Can amnesic patients learn without awareness?
New evidence comparing deterministic and probabilistic sequence learning

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Abstract
Can associative learning take place without awareness? We explore this issue in a sequence learning paradigm with amnesic and control participants, who were simply asked to react to one of four possible stimuli on each trial. Unknown to them, successive stimuli occurred in a sequence. We manipulated the extent to which stimuli followed the sequence in a deterministic manner (noiseless condition) or only probabilistically (noisy condition). Through this paradigm, we aimed at addressing two central issues: first, we asked whether sequence learning takes place in either condition with amnesic patients. Second, we asked whether this learning takes place without awareness. To answer this second question, participants were asked to perform a subsequent sequence generation task under inclusion and exclusion conditions, as well as a recognition task. Reaction times results show that amnesic patients learned the sequence only in the deterministic condition. However, they failed to be able to reproduce the sequence in the generation task. In contrast, we found learning for both sequence structures in control participants, but only control participants exposed to a deterministic sequence were successful in performing the generation task, thus suggesting that the acquired knowledge can be used consciously in this condition. Neither amnesic nor control participants showed correct old/new judgments in the recognition task. The results strengthen the claim that implicit learning is at least partly spared in amnesia, and the role of contextual information available for learning is discussed.

Keywords: Amnesia; Sequence learning; Awareness

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1. Introduction
Whether associative learning can take place without awareness is a central issue for the cognitive neurosciences. Amnesic patients, whose explicit memory is severely impaired, provide us with a unique opportunity to explore this issue. In this paper, we explored the extent to which such patients are able to learn about the regularities contained in deterministic or probabilistic sequences of events presented visually in the context of a choice reaction time task – a robust paradigm known as sequence learning, and in which incidental learning has been abundantly documented, both with normal participants (Nissen & Bullemer, 1987; Cleeremans & McClelland, 1991; Reed & Johnson, 1994) as well as with special populations (Nissen & Bullemer, 1987; Reber & Squire, 1998). In the following, we first provide an overview of the contribution that studies of amnesic patients can bring in the debate concerning the possibility of learning without awareness. Next, we focus on the sequence learning paradigm itself, and finally on the comparison between deterministic and probabilistic sequence learning.

1.1. Amnesic patients studies: evidence for learning without awareness?

The possibility that learning may occur without awareness remains a controversial issue (Shanks & St. John, 1994; Cleeremans & Jiménez, 2002; Perruchet & Vinter, 2002). The most compelling evidence for the existence of two distinct and independent systems has been accumulated in studies with amnesic patients. Indeed, while their declarative or explicit memory is poor, amnesic patients exhibit intact learning in various tasks of non-declarative memory, such as eye blink con-
studies performed with amnesic patients suggest that they can learn a repeating sequence while remaining unable to consciously recognize it (Curran, 1997; Reber & Squire, 1998). However, we do not know whether amnesic patients can also learn probabilistic (or noisy) sequences, and we only have little information about the implicit or explicit nature of the knowledge acquired during the SRT task. In a typical sequence learning experiment, participants first perform a serial reaction time task (Nissen & Bullemer, 1987), in which they are asked to react to each element of a sequentially structured and typically visual sequence of events. On each trial, they see a stimulus appear at one of several locations on a computer screen and are asked to press on the corresponding key as fast and as accurately as possible. Unknown to them, the sequence of successive stimuli follows a repetitive pattern. Reaction times (RTs) tend to decrease progressively during practice but to increase dramatically when the repetitive pattern is modified in any of several ways (Reed & Johnson, 1994; Shanks & Johnson, 1999; Destrebecqz & Cleeremans, 2001). This finding suggests that healthy participants learn the pattern and tend to respond on the basis of their knowledge of the sequence. However, the extent to which the acquired knowledge is implicit or explicit remains controversial.

To address this issue, and based on the central assumption that any task will always tend to involve both implicit and explicit influences, Destrebecqz and Cleeremans (2001) adapted the Process Dissociation Procedure (Jacoby, 1991) to sequence learning. To probe participants’ knowledge of the sequential material after training on the SRT task was completed, they used a so-called “free generation” task – previously shown to be a very sensitive test of sequence knowledge (Perruchet & Amorim, 1992).

