2000; Schmidtke *et al*., 2002), Parkinson's disease (Frith *et al*., 1986; Ferraro *et al*., 1993; Jackson *et al*., 1995; Agostino *et al*., 1996; Doyon *et al*., 1997; Stefanova *et al*, 2000; Swinnen *et al*., 2000) and Huntington's disease (Heindel *et al*., 1988; Knopman and Nissen, 1991; Gabrieli *et al*., 1997), as well as functional neuroimaging studies (Seitz *et al*., 1990, 1994; Friston *et al*., 1992; Grafton *et al*., 1992, 1994, 1995; Rauch *et al*., 1995, 1997; Flament *et al*., 1996; Imamura *et al*., 1996; Hazeltine *et al*., 1997; Krebs *et al*., 1998; Imamizu *et al*., 2000; Doyon *et al*., 2002), indicate that the basal ganglia, cerebellum and the prefrontal/premotor regions are involved in perceptual–motor skill learning.

Since some procedural memory systems are anatomically distinct from the declarative memory system, amnesic patients should be able to acquire skills with major implications for daily functioning. To date, however, this notion has had little impact on neurorehabilitation. One reason for this may be the limited number of experimental tasks that have been used to study procedural memory. The mirror tracing, rotor pursuit and serial reaction time tasks all allow careful experimental control, but have a limited range of perceptual–motor requirements and no clear linkage to real-world activities. Although such tasks have been extremely valuable in the early studies of procedural memory, little is known about the phenomenon outside of behaviour on these tasks, which have no easy generalization to daily life or potential rehabilitation applications. Thus, the scope and range of perceptual–motor skills that are preserved in amnesia remain largely unknown.

To address this issue, we measured the performance of a group of amnesic subjects on five novel experimental tasks that test procedural memory. The design of each task was inspired by a real-world activity (e.g. work on an assembly line or in construction). The tasks were designed to differ from one another in the specific cognitive, perceptual and motor demands (e.g. moving versus static stimuli; uni-manual versus bi-manual; uni-step versus multi-step routine; continuous feedback during performance versus feedback after performance; sequential versus non-sequential). These tasks allowed us to address two questions: (i) is preserved perceptual–motor skill learning in amnesia restricted to a small number of laboratory tasks, or is it a more general characteristic of amnesia? and (ii) can patients with amnesia acquire and retain new skills relevant to activities of daily living? We hypothesized that amnesic subjects would be able to acquire and retain (over delays of 24 h and 2 months) a diverse set of complex and ecologically based perceptual–motor skills, and that they would do so as efficiently as normal subjects. If this hypothesis is true, then occupationally relevant, perceptual–motor tasks could have an essential role in the development of new strategies for the neurorehabilitation of amnesic individuals.

Methods

Subjects

The subjects (Table 1) were 10 patients (seven men and three women) with moderate to severe chronic memory impairment (amnesic group) and 25 normal comparison subjects. The amnesic patients were obtained from the Patient Registry of the University of Iowa's Division of Behavioral Neurology and Cognitive Neuroscience. Aetiologies for the memory impairment included herpes simplex encephalitis (HSE) (n = 4), anoxia (n = 5) and thalamic stroke (n = 1). All were studied at least 5 months after their neurological event, at which time their neurological status and neuropsychological profiles were stable. All had normal educational and occupational histories prior to their neurological event, and all had become disabled due to their amnesia. The primary inclusion criterion was the presence of amnesia, which was operationally defined as severe impairment on standardized measures of both verbal and visual memory (at least 1 Z-score below the mean on the 30 min delayed recall of both the Rey Auditory Verbal Learning Test and the Complex Figure Test). As shown in Table 1,

Table 1 *Amnesic subjects*

Subjects	Gender	Age (years) mean = 50 (9.7)	RH/LH*	Years of education mean = 15 (2.4)	Aetiology	Time since onset (months)	AVLT—30 min recall		Complex Figure Test—30 min recall	
							Raw score	Z-score^{+}	Raw score	Z-score†
1	Male	72	+100 RH	14	HSE	119	0	−2.83	0	−3.86
2	Male	45	−100 LH	18	HSE	31	0	−3.24	0	−3.57
3	Male	50	+100 RH	16	HSE	258	1	−2.92	4	−2.86
4	Female	41	+100 RH	13	HSE	5	2	−2.59	8	−2.15
5	Male	57	+50 RH	19	Infarct	62	1	−2.92	13	−1.26
6	Male	45	+100 RH	16	Anoxia	34	0	−3.24	5	−2.68
7	Female	52	+100 RH	12	Anoxia	53	1	−2.92	3	−3.04
8	Male	54	+100 RH	12	Anoxia	131	0	−3.24	11	−1.61
9	Female	38	+100 RH	14	Anoxia	98	1	−5.65	6	−2.6
10	Male	46	−80 LH	16	Anoxia	22	2	−2.59	5.5	−2.59

AVLT = Rey Auditory Verbal Learning Test; *Geschwind–Oldfield questionnaire (Oldfield, 1971); $^{+}$ the Z-scores were calculated with the normal mean and standard deviation for the subject's age (R. D. Jones, unpublished data); †the Z-scores were calculated with the normal mean and SD for the subject's age (J. S. Wefel and K. E. Boward, unpublished data).

most subjects were significantly more impaired than the criteria. Exclusion criteria included evidence of progressive dementia (assessed with serial neurological and neuropsychological evaluations), significant motor and sensory impairment, history of psychiatric disorder or neurological event other than that which caused the amnesia.

Twenty-five healthy normal subjects (11 men and 14 women), with no history or evidence of neurological or psychiatric disorder, constituted the comparison group. The comparison group was matched to the amnesic group in terms of age (mean = 51.4 years, SD = 15.4) and years of education (mean = 16 years, SD = 3.2).

All subjects provided informed consent to participate in this experiment, according to the Declaration of Helsinki and the regulations of the University of Iowa Institutional Review Board.

Neuropsychological characterization

A battery of standardized neuropsychological tests was used to characterize the amnesic subjects' cognitive profile further. The battery consisted of: verbal IQ and the performance IQ indexes of the Wechsler Adult Intelligence Scale (1998); Judgement of Line Orientation; Complex Figure Test (copy); Grooved Pegboard Test; Trail Making Test (parts A and B); and Logical Memory (immediate and 30 min recall) of the Wechsler Memory Scale (1987). These findings show generally well-preserved cognitive abilities of these subjects, with the exception of their severe memory impairment (Tables 1 and 2).

Neuroanatomical characterization

The anatomical characterization of the amnesics was performed on high-resolution magnetic resonance scans, using the standard procedures of the Laboratory of Neuroimaging and Human Neuroanatomy, University of Iowa.

Thin cut MRIs were obtained in a GE Signa scanner operating at 1.5 Tesla, using the following protocol: SPGR (spoiled gradient recalled) Flip angle 50°, TR (repetition time) 24 ms, TE (echo time) 7 ms, NEX (number of excitations) 1, matrix 256 × 192, FOV (field of view) 24 cm. We obtained 124 contiguous coronal slices, 1.5 or 1.6 mm thick, with an interpixel distance of 0.94 mm. The slice thickness was adjusted to the size of the brain so as to sample the entire brain, while avoiding wrap artefacts. Three data sets were obtained for each brain during each imaging session. These were co-registered and averaged *post hoc* using automated image registration (AIR 3.03, UCLA; Woods *et al*., 1992), to produce a single data set of enhanced quality with pixel dimensions of 0.7 mm in plane and interslice spacing of 1.5–1.6 mm between planes (Holmes *et al*., 1998).

All brains were reconstructed in three dimensions using Brainvox (Frank *et al*., 1997), an interactive family of programs designed to reconstruct, segment and measure brains from MRIs. An automated program, extensively validated against human experts (Grabowski *et al*., 2000), was used to segment the images into the three primary tissue types (white matter, grey matter and CSF). Before tracing regions of interest (ROIs), brains were realigned (but not resized) along a plane running through the anterior and posterior commissures (i.e. the AC–PC line); this ensured that coronal slices in all subjects were perpendicular to a uniformly and anatomically defined axis of the brain. Volume determinations from ROIs were made using image analysis programs developed in our laboratory (Frank *et al*., 1997).

The visual inspection and description of the lesion were performed in the HSE and thalamic stroke patients (Table 3). As a summary, all four HSE patients had extensive or complete damage to the hippocampal region bilaterally, and three also showed amygdala damage. The only subject without hippocampal damage had a medial and anterior thalamic lesion.

A quantitative analysis of the brains of the anoxic patients was performed using Brainvox and automated tissue segmentation (Grabowski *et al*., 2000). ROIs were traced by hand on contiguous coronal slices of the brain. Criteria for tracing the amygdala and hippocampus were derived from the atlas of Duvernoy (1988). Using a method similar to that of Convit *et al*. (1999; see also Szabo *et al*., 2001), point sets outlining the boundaries of the amygdala and hippocampus were first made in parasagittal and axial planes; these point sets were then projected to the coronal slices to guide tracing of the ROIs. In a reliability study (two raters, 59 normal subjects) conducted in our laboratory using these criteria for tracing the amygdala and hippocampus, inter-rater Pearson *r*s were 0.917 for the left amygdala, 0.952 for the right amygdala, 0.93 for the left hippocampus and 0.946 for the right hippocampus. The quantitative MRI results of the anoxics can be seen in Table 4. Of the four anoxic

Table 2 *Neuropsychological characteristics of the amnesic subjects*

Subjects	WAIS (R, III)—verbal IQ*	WAIS (R, III)—performance IQ*	Line orientation+	Complex Figure Test—copy+	Grooved Pegboard		Trail Making Test		Wechsler Memory Scale—logical memory	
					Dominant hand+	Non-dominant hand+	A+	B+	Immediate+	30 min recall+
1	103	91	NA	27	133	108	79	102	14	0
2	95	78	26	32	78	92	55	147	10	0
3	105	106	30	32	75	73	27	53	17	6
4	84	98	27	28	69	70	34	79	37	6
5	103	113	31	32	67	68	39	84	NA	NA
6	111	83	26	25	113	153	43	118	24	1
7	102	94	25	33	70	70	27	48	32	0
8	94	89	24	34	104	93	39	145	21	0
9	89	79	22	28	65	72	21	59	23	0
10	91	98	29	36	69	90	51	99	36	17

*Standard scores; + raw scores; NA = data not available; WAIS = Wechsler Adult Intelligence Scale.

subjects, three had a significantly smaller hippocampal volume when compared with age- and gender-matched normal comparison subjects; the amygdala and the temporal lobe volume of the four anoxic subjects was within the range of normal comparison subjects.

Table 3 *Description* of the lesion sites of patients 1,2,3,4 and 5*

Brain areas	Subjects				
	1	2	3	4	5
Right hemisphere					
Temporal pole	**3**	**2**	**3**	0	0
Superior temporal gyrus	**2**	0	**3**	0	0
Middle temporal gyrus	0	0	**3**	0	0
Inferior temporal gyrus	0	0	**3**	0	0
Fourth temporal gyrus	**2**	0	**3**	0	0
Fifth temporal gyrus	**2**		**3**	0	0
Insula	0	0	**3**	0	0
Dorsolateral frontal lobe +	0	0	0	0	0
Orbitofrontal area	0	0	**2**	0	0
Basal forebrain area	0	0	**3**	0	0
Medial and anterior thalamic nuclei	0	0	0	0	**2**
Basal ganglia	0	0	0	0	0
Hippocampus	**3**	**2**	**3**	**2**	0
Amygdala	**3**	**2**	**3**	0	0
Cerebellum	0	0	0	0	0
Left hemisphere					
Temporal pole	**2**	**3**	**2**	0	0
Superior temporal gyrus	0	0	0	0	0
Middle temporal gyrus	0	**2**	0	0	0
Inferior temporal gyrus	0	**2**	0	0	0
Fourth temporal gyrus	2	2	2	0	0
Fifth temporal gyrus	**2**	**3**	**2**	0	0
Insula	0	**2**	0	0	0
Dorsolateral frontal lobe +	0	0	0	0	0
Orbitofrontal area	0	0	0	0	0
Basal forebrain area	0	**3**	**3**	**2**	0
Medial and anterior thalamic nuclei	0	0	0	0	0
Basal ganglia	0	0	0	0	0
Hippocampus	**3**	**3**	**2**	**2**	0
Amygdala	**3**	**3**	**3**	0	0
Cerebellum	0	0	0	0	0

*0 = no damage to the structure; 1 = lesion involves <25% of the structure; 2 = lesion involves 25–75% of the structure; 3 = lesion involves >75% of the structure. + The dorsolateral frontal lobe included the motor, premotor and prefrontal areas.

Procedures

Five new procedural memory tasks were developed to measure the capacity to acquire and retain a range of perceptual–motor skills. Procedural memory was defined as improvement in performance on a perceptual–motor task over repeated trials, as reflected in increased speed and/or accuracy across trials. The design of each task was inspired by real-life situations. There are several similarities and differences among the five tasks. All of the tasks are highly structured, i.e. the goal and the means to achieve it are apparent. To complete the tasks successfully, subjects need not recall, recognize or reflect on prior experiences. The tasks differ from one another in the specific perceptual and motor demands (e.g. moving versus static stimuli; uni-manual versus bi-manual; uni-step versus multi-step routine; continuous feedback during performance versus feedback after performance; and sequential versus non-sequential). Subjects were tested individually in a quiet, well-lit room. Each subject performed each task on three different occasions: initial learning at time 1; retention at time 2 (24 h later); and retention at time 3 [the mean interval between time 1 and time 3 for the qmnesic group was 85 days (SD = 51.8) and for the comparison group was 57 days (SD = 5.3)].

Description of the experimental tasks

First task—weaving task

Description. This task involved weaving a small piece of fabric from woollen strings, using an actual weaver's loom. Each trial consisted of performing a consistent and recurrent five-step routine that required the use of both hands.

Apparatus and stimuli. The apparatus included a weaver's loom (42 cm/66 cm), a stick ('shuttle') with a string attached, and strings of a constant length (1.60 m) (Fig. 1).

Instructions and training. Each subject was provided with verbal instructions in the presence of the apparatus. The subject was asked to perform the weaving routine as quickly as possible. The routine consisted of five steps: (i) pull back the beater; (ii) press the lever on the same side of the stick; (iii) push the beater forward, while holding the lever; (iv) pass the stick through the middle of the two layers of strings; and (v) pull back the beater to press the fabric. In time 1, prior to testing, and in addition to the verbal instructions, the subject performed three practice rows while following the experimenter's instructions and feedback.