After performing the SRT task, participants were informed about the presence of a sequence in the task they had just performed and were required to freely generate a sequence under inclusion and exclusion instructions. Under inclusion instructions, participants were asked to reproduce the sequence as much as possible. This is a facilitation task because both explicit and implicit knowledge may help participants generate the sequence on which they have been trained. Under exclusion instructions, in contrast, participants were instructed to generate a different sequence, and to avoid reproducing the training sequence. This is an interference task because explicit and implicit knowledge of the repetitive pattern act in opposition: only explicit knowledge can help participants reproduce the repetitive pattern to improve their performance. If the repetitive pattern is nevertheless produced under exclusion instructions, such responses can only be interpreted as reflecting the implicit influence of learned sequential regularities. Finally, participants perform a recognition task on fragments of the training sequence (Perruchet & Amorim, 1992) to assess the extent to which sequence knowledge is available to consciousness. By using this methodology, Destrebecqz and Cleeremans (2001) showed that sequence learning could be implicit with healthy participants, under some specific temporal conditions (i.e., when they were denied preparation to the next stimulus – that is, when the interval that separates participants’ responses and the onset of the next stimulus was eliminated. However, for a failure to replicate, see Shanks, Wilkinson, & Channon, 2003; Wilkinson & Shanks, 2004).
In the present experiment, we sought to adapt Destrebecqz and Cleeremans (2001) methodology to the study of amnesic participants. In addition, we compared learning under two conditions defined by the nature of the sequential material. The sequential material could either consist of a repeating deterministic sequence (noiseless condition) or of a comparable probabilistic sequence (noisy condition). We describe and motivate these conditions in the next section.

1.3. Deterministic and probabilistic sequence learning

Typically, the structure of the repetitive pattern used in the SRT task is either deterministic (noiseless) or probabilistic (noisy). Under deterministic conditions, a fixed sequence of stimulus positions is repeated all through the SRT task, except during a transfer block in which a different sequence is presented. In most experiments, the fixed sequence and the transfer sequence are composed entirely of second-order conditionals (SOC, Reed & Johnson, 1994), in which (1) every location that the target can visit is fully determined by the previous two locations and (2) knowing the previous location alone provides only limited information regarding the next location. Early studies revealed that RTs tend to decrease with practice and to increase during the transfer phase, leading authors to conclude that participants exhibit sequence-specific learning. The major limitation of using fixed sequences of events in the context of implicit learning research is that participants tend to learn parts of the repeated sequence explicitly (Perruchet & Amorin, 1992; Cleeremans & Jiménez, 1998). This led some authors to introduce noise in the repeated sequence so as to make conscious detection of sequential structure much more difficult. Cleeremans and McClelland (1991) first introduced such sequences by using material generated based on a probabilistic finite-state grammar. More recently, Schvaneveldt and Gomez (1998) developed a probabilistic version of deterministic SOC sequences by manipulating the conditional probabilities of transitions. For instance, the sequence fragment 1–4 could be followed by Location 3 with a probability of 0.90, and by Location 2 with a probability of 0.10 (whereas in the deterministic SOC sequence, 1–4 was followed by Location 3 with a probability of 1.00). Schvaneveldt and Gomez showed that healthy participants were able to learn about the probabilistic structure of sequences, as shown by lower error rates and faster RTs to highly probable as compared to less probable transitions.

Comparing deterministic and probabilistic material is interesting both in healthy participants and in amnesic patients. Indeed, we assume that the noiseless and repeating character of the deterministic sequence makes it possible for healthy participants to acquire more explicit knowledge than in under probabilistic conditions. This knowledge can be subsequently assessed using direct measures such as generation and recognition tasks. The only experiments using the same probabilistic sequences as Schvaneveldt and Gomez and a subsequent recognition task noted a learning effect with healthy participants, and showed that the participants were able to recognize 6-elements sequences from the 12-elements training sequence (Shanks et al., 2003, experiment 3).

Moreover, if we assume that probabilistic sequences lead amnesic patients to acquire knowledge that is less available to consciousness than when learning deterministic sequences, we may wonder whether they would still be able to exhibit sequence learning effects during the SRT task. Probabilistic sequences (Schvaneveldt & Gomez, 1998) offer the possibility of examining anticipation errors (i.e., when a response that is appropriate for a highly probable transition is produced after a less probable transition), which would be particularly informative about the nature of what is learned by amnesic patients. We stated that under deterministic sequence learning conditions, previous experiments using SOC sequences with amnesic patients had revealed significant learning effects (Reber & Squire, 1994, 1998; Curran, 1997), although no explicit recognition of the repeated pattern was found in the amnesic groups, in contrast to the control groups (Reber & Squire, 1994, 1998).

This dissociation led authors to consider that learning in this situation was implicit in amnesic patients. Only two studies using different types of probabilistic material have been performed with amnesic patients. First, Cleeremans (1993, Chapter 4) reported on an amnesic patient exposed to a probabilistic sequence generated from an artificial grammar and found a learning effect similar to that of the control participants. Second, Curran (1997) showed that amnesic patients were able to learn “FOC” sequences (“first-order conditionals”, in which elementary associations between adjacent stimuli may be predicted: each element is followed by another element in a 67/33 ratio). However, no probabilistic sequence learning study has investigated performance in amnesic patients with the Schvaneveldt and Gomez (1998) methodology.