Feedback. The experimenter monitored the subject's performance and corrected any missteps.

Table 4 *Volume of the hippocampus, amygdala and temporal lobe of four anoxic subjects (Z-scores)**

Subjects	Age (years) +	Cause of anoxic event	Amygdala volume		Hippocampus volume		Hippocampus: temporal volume ratio		Temporal	
			Left	Right	Left	Right	Left	Right	Left	Right
6	43	Cardiac arrest	−1.35	0.09	−1.44	−1.45	−0.78	−0.52	−0.85	−0.96
7	49	Seizure	0.13	−0.43	**−3.52**	**−3.18**	**−4**	**−3.82**	−0.33	−1.16
8	51	Cardiac arrest	−0.94	−0.96	**−2.3**	**−2.18**	−1.28	−1.63	−1.86	−1.03
9	38	Status epilepticus	−0.77	−0.82	**−5.18**	**−3.82**	**−5.01**	**−4.72**	−1.71	0.03

*The significant *Z*-scores are in bold. + Subject's age when MRI data were acquired. Subject 7 was compared with a group of 13 women (40–59 years, mean = 50.8, SD = 7.3). Subjects 6 and 8 were compared with a group of nine men (40–59 years, mean = 47.8, SD = 5.7). Subject 9 was compared with a group of 23 women (23–47 years, mean = 32.6, SD = 7.5). The hippocampus was particularly atrophic in these anoxics. The fifth anoxic subject underwent CT imaging rather than MRI because he had a cardiac pacemaker. No abnormalities were evident on CT imaging. Volumetric analysis was not possible for this subject.

Fig. 1 Weaving loom (42 cm/66 cm).

Dependent measures. The first dependent measure was time spent to perform the routine seven times. The second dependent measure was the number of errors committed per trial.

Protocol. Each trial consisted of completing the five-step routine seven times in a row (one string per trial). On each testing day, there were four trials, with a 2 min interval. The interval was filled with a manual distractor task. The manual distractor task consisted of tying knots between strings (i.e. part of the resetting the loom procedure).

The weaving task is a bi-manual, multi-step, explicit sequential task that requires speed of accurate performance. It requires constant alternation between the left and right hand, and places demands on working memory.

Second task—geometric figures task

Description. The geometric figures task was inspired by assembly line work, particularly the type of work that involves operating with objects in motion in a conveyer belt. Each trial of the task consisted of tracing eight horizontally moving geometric figures with a stylus on a touch screen monitor.

Apparatus and stimuli. The apparatus included a touch screen monitor (Keytec 15 inch Touch Screen Monitor; Sony 110GS) and a stylus (Fig. 2). After the instructions, the subjects were oriented to the monitor where the figures appeared one at a time, and moving horizontally from left to right. The stimuli consisted of complete geometric figures that appeared and disappeared at 3.5 cm of the left and right edge of the screen, respectively. Each figure was on the screen for 25 s (average speed of 0.5 cm/s). There was no interval between the disappearance of the figure and the appearance of the next figure. The computer program continuously sampled the subject's response and compared it with the location of several pre-defined points in the figure. The number of pre-defined points ranged from 850 to 1192 per figure.

Instructions. Each subject was provided with verbal instructions in the presence of the apparatus. The subject was asked to trace over each geometric figure with a stylus as accurately as possible.

Dependent measures. The first dependent measure was distance from target (DFT), summed across all of the pre-defined points for each figure. The second variable was the number of points available for sampling. Learning was defined as a decrease in the DFT.

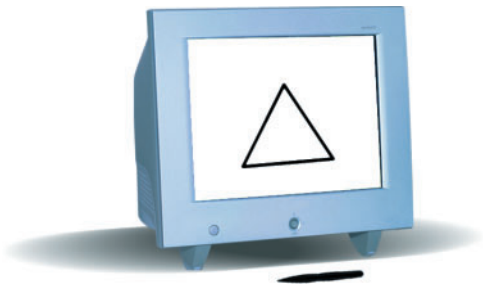

Fig. 2 Geometric figures apparatus.

Fig. 3 Control stick apparatus.

Protocol. The protocol consisted of five trials on each testing day.

The geometric figures task is a uni-manual task that requires direct visual control, ongoing mapping of visual cues and motor responses, ongoing prediction of direction and speed of the stimulus movement, and ongoing adjustment of the motor response according to visual feedback. The task requires accuracy in a time-constrained context.

Third task—control stick task

Description. The control stick task was inspired by the operation of construction and manufacturing machinery. The task involved tracking a specific sequence of eight target locations using a joystick in the reverse mode (i.e. the controlled cursor moves in the opposite direction to the joystick).

Apparatus and stimuli. The apparatus included a computer screen and a joystick. On the computer screen, there was an horizontal bar with a blue line (target) and a red line (cursor) (Fig. 3). The targets appeared one at a time. The next target only appeared following an accurate response to the prior target. The response was considered accurate within an 80 pixel distance between the two lines.

Instructions. Each subject was provided with verbal instructions in the presence of the apparatus. The subject was asked to track a blue line (target) with a red line (cursor), and press the trigger on the joystick when the two lines were matched.

Dependent measures. The first dependent measure was time to produce an accurate response, beginning with the appearance of the stimulus and ending with an accurate control stick button press response. The second dependent measure was the number of false alarms per trial.

Protocol. The protocol consisted of five repetitions of the eight target sequence without a break between sequences for a total of 40 trials on each testing day.

The control stick task is a uni-manual, implicit sequential task that requires arbitrary perceptual–motor mapping of visual cues and motor responses. The task provides ongoing visual cues and post-response feedback, and requires speed of accurate performance.

Fourth task—pouring task

Description. The pouring task was inspired by the need to handle liquids carefully in several vocational activities (e.g. food preparation and manufacturing). Each trial of the task consisted of pouring 200 ml of water from a small watering can into eight graduated cylinders, from a point at 20 cm distance above the cylinders.

Apparatus and stimuli. The apparatus included a small plastic watering can (with a spout of 7 mm diameter) and eight graduated cylinders, each of 2 cm diameter. The eight cylinders were positioned in a plastic container (60 cm × 40 cm × 30 cm) (Fig. 4). There was a barrier wire positioned 20 cm above the top of the cylinders, preventing the subjects from getting any closer. Each graduated container had an easily seen black line printed at the 25 ml level.

Instructions. Each subject was provided with verbal instructions in the presence of the apparatus. The subject was asked to fill all the graduated cylinders up to the black mark printed on each cylinder without splashing liquid, and to do it as quickly as possible.

Dependent measure. The dependent measure was the total volume of liquid poured into the eight cylinders, excluding any liquid poured above the mark. Pouring inaccuracy was penalized by disregarding the liquid poured above the black mark or outside the cylinders. This inaccurately poured liquid could not be reused, and subjects were not provided with additional liquid.

Protocol. The protocol consisted of five consecutive trials on each testing day.

The pouring task is a direct visual control task that requires ongoing mapping of visual cues and motor responses. Direct visual feedback regarding response accuracy is inherent in the task.

Fig. 4 Pouring apparatus.

Fifth task—spatial sequence task

Description. The activity of entering frequent numbers on a keyboard (e.g. data entry, alarm codes or phone numbers) inspired the design of the spatial sequence task. The task involved learning an ordered sequence of pushing five spatially distributed buttons without visual guidance.