To sum up, in this experiment, severely memory impaired patients and control participants first performed an SRT task (with a deterministic or probabilistic sequence) and then two direct tasks (generation and recognition) to assess the extent to which knowledge acquired during the SRT task is available to conscious awareness. This study was thus aimed at addressing two central questions. First, we wondered whether learning is preserved in amnesia, in either deterministic or probabilistic conditions. Previous studies (Reber & Squire, 1994, 1998; Curran, 1997) suggest that amnesic patients exhibit implicit learning under deterministic conditions, but to the best of our knowledge, no study has compared deterministic and probabilistic sequence learning in amnesia. Second, if amnesic patients acquire sequential knowledge during the SRT task, we wondered whether this knowledge is available to consciousness. The methodology proposed by Destrebecqz and Cleeremans (2001), with a generation task following inclusion and exclusion instructions and a recognition task, should allow us to obtain more information concerning this second issue.

2. Method

2.1. Subjects

Six individuals with anterograde amnesia and 24 matched control participants took part in the study. They were all unfamiliar with the SRT task. Amnesic...
Table 1: Demographic data, diagnosis informations and results of the amnesic patients in the Raven’s Progressive Matrices (PM38), the Spans and the Executive Functioning tasks

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Months since diagnosis</th>
<th>PM38</th>
<th>Span</th>
<th>Executive Functioning</th>
</tr>
</thead>
<tbody>
<tr>
<td>JMD</td>
<td>49</td>
<td>M</td>
<td>Male</td>
<td>9</td>
<td>105</td>
<td>60</td>
<td>275</td>
</tr>
<tr>
<td>GR</td>
<td>43</td>
<td>M</td>
<td>Male</td>
<td>15</td>
<td>90</td>
<td>60</td>
<td>240</td>
</tr>
</tbody>
</table>

Note: "ED", years of formal education. In the Stroop test; "C", number of self-corrected errors and "NC", number of uncorrected errors. AC did not perform the Stroop test because of color-blind. In the Hayling test, mean performance was given their approval orally or signed statements of informed consent prior to participation. All participants received oral information about the experiment and were screened via self-reports for absence of any existing neurological or psychiatric condition and for absence of any medication that could affect cognition. All participants showed global intellectual efficiency and verbal and spatial spans within the normal range. To measure these attentional and cognitive capacities, all patients performed the Stroop test and the verbal inhibition Hayling test. Results presented in Table 1 suggest that the executive functioning of some patients was not completely intact (see GR in the Stroop task, or HV, GR or JMD in the Hayling test). However, clinical observations revealed that these patients were forgetting the instructions during the task itself, so that these deficits did not interfere with the generation performance of these patients. Lastly, measures of attentional capacities were taken during the SRT task itself (described below) and revealed that in some of the patients, any attentional deficit interfered with the experiment.

To assess their degree of amnesia, all patients were given various tests of immediate and delayed recall, such as the “Grober and Buschke’s Test” (Grober & Buschke, 1987) for verbal learning and “Test de la Ruche” (Violon & Wijns, 1984) for visuo-spatial learning or “Doors Recognition Test” (Baddeley, Emslie & Nimon-Moore, 1994) for pictorial memory. Results are presented in Table 2. The Grober and Buschke’s Test is a verbal learning task in which 16 foils-bidimensional words were presented to the patients, with semantic encoding being missing for four words at a time. The “recall phase” of the 16 words included three trials. Each trial consisted of an extended period of free recall (“free recall 1–2–3”), up to 2 min, immediately followed by cued recall for those items not retrieved at free recall (the category cue of each of these was verbally provided). Patients also performed a recognition task amongst 48 words and a delayed recall (after a 20 min delay). The “Test de la Ruche” was a visuo-spatial learning task in which patients have to learn the position of 10 black boxes in a 4×4 boxes-matrix. The learning phase included five trials (“Recall 1–2–3–4–5”). In the “Recognition phase”, four matrices were presented to the patients who had to recognize the one they had to learn. A "Delayed Recall phase" occurred after a 10min delay. The “Doors Recognition Test” is a visual recognition task in which patients had to watch 24 door pictures and then to recognize them amongst other door pictures. Results presented in Table 2 show the number of positions correctly recalled or recognized in the “Test de la Ruche”, and the number of pictures correctly recognized in the “Doors Recognition Test”. Table 2 shows that all patients exhibited recall and recognition performance on the verbal learning task well below two standard deviations under the controls’ mean performance, as well as on the visual memory measurements. We also checked that patients did not have visual impairments preventing them from perceiving precisely the whole screen.
Recognition False

"Test de la Ruche"

Table 2

<table>
<thead>
<tr>
<th>Patient</th>
<th>Recall</th>
<th>Cued Recall</th>
<th>Free recall</th>
<th>Delayed Recollection</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. V.</td>
<td>8/16</td>
<td>7/16</td>
<td>8/24</td>
<td>9/24</td>
</tr>
<tr>
<td>B. C.</td>
<td>7/16</td>
<td>6/16</td>
<td>6/24</td>
<td>7/24</td>
</tr>
</tbody>
</table>

Note: "Recall" scores were determined by the number of standard deviations from the mean of words correctly evoked on the three successive trials. "Cued Recall" scores were determined by the number of words correctly evoked at cued recall on the three successive trials. Normative data with age and educational level come from van der Linden et al. (2004).