Apparatus and stimuli. The apparatus included a computer screen and a special keyboard. The computer screen had five distributed squares, each identified by a number (1–5). The word 'start', framed in a green box, appeared on the left lower corner of the screen at the beginning of each trial. The special keyboard had five buttons (Fig. 5). The keyboard was shielded from the subject's view by an inverted U-shape cardboard box with a front opening. The spatial distributions of the squares on the screen and the buttons on the keyboard were identical. There were no changes in the spatial configuration or in the number of the squares across trials, i.e. the same sequence was used for each trial.

Instructions. Each subject was provided with verbal instructions in the presence of the apparatus. The subject was asked to press the sequence of buttons as quickly as possible, according to the order of the numbers on the squares. The subject was also instructed to perform the sequence only after the word 'start' appeared on the screen.

Feedback. At the end of each trial, the squares on the screen were coloured green or red depending upon the accuracy of the response.

Dependent measure. The dependent measure was time to perform the sequence accurately, beginning with the appearance of the stimulus and ending with the fifth button press response.

Protocol. The protocol consisted of 20 successfully performed trials on each testing day. After pushing five buttons on the keyboard, there was an inter-trial interval of 2.5 s until the word 'start' appeared again.

The spatial sequence task is a blinded, uni-manual, explicit sequential task that requires speed of accurate performance. The task provides post-response feedback.

Declarative memory of the tasks

Declarative memory for the experiment was evaluated with two memory tests, administered at time 2. The first declarative memory measure was a recognition test that required a 'yes' or 'no' answer as to whether each of a series of statements described a task that they had performed before. Each of the 40 sentences described a different task: six of them pertained to the tasks performed at time 1, and 34 were foils. The recognition questionnaire was administered orally prior to the experimental tasks for time 2, in a separate room.

Following the recognition test, the subject was escorted to the testing room and given the cued recall questionnaire. The subject

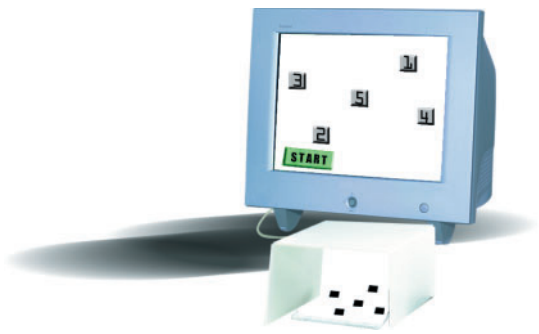

Fig. 5 Spatial sequence apparatus.

was asked to answer four open-ended questions read aloud by the examiner. These questions concern aspects of the tasks performed at time 1 (e.g. 'When you performed a task with this keyboard, what appeared on the computer screen?'). Responses were scored 0, 1 or 2, with 0 being no specific content accurately recalled, 1 being some specific content accurately recalled, and 2 being complete and accurate recall.

Results

First task—weaving task (Fig. 6)

The dependent measure was the time between initiation of the first step of the first routine and the completion of the last step of the seventh routine. Learning was defined as the difference between baseline and the last trial of time 1. Baseline was defined as time spent in the first trial of time 1.

The amnesics spent significantly more time ($t = 4.83$, $P < 0.01$) performing the task at baseline than comparison subjects. t tests for paired samples were used to assess learning of the task by each group. Both groups significantly reduced the amount of time needed to perform the task (amnesics $t = 6.58$, $P < 0.01$; comparison subjects $t = 6.17$, $P < 0.01$). A 2 × 2 ANOVA (analysis of variance) showed significant learning effects ($F = 92.85$, $P < 0.01$), significant group effects ($F = 44.41$, $P < 0.01$) and significant learning × group interaction ($F = 12.68$, $P < 0.01$). To make sure this significant learning × group interaction was not due to different baseline performances of the two groups, we performed a 2 × 2 ANOVA for repeated measures with trial 2 and trial 4 of time 1 as the levels of analysis, and baseline competency as the covariate. The analysis showed no significant learning × group interaction ($F = 0.04$, $P = 0.84$). This analysis demonstrates that when taking into account baseline performance, the amnesic and the comparison groups have similar learning curves after the second trial.

The 24 h retention was defined as the difference between baseline and the first trial of time 2. The t tests for paired samples revealed a significant retention for both groups (amnesics $t = 6.4$, $P < 0.01$; comparison subjects $t = 5.61$, $P < 0.01$). The 2 × 2 ANOVA showed significant retention effects ($F = 78.07$, $P < 0.01$), significant retention × group interaction ($F = 10.77$, $P < 0.01$), and significant group effects ($F = 40.27$; $P < 0.01$). To make sure the significant learning × group interaction was not due to different baseline performance of the two groups, we performed a 2 × 2 ANOVA for repeated measures with trial 2 of time 1 and trial 1 of time 2 as the levels of analyses, and baseline competency as the covariate. This analysis showed no significant retention × group interaction ($F = 0$, $P = 1$). This analysis demonstrates that when taking into account baseline performance, the amnesic and the comparison groups have similar retention after the second trial.

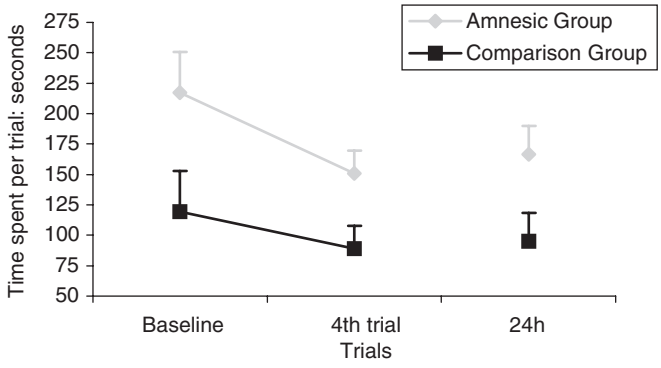

Fig. 6 Results of the weaving task.

For the comparisons between time 1 and time 3, only subjects with complete data sets for time 3 were used. At time 3, complete data were only available for nine amnesics and 13 comparison subjects. As a result of the reduction of the number of subjects in both groups, the groups were no longer matched for age and education. The comparison group was significantly younger (mean = 42.69 years, SD = 9.45, $t = 2.13$, $P = 0.05$) and more educated (mean = 18.08 years, SD = 3.45, $t = -2.2$, $P = 0.04$) than the amnesic group. There was no significant difference between groups on the number of days interval between time 1 and time 3. At this follow-up, the amnesics ($t = 3.08$, $P = 0.01$) and the comparison subjects ($t = 2.82$, $P = 0.02$) showed significant retention of the weaving skill. The 2 × 2 ANOVA demonstrated a significant retention effect ($F = 19.3$, $P < 0.01$), significant group effect ($F = 36.49$, $P < 0.01$) and significant retention × group interaction ($F = 4.94$, $P = 0.04$). To make sure that the significant learning × group interaction is not due to different baseline performance of the two groups, we performed a 2 × 2 ANOVA for repeated measures with trial 2 of time 1 and trial 1 of time 3 as the levels of analyses, and baseline competency as the covariate. This analysis showed no significant retention × group interaction ($F = 0.39$, $P = 0.54$). This analysis demonstrates that when taking into account baseline performance, the amnesic and the comparison groups have similar retention after the second trial.