2.2. Procedure

The first part of the experiment consisted of a serial reaction time task. After this task, participants performed two free generation tasks (one under "inclusion" instructions and one under "exclusion" instructions), a serial recall task, a transfer task, and a recognition task.

During the SRT task (Nissen & Bullemer, 1987), a stimulus appeared on each trial at one of four possible screen locations arranged horizontally on a computer screen. Participants were instructed to respond as fast and as accurately as possible by pressing one of four corresponding keys organized in a 2 × 2 grid. The target stimulus appeared on one of the four locations, and there was no repetition of the same stimulus location on different trials. The next stimulus appeared after a 250 ms interval. Erroneous responses were recorded as participants by means of a tone. Participants did not know how many stimuli to expect, nor did they know whether or not the target stimulus had been presented during the previous trial. The order of trials was different for each participant in order to ensure that the participants were not biased by their previous experience.

2.2.1. Deterministic condition

The experiment consisted of 18 experimental blocks of 96 trials for a total of 1728 trials. Each block consisted of eight repetitions of the sequence. Block 16 was the transfer block: the training sequence (grammatical trials) was replaced by the transfer sequence (non-grammatical trials). Thus, participants trained on SOC1 during the first 15 blocks were exposed to SOC2 during block 16 and then to SOC1 again during blocks 17 and 18. This design was reversed for the other half of the participants. Increased RTs during block 16 were thus expected only when participants had acquired SOC knowledge during training over blocks 1–15.

2.2.2. Probabilistic condition

The experiment consisted of 21 experimental blocks of 96 trials for a total of 2016 trials (more experimental blocks were necessary to expose participants to the second-order transitions of SOC1 and in 20% of the trials to those of SOC2). This design was reversed for the participants trained on SOC2 for the second one, and conversely for the others.
stimulus appearing at any of the four locations, and asked to freely generate a series of 95 trials that “resembled the training sequence as much as possible”. The stimulus moved whenever participants had pressed one of the keys, and appeared at the corresponding location after a delay of 250 ms. They were told to rely on their intuitions when feeling unable to recollect the location of the next stimulus. Second, they were asked to generate another sequence of 95 trials, now following exclusion instructions (that is, avoiding the reproduction of the sequential regularities of the training sequence). In both generation tasks, participants used the same keys as in the SRT task, and were told not to repeat responses. They were not instructed to respond as fast as possible, and did not receive any feedback about their responses.

3. Results

In all analyses, a significance criterion of $\alpha = .05$ was used.

3.1. SRT task

We calculated mean RTs by block, for each group of participants (amnesic versus control) and for each condition (deterministic versus probabilistic). RTs associated with the first two stimuli of each block were excluded, because their locations could not be predicted. RTs associated with erroneous responses were also excluded, as were RTs beyond two standard deviations above the subject mean per block. The percentages of excluded RTs were around 5% in each condition, and did not differ between amnesic and control groups, neither in the deterministic condition ($t(16) = .515$, $p > .5$, two-tailed), nor in the probabilistic condition ($t(5.178) = .216$, $p > .5$, two-tailed). This suggests that in none of the patients, any attentional deficit interfered with the experiment. As the two subgroups of participants were matched, in both conditions, with either SOC1 or SOC2, were trained identically and performed similarly, their RTs were combined for subsequent analyses.

3.1.1. Deterministic condition

3.1.1.1. Reaction time analyses. Fig. 1 shows the average RTs obtained over the entire SRT task with a deterministic sequence plotted separately for amnesic and controls participants. Prior to each analysis of variance (ANOVA), data were tested with Mauchly’s test of sphericity. Where sphericity was of concern, the degrees of freedom were modified with the Greenhouse–Geisser epsilon and effects were also excluded. The Greenhouse–Geisser correction was of concern, the degrees of freedom were modified with the Greenhouse–Geisser epsilon and effects were also excluded. The Greenhouse–Geisser correction was applied. The Greenhouse–Geisser correction was applied. The Greenhouse–Geisser correction was applied. The Greenhouse–Geisser correction was applied. The Greenhouse–Geisser correction was applied. The Greenhouse–Geisser correction was applied. The Greenhouse–Geisser correction was applied. The Greenhouse–Geisser correction was applied. The Greenhouse–Geisser correction was applied. 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level. An ANOVA with Training Blocks (15 levels, the first 15 blocks) as a within-subjects variable and Group as a between-subjects variable revealed significant effects of Training Blocks \( F(1, 58) = 9.57, \text{MSE} = 47700.49, p < .001 \) and Group \( F(1, 16) = 6.23, \text{MSE} = 991199.11, p < .05 \). The interaction also reached significance \( F(1, 58) = 2.85, \text{MSE} = 14230.439, p < .05 \). Next, independent ANOVAs conducted on both control and amnesic groups revealed a significant effect of Training Blocks for control participants \( F(14, 541) = 17.33, \text{MSE} = 93396.281, p < .001 \), but not for amnesic patients \( F(3, 226) = 1.58, \text{MSE} = 20612.35, p > .1 \). Thus, RTs decreased during the first 15 blocks of the SRT task in both groups, but the decrease was significant only in the control group.

Most importantly, RTs increased in both groups when participants were exposed to the transfer sequence on block 16. Further, presenting participants with the training sequence anew on blocks 17 and 18 allowed them to recover their pretransfer performance level. This observation was confirmed by another ANOVA with Transfer (two levels, block 16 and mean of blocks 15 and 17) as a within-subjects variable and Group as a between-subjects variable. This analysis showed significant effects of Transfer \( F(1, 16) = 34.81, \text{MSE} = 37339.87, p < .001 \) and Group \( F(1, 16) = 5.64, \text{MSE} = 98882.23, p < .05 \) but the corresponding Transfer \( \times \) Group interaction failed to reach significance \( F(1, 16) = 0.70, \text{MSE} = 753.93, p > .1 \). Thus, both groups are sensitive to the sequence modification, and the absence of interaction indicates that these learning effects are of similar extent. To probe the data more precisely, we checked directly that each of the amnesic patients had been sensitive to the sequence modification. Fig. 2 shows the transfer effect in the SRT task, plotted separately for each of the six amnesic patients. The figure shows that five of the six patients exhibit a transfer effect, that is, reacts more slowly when the sequence is changed. As transfer effects are not of similar extent for each patient, we computed the mean extent of the control group’s transfer effect in order to verify that each of the patient performed like the control participants during the transfer phase. For the control group, we obtained a ratio between the transfer block RTS and the mean of the two adjacent blocks RTS of 1.18 (S.D. = 0.12; Min = 1.06 and Max = 1.32), and a ratio of 1.14 for the amnesic group (S.D. = 0.08; Min = 1.03 and Max = 1.22). That is, the patient with the smallest ratio was only 1.25 S.D. under the control group’s mean ratio.

3.1.2. Error analyses. Fig. 3 shows mean errors rates obtained over the entire SRT task with a deterministic sequence, plotted separately for the amnesic and control groups. An ANOVA showed only a significant effect of Transfer [two levels, block 16 and mean of blocks 15 and 17; \( F(1, 16) = 5.73, \text{MSE} = 20.37, p < .05 \], but Group and the Transfer \( \times \) Group interaction failed to reach significance (all \( p > .5 \)). This confirms that mean error rates were higher during the transfer block than during adjacent blocks, for both amnesic and control participants. In the transfer block, the proportion of anticipation errors (that is, errors in which the training sequence response is produced when exposed to the transfer sequence) was 36% of the total errors for amnesic patients (32% of the total errors were repetitions errors and 32% were other errors), and 43% for control patients (19% of the total errors were repetitions errors and 36% were other errors).

We can thus conclude, both from RT and error analyses, that although amnesic patients were generally slower than their matched control participants, both groups have been disturbed by the sequence modification. No consistent decline in RTs of amnesic patients had been observed during the first 15 blocks, but error analyses suggest that amnesic patients behaved in a conservative manner: they committed few errors during the first 15 blocks (maximum 3%), suggesting that they privileged the precision with the detriment of the speed. Thus, although their RTs did not decrease significantly with practice, transfer block results show that amnesic patients, as well as their control participants, clearly learned the training sequence in the deterministic condition.

3.1.2. Probabilistic condition

3.1.2.1. Reaction time analyses. Fig. 4 shows mean RTs to stimuli were divided all through the task, so that each group
is represented by two curves (for highly probable and less probable transitions, respectively). An ANOVA with probability (two levels, highly probable and less probable transitions) and Training Blocks (21 levels) as within-subjects variables and Group as a between-subjects variable revealed significant effects of Probability [$F(1,16) = 4.70$, $MSE = 9805.81, p < .05$] and Group [$F(1,16) = 5.19$, $MSE = 421009.8$, $p < .05$]. Most important is the significant Probability × Group interaction [$F(1,16) = 5.50$, $MSE = 1147.76, p < .05$], which demonstrated that learning of the sequence was not of similar extent in amnesic and control groups. None of the remaining effects or interactions was significant (all $p > .1$). To measure learning effects in each group, two ANOVAs were conducted separately for control and amnesic groups. For the control group, the Probability × Training Blocks interaction reached significance [$F(5,139,56.53) = 2.62$, $MSE = 7161.95$, $p < .05$], revealing a greater probability effect later in practice than earlier (inductive of sequence learning). In contrast, the second ANOVA performed on amnesic patients’ RTs, failed to reveal any significant effect (all $p > .1$), suggesting that amnesic patients did not learn the probabilistic material. Moreover, in contrast to the deterministic condition in which five on the six patients exhibited a learning effect, the observation of individual performances for each of the six amnesic patients shows that none of them exhibited a learning effect with probabilistic sequence.