Frequency of errors

At baseline, the frequency of errors ranged from 0 to 7 (mean = 3.4, SD = 2.8) for the amnesic group, and from 0 to 3 (mean = 0.48, SD = 0.82) for the comparison group. t tests for independent samples were used to compare the two groups on the number of errors committed per trial. The amnesics committed significantly more errors at baseline ($t = 3.3$, $P < 0.01$) and at the last ($t = 2.36$, $P < 0.05$) trial of time 1 than the comparison group. No significant difference in number of errors was found between groups at time 2 ($t = 2.14$, $P = 0.06$) or time 3 ($t = 2.05$, $P = 0.07$). The amnesic group reduced the number of errors from baseline to the last trial of time 1 ($t = 3.47$, $P < 0.01$), and from baseline to time 2 ($t = 2.27$, $P = 0.05$). No significant difference was found for the amnesic group between baseline and time 3. The comparison group did not show any significant reduction or increase in number of errors across trials.

Second task—geometric figures task (Fig. 7)

The dependent measure for this task was the total DFT, summed across all of the pre-defined points for each figure. Learning was defined as the difference between the DFT at the baseline and at the last trial of time 1. Baseline was defined as the DFT in the first trial of time 1.

The groups did not differ from one another on the DFT at baseline ($t = 1.3$, $P = 0.09$). *t* tests for paired samples were used to assess learning of the task by each group. Both groups demonstrated learning (amnesics $t = 3.6$, $P < 0.01$; comparison subjects $t = 3.31$, $P < 0.01$). A 2 × 2 ANOVA showed significant learning effects ($F = 20.13$, $P < 0.01$), significant group effects ($F = 4.62$, $P = 0.04$) and no significant learning × group interaction ($F = 0.62$, $P = 0.44$). An ANOVA for repeated measures, with trial 2 and trial 5 of time 1 as the levels of analysis, and baseline competency as the covariate, showed no significant learning × group interaction ($F = 0.08$, $P = 0.78$).

The 24 h retention was defined as the difference between baseline and the first trial of time 2. On *t* tests for paired samples, the retention level of the DFT reached significance for the amnesic group ($t = 3.05$, $P = 0.01$) and the comparison group ($t = 2.38$, $P = 0.03$). The 2 × 2 ANOVA showed significant retention effects ($F = 13.17$, $P < 0.01$). This test did not show significant group effects ($F = 3.61$, $P = 0.07$) nor significant retention × group interaction ($F = 1.01$, $P = 0.32$). An ANOVA for repeated measures, with trial 2 of time 1 and trial 1 of time 2 as the levels of analysis, and baseline competency as the covariate, showed no significant retention × group interaction ($F = 0.21$, $P = 0.65$).

For the comparisons between time 1 and time 3, only subjects with complete data sets for time 3 were used. At time 3, complete data were only available for nine amnesics and 10 comparison subjects. These two groups were not significantly different in terms of age, years of education and days of interval between time 1 and time 3. At time 3, the amnesics' distance from the figures was significantly smaller than at baseline ($t = 4.01$, $P < 0.01$). The comparison subjects' DFT did not differ from baseline ($t = 1.55$, $P = 0.16$). The 2 × 2 ANOVA demonstrated a significant retention effect ($F = 10.26$, $P < 0.01$), no group effects ($F = 1.92$, $P = 0.18$) and no significant retention × group interaction ($F = 0.34$, $P = 0.57$). The ANOVA for repeated measures with trial 2 of time 1 and trial 1 of time 3 as the levels of analysis, and baseline competency as the covariate, showed no significant retention × group interaction ($F = 0.69$, $P = 0.42$).

Number of points available

To address the issue of whether subjects might adopt a strategy that sacrifices completeness of tracing for accuracy, we analysed the total number of points available for sampling. The outline of each figure was divided into a number of points varying from 850 and 1192, depending on the size of the figure. If a subject goes slowly in order to increase accuracy, fewer points will be available for sampling. There were no significant differences between groups, or within groups over time in the number of points available for sampling.

Third task—control stick task (Fig. 8)

The dependent measure was time between the appearance of the target and the control stick button press response, when the cursor was aligned with the target. Only accurate responses, as defined in the procedures, were considered in this analysis. Learning was defined as the difference between baseline and the last trial of time 1. Baseline was defined as time spent in the first trial of time 1.

The amnesics spent significantly more time ($t = 2.19$, $P = 0.04$) to perform the task at baseline than comparison subjects. *t* tests for paired samples were used to assess learning of the task by each group. Both groups demonstrated learning (amnesics $t = 6.85$, $P < 0.01$; comparison subjects $t = 6.19$, $P < 0.01$). A 2 × 2 ANOVA showed significant learning effects ($F = 67.42$, $P < 0.01$), significant group effects ($F = 6.23$, $P = 0.02$) and no significant learning × group interaction ($F = 1.39$, $P = 0.25$). An ANOVA for repeated measures, with trial 2 and trial 5 time 1 as the levels of analysis, and baseline competency as the covariate, showed no significant learning × group interaction ($F = 0.13$, $P = 0.72$).

The 24 h retention was defined as the difference between baseline and the first trial of time 2. On *t* tests for paired samples, the retention level nearly reached significance for both the

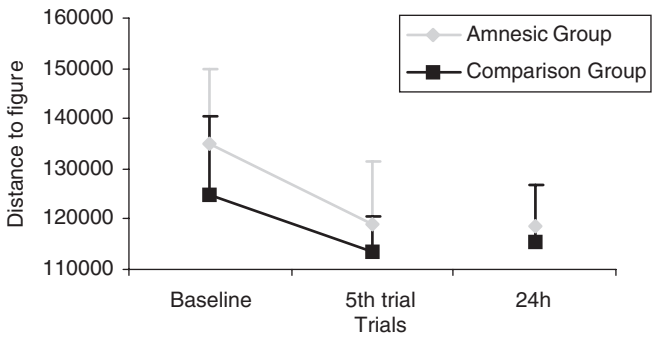

Fig. 7 Results of the geometric figures task.

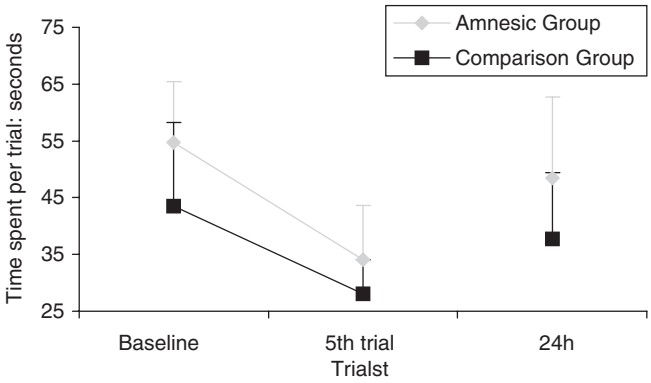

Fig. 8 Results of the control stick task.

comparison group ($t = 2.07$, $P = 0.05$) and the amnesic group ($t = 2.1$, $P = 0.06$). The 2 × 2 ANOVA showed significant retention effects ($F = 6.2$, $P = 0.02$) and group effects ($F = 6.68$, $P = 0.01$), and no significant retention × group interaction ($F = 0.01$, $P = 0.93$). An ANOVA for repeated measures, with trial 2 of time 1 and trial 1 of time 2 as the levels of analysis, and baseline competency as the covariate, showed no significant retention × group interaction ($F = 2.87$, $P = 0.1$).