3.1.2. Error analyses. Fig. 5 shows mean error rates to sequential and noisy transitions over the entire SRT task with a probabilistic sequence, plotted separately for the amnesic and control groups. Of particular interest, there was a significant effect of Probability [$F(1,16) = 6.80$, $MSE = 145.12, p < .05$], showing that more errors occurred on noisy transitions than on sequential ones. Neither the effect of Group nor other interactions reached significance (all $p > .1$). Thus, error rates seemed to evolve similarly in both groups.

The observation that more errors occur on less probable transitions suggests that participants have learned sequential transitions occurring with a higher probability and frequently make highly probable responses to less probable transitions. An additional analysis of the subset of errors called “wrong-sequence” errors (that is, the set of highly probable responses being made to the less probable transitions, also called “anticipation errors”), or of the less probable responses being made to the highly probable transitions, see Schvaneveldt & Gomez, 1998] confirmed this inference: there were marginally significant effect of Probability [$F(1,16) = 3.76, MSE = 41.15, p < .075$], and significant effect of Training Blocks [$F(5,41,86.57) = 2.35, MSE = 35.05, p < .05$]. The Probability × Training Blocks interaction was marginally significant [$F(5;38,86.07) = 1.95, MSE = 32.79, p < .1$]. Neither the effect of Group nor other interactions reached significance (all $p > .4$). Participants of both groups were thus making increasingly more wrong-sequence errors to less probable than to highly probable transitions, hence engaging in anticipation behaviour. In contrast to the results of the RT data, which showed differences between amnesic and control groups in the probabilistic condition, the error data suggests similar learning for both groups.

We can thus conclude that amnesic patients showed sequence learning under deterministic conditions, and, to a much smaller extent under probabilistic conditions. In contrast, control participants showed sequence learning in both conditions. Before examining generation and recognition tasks results, we wondered if the first experiment would lead to a general procedural learning effect, so that each patient would begin the second experiment faster than he began the first one. An ANOVA on amnesic patients RTs during the five first blocks of the SRT task, for both experiments, revealed a significant effect of Order [$F(1,15) = 18.10, MSE = 1130153.8, p > .01$]. Neither the effect of Blocks nor the Blocks × Order interaction were significant (all $p > .1$). A detailed observation of individual performances confirms this order effect: all patients began the second experiment with faster RTs than in the first experiment, regardless of the structure of the sequence they were first exposed to. This suggests that 5 weeks after the first experiment, amnesic patients still showed a general procedural learning effect.

In the next section, we examine whether amnesic and control participants differ in their ability to project their knowledge of the sequence in generation and recognition tasks.

Fig. 4. Mean reaction times (RT) in milliseconds across blocks in the SRT task with a probabilistic sequence (80/20 ratio of sequential to noisy transitions), plotted separately for amnesic and control participants.

Fig. 5. Mean error rates (percent) across blocks in the SRT task with a probabilistic sequence (80/20 ratio of sequential to noisy transitions), plotted separately for amnesic and control participants.
3.2. Generation tasks

In this generation task, participants were first asked to genera-
te a sequence that resembles the training sequence as much
as possible (inclusion instructions) and second to generate a
different sequence, avoiding reproducing the training sequence
(exclusion instructions). Even if amnesic patients did not always
remember having performed the learning task, they were told to
rely on their intuition under inclusion instructions and to try
to counteract their intuition feelings under exclusion instruc-
tions. As the generation task is very similar to the SRT task,
patients managed to perform it without difficulties. To measure
generation performance, we computed the number of generated
chunks of three-elements (triplets) that were part of the training
sequence. To obtain inclusion and exclusion scores for each sub-
ject, we divided the corresponding number of correct triplets by
the sum of the triplets that were part of the training sequence (cor-
rect triplets) and those that were part of the transfer sequence.1
As only triplets from the training and from the transfer sequence
were considered, chance level was 50.

Fig. 6 shows average inclusion and exclusion scores for
both groups and both conditions. To find out whether genera-
tion performance reflects knowledge acquired during the SRT
task, paired samples t-tests were conducted to compare gener-
ation scores with those expected at chance level, that is, with
the number of generated triplets that were part of the transfer
sequence. Let us first examine the results of the determinis-
tic condition (left panel of Fig. 6). Amnesic patients gener-
ated as many training triplets as transfer triplets under inclu-
sion \( t(15) = -0.02, p > 0.5 \) (one-tailed) and exclusion instructions \( t(15) = -0.02, p > 0.5 \) (two-tailed). In contrast, control partici-
pants generated more training triplets than transfer triplets under
inclusion instructions \( t(11) = -2.01, p < 0.05 \), one-tailed) but not
under exclusion instructions \( t(11) = 0.19, p > 0.5 \), two-tailed).

Concerning the probabilistic sequence (right panel of Fig. 6),
both amnesic and control participants generated as many training
triplets as transfer triplets under inclusion \( t(5) = -0.14, p > 0.5 \);
\( t(11) = 0.95, p > 0.1 \), one-tailed, for amnesic and control subjects,
respectively) and exclusion instructions \( t(5) = -0.31, p > 0.5 \);
\( t(11) = -0.66, p > 0.5 \), two-tailed, for amnesic and control group,
respectively). This suggests that the generation performance of
both amnesic and control participants after training under prob-
alistic conditions fails to reflect knowledge acquired during
the SRT task. To summarize, only control participants exposed
to a deterministic sequence generated a high percentage of cor-
rect triplets under inclusion instructions. Other generation scores
were at baseline.

Moreover, an ANOVA with Group as a between-subjects variab
le, Condition (two levels, deterministic and probabilistic) and
instructions (two levels, inclusion and exclusion) as within-
subjects variables2 only revealed a significant triple interac-
tion between Group, Condition and Instructions \( F(1,16) = 5.83,\nMSE = 432.12, p < 0.05 \); all other \( p > 0.25 \). Independent ANOVAs
on the amnesic group did not reveal any significant effect
(all \( p > 0.4 \)). By contrast, the ANOVA performed on the con-
trol participants generation scores revealed a significant inter-
action between Condition and Instructions \( F(1,11) = 8.49,\nMSE = 704.03, p < 0.05 \); other \( p > 0.25 \). Paired samples two-tailed
\( t \) tests confirm that the control participants generated sig-
ificantly more training triplets under inclusion than exclu-
sion instructions under deterministic conditions \( t(11) = -2.38,\np < 0.05 \), but not under probabilistic conditions \( t(11) = 1.44,\np > 0.2 \). Thus, control participants exposed to deterministic mate-
rial were able to generate parts of the training sequence or
to avoid reproducing them, according to the instructions. We
can thus conclude that these participants have acquired explicit
knowledge in the deterministic condition, but not in the prob-
alistic condition. In contrast, the generation performance of
amnesic patients fails to reveal any learning, either in the deter-
mindistic or in the probabilistic condition.

One might wonder whether an inhibition deficit might inter-
fere with our measures of implicit and explicit influences as
computed in the generation task. Executive functioning of some
patients was not indeed completely intact (see Table 1: GR in
the Stroop task, or HV, GR or JMD in the Hayling test). How-
ever, in the generation task, each of these patients obtained a
score that was below chance level under exclusion instructions,
which indicates that they successfully avoided reproducing the
training sequence. This is turn suggests that inhibition deficit is
not a significant issue in our study.

3.3. Recognition task

Participants were asked to react to three-elements sequences
(triplets) and to rate from 1 to 6 the extent to which they

1 As training and transfer sequences share the same abstract structure, this
comparison allows us to make sure that generation performance reflects learn-
ing of the sequential contingencies of the training sequence and not merely
baccal frequency information (see Shanks & Johnstone, 1999; Destrebecqz &
Cheremans, 2001).

2 Condition may be considered as a within-subjects factor because the same
amnesic patients were exposed to both conditions and their control participants
were pared two by two in terms of age, sex and education level (see Curran,
1997).
felt these sequences were familiar. Sequences with erroneous responses were excluded. Mean recognition ratings for both conditions, both groups and both structures of sequence (old versus new) are shown in Fig. 7 (recall that high ratings correspond to judgments of novelty and are expected for triplets from the transfer sequence). An ANOVA performed on recognition ratings revealed no significant effect (all p > .1), except for Group [F(1, 14) = 3.66, MSE = 5.86, p < .05], consistent with the amnesic group’s tendency to generally use higher recognition ratings. Therefore, neither amnesic nor control participants were able to differentiate triplets from the training (old) and from the transfer (new) sequence.

Nevertheless, we compared, for each group, the mean RTs associated to the third element of the 12 training triplets with the mean RTs associated to the third element of the 12 transfer triplets. One-tailed paired samples t tests showed that these differences were significant only for the control group [mean difference = 89 ms, S.D. = 155 ms, t(11) = −1.98, p < .05 and mean difference = 104 ms, S.D. = 79 ms, t(11) = −2.02, p < .05, for deterministic and probabilistic conditions, respectively]. This was not the case for the amnesic patients [mean difference = 32 ms, S.D. = 85 ms, t(5) = 0.92, p > .1] and mean difference = 279 ms, S.D. = 540 ms, t(5) = −1.27, p > .1, for deterministic and probabilistic condition, respectively]. Hence, only control participants were able to respond significantly faster to the old than to the new triplets, suggesting perceptual fluency effects.

4. Discussion

In this study, we sought (1) to assess the extent to which amnesic patients can learn about probabilistic structure and (2) to assess the extent to which knowledge possibly acquired by such patients under incidental learning conditions is available to conscious awareness. To explore these issues, we compared the performance of six amnesic patients with that of 24 matched control participants in two conditions differing only in terms of sequence structure. In the deterministic (noiseless) condition, a standard 12-element sequence was repeated during the entire SRT task, while in the probabilistic condition, noise was introduced so as to prevent explicit learning. Each participant first performed an SRT task (with a deterministic or probabilistic sequence) and then two direct tasks (generation and recognition) assessing the extent to which the acquired knowledge is available to conscious control and to conscious recollection.