For the comparisons between time 1 and time 3, only subjects with complete data sets for time 3 were used. At time 3, complete data were only available for 10 amnesics and 16 comparison subjects. As a result of the reduction of the number of subjects in the comparison group, the groups were no longer matched for age and education. There was a tendency for the comparison group to be younger (mean = 42.4 years; SD = 9.1) than the amnesic group ($t = 2.02$, $P = 0.05$). The comparison group was significantly more educated than the amnesic group ($t = -2.47$, $P = 0.02$). There was no significant difference between groups on the number of days interval between time 1 and time 3. At time 3, the amnesics did not show a significant difference from baseline ($t = 1.28$, $P = 0.23$). The comparison subjects demonstrated a significant retention of the skill ($t = 2.33$, $P = 0.03$). The 2 × 2 ANOVA demonstrated a significant retention effect ($F = 5.69$, $P = 0.02$), nearly significant group effects ($F = 4.34$, $P = 0.05$) and no significant retention × group interaction ($F = 0.71$, $P = 0.41$). An ANOVA for repeated measures, with trial 2 of time 1 and trial 1 of time 3 as the levels of analysis, and baseline competency as the covariate, showed significant retention × group interaction ($F = 6.71$, $P = 0.02$).

False alarms

The overall rate of false alarms per trial ranged between zero and eight in both amnesics and comparison groups. There were no trial × false alarm effects for either group, nor any group × false alarm interaction.

Fourth task—pouring task (Fig. 9)

The total volume of water poured within the pre-defined limits, as described in the procedures, was the dependent measure. Learning was defined as the difference between the baseline and the last trial of time 1. Baseline was defined as the total volume poured within the pre-defined limits in the first trial of time 1.

The amnesics poured a significantly smaller amount of water ($t = -3.56$, $P < 0.01$) than comparison subjects on the first trial of time 1. *t* tests for paired samples were used to assess learning of the task by each group. Both groups significantly increased the volume of water successfully poured (amnesics $t = -2.79$, $P = 0.02$; comparison subjects $t = -4.5$, $P < 0.01$). A 2 × 2 ANOVA showed significant learning effects ($F = 20.14$, $P < 0.01$), significant group effects ($F = 20.69$, $P < 0.01$) and no significant learning × group interaction ($F = 0.38$, $P = 0.54$). An ANOVA for repeated measures, with trial 2 and trial 5 of time 1 as the levels of analysis, and baseline competency as the covariate, showed no significant learning × group interaction ($F = 0.25$, $P = 0.62$).

As opposed to the comparison group ($t = -2.38$, $P = 0.03$), the amnesic group did not show a significant difference ($t = -0.3$, $P = 0.77$) between baseline and the first trial of time 2. The 2 × 2 ANOVA did not show significant retention effects ($F = 2.45$, $P = 0.13$) nor retention × group interaction ($F = 1.55$, $P = 0.22$). There were significant group effects ($F = 22.75$, $P < 0.01$). An ANOVA for repeated measures, with trial 2 of time 1 and trial 1 of time 2 as the levels of analysis, and baseline competency as the covariate, showed no significant retention × group interaction ($F = 1.53$, $P = 0.22$).

For the comparisons between time 1 and time 3, only subjects with complete data sets for time 3 were used. At time 3, complete data were only available for 10 amnesics and 14 comparison subjects. As a result of the reduction of the number of subjects in the comparison group, the groups were no longer matched for education. The comparison group had significantly more years of education (mean = 18 years; SD = 3.3; $t = -2.41$, $P = 0.02$) than the amnesic group. The two groups were not significantly different in terms of age nor on the number of days interval between time 1 and time 3. At time 3, neither the amnesics ($t = 0.35$, $P = 0.74$) nor the comparison subjects ($t = -1.93$, $P = 0.08$) showed a significant difference from baseline. An ANOVA for repeated measures, with trial 2 of time 1 and trial 1 of time 3 as the levels of analysis, and baseline competency as the covariate, showed no significant retention × group interaction ($F = 0.52$, $P = 0.48$).

Fifth task—spatial sequence task (Fig. 10)

The dependent measure was the time between the appearance of the word 'start' and the fifth button press response. Learning was defined as the difference in speed between baseline performance and the last trial of time 1. Baseline was defined as time spent in the first trial of time 1.

The groups did not differ from one another in the time spent to perform the task at baseline ($t = 0.94$, $P = 0.35$). Only trials performed without error were considered in this analysis. One amnesic and one comparison subject were not able to perform

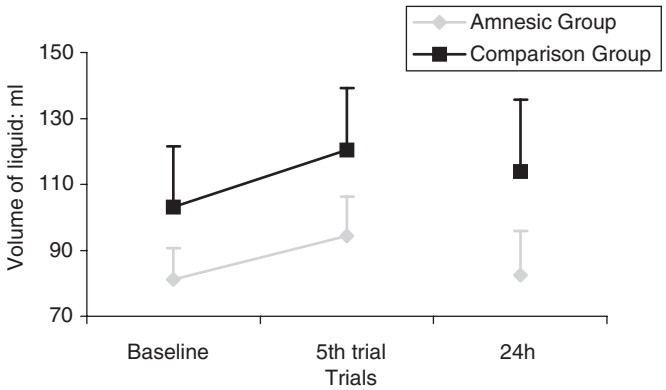

Fig. 9 Results of the pouring task.

a successful trial after 20 consecutive trials. The task was discontinued at that point. *t* tests for paired samples were used to assess learning of the task by each group. Significant learning was demonstrated by the comparison subjects (t = 7.02, $P < 0.01$) as well as the amnesics (t = 2.46, P = 0.04). The 2 × 2 ANOVA showed a significant learning effect (F = 34.98, $P < 0.01$). No significant learning × group interaction ($F = 0.41$, $P = 0.53$) nor a significant group effect ($F = 3.56$, P = 0.07) were found. An ANOVA for repeated measures, with trial 2 and trial 20 of time 1 as the levels of analysis, and baseline competency as the covariate, showed no significant learning × group interaction (F = 3.45, P = 0.07).

Neither group demonstrated retention of their task at time 2 or time 3. There was no significant difference between baseline performance and performance on the first trial of time 2 and 3, in either speed or number of errors.

For the comparisons between time 1 and time 3, only subjects with complete data sets for time 3 were used. At time 3, complete data were only available for nine amnesics and 12 comparison subjects. As a result of the reduction of the number of subjects, the groups were no longer matched for age. The comparison group was significantly younger (mean = 40.83 years; SD = 8.64; t = 2.67, P = 0.01) than the amnesic group. The number of years of education and number of days interval between time 1 and time 3 did not differ significantly. An ANOVA for repeated measures, with trial 2 of time 1 as the first level of analyses, and baseline competency as the covariate, showed no significant retention × group interaction at time 2 (F = 0.27, P = 0.6) or time 3 (F = 0.19, P = 0.67).

Outliers

We reran the statistical analyses after excluding outlying data points identified with stem-and-leaf plots. In general, the results of these analyses did not alter the key findings. Specifically, the two groups did not significantly differ on their learning curves or retention results for any of the tasks. Only one significant retention × group interaction was found; this was for the geometric figures task at time 3. This difference appears to be due to the reduced number of data points available after excluding the outlying points, in that the comparison group was reduced to only five subjects at time 3 for this task.

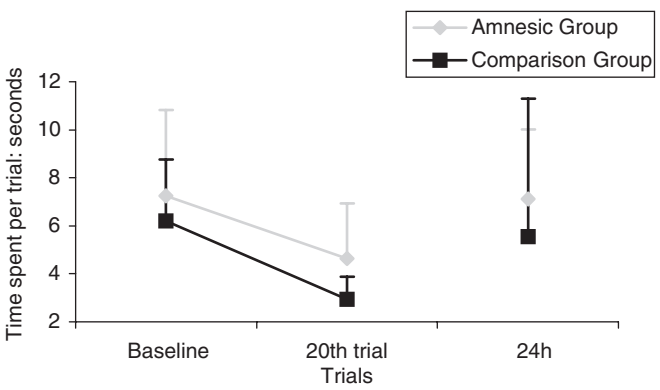

Fig. 10 Results of the spatial sequence task.

Age and education

Multiple regression analyses revealed that age and education were not significant predictors of learning ($F = 0.18$, $P = 0.32$), retention at time 2 ($F = 0.02$, $P = 1$) nor retention at time 3 (F = 0.99, P = 0.39) of the weaving task. After adjusting for these demographic factors, the independent variable group was a good predictor of learning (F = 2.98, P = 0.047) and retention at time 2 ($F = 3.54$, $P = 0.03$), and not a good predictor at time 3 (F = 1.58, P = 0.23).

Multiple regression analyses revealed that age and education were not significant predictors of learning, retention at time 2, nor retention at time 3 of the geometric figures task, control stick task and spatial sequence task. After adjusting for these factors, the independent variable group was not a good predictor of learning, retention at time 2 nor retention at time 3 of any of the tasks.

The fact that the groups were not perfectly matched for age and education raised concerns regarding the interpretation of the results at time 3. We reran the analyses for time 1 and time 2 with only those subjects who completed the protocol at time 3. The results were largely consistent with those previously presented, i.e. the groups' learning curves at time 1 continued to not differ for all tasks, and no significant retention × group interaction was found except for the pouring task (Table 5).

Effects of amnesia aetiology on performance

The amnesic group encompassed three separate aetiologies responsible for the neural damage, which raised the question of different learning patterns depending on the aetiology of the damage. In order to answer this question, the amnesic group was subdivided further into three groups: an HSE group, an anoxia group and a stroke group.

We found a significant interaction between aetiology and learning ($F = 5.98$, $P = 0.03$) and no significant group effect on learning ($F = 0.7$, $P = 0.53$) of the weaving task. When we used the ANOVA for repeated measures with trial 2 of time 1 as the first level of analyses, and baseline competency as the covariate, the analyses showed no significant learning × aetiology effect.

When we analysed only the HSE group and the anoxia group, the interaction between aetiology and learning of the weaving task was nearly significant (F = 4.12, P = 0.08), and again no significant aetiology effect (F = 0.12, P = 0.74) was found on learning the weaving task. When we used the ANOVA for repeated measures with trial 2 of time 1 as the first level of analyses, and baseline competency as the covariate, the analyses showed no significant learning × aetiology effect.

On tasks 2, 3, 4 and 5, no aetiology × learning interaction nor aetiology effect were found on the 2 × 2 ANOVA analyses.

Table 5 *Learning and retention of both groups on the experimental tasks*

Task	Baseline vs. last trial of Time 1					Baseline vs. 1st trial of Time 2					Baseline vs. 1st trial of Time 3				
	Amnesics[1]	Comparison subjects 1	Learning effects[2]	Learning by group effects[2]	Group effects[2]	Amnesics[1]	Comparison subjects 1	Retention effects[2]	Retention by group effects[2]	Group effects[2]	Amnesics[1]	Comparison subjects 1	Retention effects[2]	Retention by group effects[2]	Group effects[2]
Weaving	**6.58****	**6.17****	**92.85****	**12.68****	**44.41****	**6.4****	**5.61****	**78.07****	**10.78****	**40.27****	**3.08***	**2.82***	**19.3****	**4.94***	**36.49****
Geometric figures	**3.6****	**3.31****	**20.13****	0.62	**4.62***	**3.05***	**2.38***	**13.17****	1.01	3.61	**4.01****	1.55	**10.16****	0.34	1.92
Control stick	**6.85****	**6.19****	**67.42****	1.39	**6.23***	**2.1***	**2.07***	**6.2***	0.01	**6.68***	1.28	**2.33***	**5.69***	0.71	4.34
Pouring	**−2.79***	**−4.5****	**20.14****	0.38	**20.69****	−0.3	**−2.38***	2.45	1.55	**22.75****	0.35	−1.93	0.98	2.3	**19.27****
Spatial sequence	**2.46***	**7.02****	**34.98****	0.41	3.56	0.11	0.54	0.13	0.06	1.2	0.63	0.45	0.48	0	0.58

[1]*t* tests for paired samples (*t* values). [2]2 × 2 ANOVA (*F* values). The significant *t* or *F* values are in bold. $^{**}P < 0.01$; $^{*}P < 0.05$.

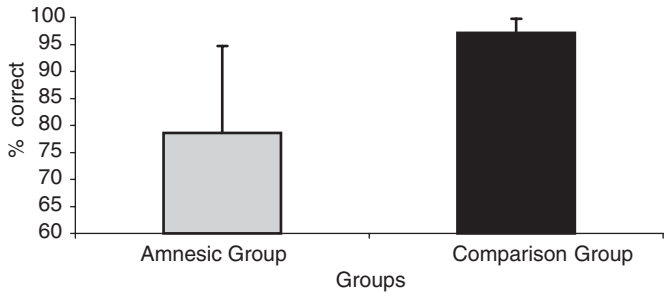

Fig. 11 Results of the recognition test.

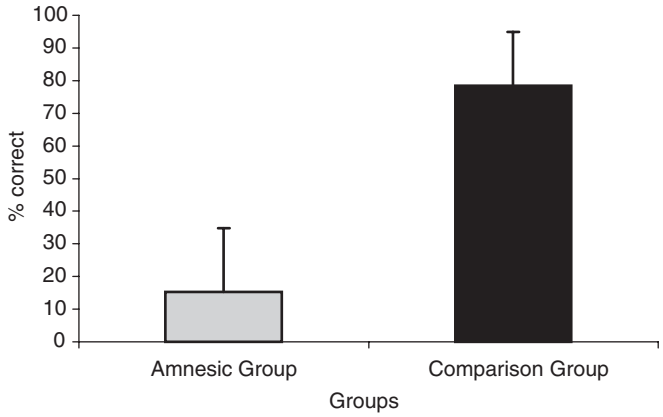

Fig. 12 Results of the cued recall questionnaire test.

Declarative memory for the experimental tasks

t tests for independent samples were used to compare the two groups on the declarative memory tests for the experimental tasks (recognition test and cued recall test). In the recognition test, the amnesic group (mean = 78.6%, SD = 16.11) also performed worse than the comparison group (mean = 97.1%, SD = 2.67) ($t = 3.43$, $P < 0.01$). The amnesic group (mean = 15.28%; SD = 19.54) performed worse than the comparison group (mean = 78.5%, SD = 16.35) on the recall questionnaire ($t = 9.45$, $P < 0.01$). Three amnesics were not able to recall any explicit information about the tasks. The amnesics' declarative memory for the tasks performed in the previous session was significantly impaired.

Motor skills

The performances of the amnesics on the five perceptual–motor tasks were examined relative to their performance on a non-memory visuomotor coordination test—the Grooved Pegboard Test. No significant correlation was found between the Grooved Pegboard (raw) data (performed with the dominant hand) and the baseline performances on tasks 2, 3, 4 and 5. The performances on the weaving task were significantly correlated with the Grooved Pegboard with both the dominant (Pearson's correlation = 0.655, $P = 0.04$) and the non-dominant hands (Pearson's correlation = 0.67, $P = 0.03$).

Discussion

These findings demonstrate that preserved perceptual–motor skill learning in amnesia is not a restricted laboratory phenomenon. Rather, the ability of amnesic subjects to learn and retain a diverse set of new procedural skills with clear translation to real-world activities indicates that this is a robust phenomenon that probably is relevant to many aspects of daily living. Our results also help refine our understanding of the dissociation between declarative and procedural memory systems in the human brain.

Although amnesic subjects showed significant improvement for each of the five ecologically relevant procedural memory tasks studied, the findings obtained from the weaving task were particularly interesting. Amnesic subjects demonstrated more improvement across trials (at time 1) and better delayed retention (at times 2 and 3) than the non-amnesic subjects. The significant differences on the learning and retention curves may be due to the baseline differences between groups. When we used the second trial (instead of the first trial) as the first level of analysis and controlled for baseline, the differences disappeared.

Within the amnesic group, the HSE subgroup tended to show more improvement on the weaving task than the anoxic subgroup. With respect to this difference in performance, it is interesting to note that the HSE subjects had substantially more extensive temporal lesions than the anoxic subjects. While lesions in the anoxic subjects were limited to the hippocampus, all four HSE subjects had damage to the hippocampus, and three of the four had damage to the temporal poles, the amygdala, and the fourth and fifth temporal gyri (including entorhinal, parahippocampal and perirhinal cortices). We know that combined lesions of the hippocampus and surrounding areas (i.e. the parahippocampal region and the amygdala) tend to cause more severe declarative memory deficits than do lesions restricted to the hippocampus proper (for a review see Eichenbaum and Cohen, 2001). Therefore, the tendency for the HSE subgroup to perform better than the anoxic subjects on the weaving task raises the possibility that extensive bilateral lesions of the medial temporal region may actually 'facilitate' certain types of procedural learning by freeing them from declarative interference. This would be consistent with recent findings suggesting that there is competition between memory systems (Packard *et al.*, 1989; Poldrack *et al.*, 2001; for a review see Poldrack and Packard, 2003).

A significant difference in performance between groups was seen only in the weaving task. This task differs from the others in several ways. First, this task was completely novel to the subjects. No subject had prior experience operating a weaving loom, but most had some prior experience with apparatus such as a joystick, a watering can and a key pad. Secondly, the weaving task comprised the most complex routine of the five tasks, incorporating continuous ongoing feedback from the experimenter. Thirdly, it required the coordinated use of both hands. Further research will be necessary to isolate the task components that influence performance, and their relationship to different neuroanatomical subsystems.

In the weaving task, an unblinded examiner provided ongoing verbal correction of errors, raising the possibility of experimenter bias. We cannot eliminate any possibility of bias in these situations, given that amnesia of this level of severity is quite obvious. To help address this issue, we analysed the frequency of errors committed by the comparison subjects and amnesic subjects on this task. The finding that the subjects in the amnesic group committed significantly more errors than did the comparison group, and that most of the comparison group performance was errorless, argues against any bias in favour of the amnesic subjects.

At 24 h and 2 months retention periods, both amnesic and comparison groups showed remarkable retention of the weaving and geometric figures tasks, while on the spatial sequence task neither group showed any retention of the skill. The retention results of the amnesic group and of the comparison group on the control stick and pouring tasks were less clear. However, no significant difference was found between groups on the geometric figures, control stick, pouring and spatial sequence tasks at time 2 and 3.

The results from the delayed retention phase of the experiment were less consistent across tasks than were the findings from the initial learning phase. Although the amnesic subjects demonstrated learning on all tasks, the delayed retention of the weaving skill and the ability to trace moving geometric figures contrasted with limited retention of the remaining skills. The amount of practice and the practice schedule may influence learning and retention of perceptual–motor skills (Schmidt and Lee, 1999). More practice and more spaced practice at time 1 might have resulted in better learning and retention of the skills.

The phenomenon of competing interference between tasks may have affected the consolidation of the motor skills, and consequently the retention results. It has been shown that consolidation of a motor skill can be disrupted if a second motor task is learned immediately after the first, and the critical time window beyond which little or no interference is found from a competing task is ~4–5 h (Brashers-Krug *et al*., 1996; Shadmehr and Brashers-Krug, 1997). In our study, each perceptual–motor task was administered immediately after the previous one. According to the order used for testing, the spatial sequence task was the first skill to be learned, and the weaving task was the last. These two tasks presented the worst and the best retention results, respectively.

The diversity of retention patterns also raises the possibility that different non-declarative memory systems may subserve learning and retention of different perceptual–motor skills. It has been demonstrated that different neural structures may be involved in perceptual–motor tasks that require arbitrary sensorimotor mapping versus direct visual integration of visual cues and motor responses (e.g. Sanes *et al*., 1990; Agostino *et al*., 1996; Timmann *et al*., 1996); use ongoing external visual feedback as a cue for motor programming versus present perceptual feedback as a predictor for motor programming (Gabrieli *et al*., 1997); or require learning of motor sequences versus motor adaptation (Doyon *et al*., 2003).

At time 3, the groups were no longer matched for age and/or education. Demographic characteristics of the subjects did not predict learning (at time 1) or retention (times 2 and 3) of any of the tasks. Additional statistical analyses with non-matching subgroups (i.e. composed of subjects with available data at time 3) demonstrated that the results (at time 1 and time 2) were comparable with those of the initial matched groups. The between-group differences in demographic factors, when they did occur, were always in the direction of being biased against our hypotheses, i.e. the comparison group was younger and more educated than the amnesic group.

The understanding of procedural learning in the normal population and in other brain-damaged populations is still very incomplete. It is our intent to examine in future studies issues of transfer, conflict, dual task and generalizability of learning in both normal and brain-damaged populations, with this new set of tasks.

Finally, our findings have significant implications for neurorehabilitation. Memory impairments are among the most common consequences of injury to the brain, and return to work is one of the most important rehabilitation goals of patients with brain injury. Unfortunately, treatment options for memory impairments remain limited. Although there have been a few attempts to use non-declarative methods in clinical rehabilitation settings with amnesic patients (e.g. Glisky *et al*., 1986; Zanetti *et al*., 1997; Goldstein *et al*., 1998; Suhr *et al*., 1999), this approach remains largely unexplored.

Our results substantially extend the known scope of preserved procedural memory capacity in amnesia, and make clear that this preserved ability encompasses the acquisition of skills relevant to real-world activities. They suggest that procedural memory training should be an integral component of comprehensive rehabilitation programmes for patients with memory impairments. It is worthwhile to teach even complex procedural tasks to amnesic patients, since they are generally able to perform them and derive immediate satisfaction from the achievement. At the same time, procedural memory tasks relevant to real-world activities may facilitate the integration of amnesic subjects into the workplace, provided that a sheltered environment to compensate for impaired declarative recall can be established.

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