Our main results are as follows. The SRT task data revealed that in the deterministic condition, both amnesic and healthy participants were sensitive to a modification of the sequence, as evidenced by their transfer effect of similar extent both on RTs and errors rates. We observed that the RTs of five of the six amnesic patients increased when the sequence was changed. By contrast, in the probabilistic condition, only healthy participants exhibited faster RTs on sequential trials with practice, as opposed to non-sequential trials, indicative of sequence learning. Amnesic patients’ RTs did not differ on these two types of trials. However, error analyses identified learning effects, both in amnesic and control participants.

In the generation task, only healthy participants exposed to the deterministic sequence were able to reproduce the sequence. Other scores were at baseline, suggesting that the knowledge acquired in the SRT task by healthy participants with a probabilistic sequence and by amnesic patients with a deterministic sequence was not strong enough to be projected in the generation task. Moreover, in the recognition task, regardless of the structure of the sequence participants had been presented with during the SRT task, neither amnesic nor control participants were able to explicitly differentiate between familiar and novel fragments. Nevertheless, control participants reacted faster to familiar fragments. To sum up, neither generation nor recognition data indicated any knowledge acquisition in the amnesic group, while they confirmed that control participants acquire more explicit knowledge under deterministic rather than probabilistic conditions.

Our results are congruent with previous findings (Reber & Squire, 1994, 1998; Curran, 1997) showing that amnesic patients can develop sensitivity to complex sequential knowledge when exposed to a repeated deterministic sequence. Furthermore, we found under probabilistic conditions, amnesic patients committed more and more anticipation errors with practice. This suggests that they can also develop sensitivity to complex sequential knowledge when exposed to a probabilistic sequence, as had already been suggested with other types of probabilistic materials (Cleeremans, 1993; Curran, 1997). Such learning has also been demonstrated in probabilistic classification tasks, in which amnesic patients performed similarly to matched controls, at least at the beginning of the task (see the weather forecast task, Knowlton et al., 1994, 1996). However, Hopkins et al. (2004) showed that learning was impaired when the probabilistic categories were more easily discriminable, suggesting that probabilistic learning is not always preserved in amnesia. In our
experiment, the finding that memory-impaired patients exhibit
sensitivity to a probabilistic sequence through their error pattern
but not through their reaction times is an interesting data point,
but one that should be taken with caution because of the small
percentage of errors.
Another interesting observation revealed by error analyses
concerns the transfer phase in the deterministic condition, in
which amnesic patients made fewer anticipation errors than
healthy participants, but more repetitions errors. This observa-
tion may be explained by the role that explicit episodic memory
can play in error elimination. Indeed, Baddeley and Wilson
(1994) suggested that one of the major functions of explicit
memory is the elimination of learning errors. In the case of nor-
mal participants, their explicit episodic memory of the learning
experience can be called up in order to eliminate these errors on
subsequent trials. In the absence of such explicit recollection,
amnesic patients instead perseverate in making the same errors
long after control participants have mastered the task. In our
study, healthy participants may have learned the deterministic
sequence in a more explicit way (pushing them to produce more
anticipation errors when the sequence is changed). They may
also have learned explicitly that no repetitions occurred during
the task. In contrast, amnesic patients continue to make the same
repetitions errors.

4.1. Preserved sequence learning in amnesia?

Our central goal in this study was to explore under which
conditions amnesic patients exhibit preserved ability to learn
about sequential regularities. Our results indicate preserved
learning when the sequential material is deterministic but not
when it is probabilistic. It is interesting to speculate about the
differences between these two types of sequential structures.
Beyond the obvious fact that probabilistic sequences are inher-
ently more complex than deterministic ones, some authors have
suggested that they are processed through different neural cir-
cuits. Peigneux et al. (2000), for instance, have suggested that the
fixed and repeating associations between the elements of deter-
ministic sequences make it possible for “encapsulated motor
programs” (i.e., motor chunks) to be learnt in the basal ganglia,
thus resulting in the observed speedup during the SRT task and
the ensuing interference when the sequence is modified. In con-
trast, processing probabilistic sequences, which fail to contain
as many stable, long chunks, would require the involvement of
higher-order cognitive processes that are not so dependent on
motor performance as when learning deterministic sequences.
Such higher-order cognitive processes would thus be impaired
in amnesia, while their motor abilities would remain relatively
intact. Further research will need to find independent evidence
to support this conclusion.

Another account of the better learning of deterministic
sequences in both amnesic and control participants is based on
the role of context. By assumption, participants in sequence
learning tasks anticipate (consciously or not) the location
where the next stimulus will appear so as to prepare their
response even before the onset of the next stimulus. This
preparation is necessarily based on the temporal context set
by previous elements of the sequence. By construction, the
contextual information conveyed by deterministic sequences
is more predictive of forthcoming events than in probabilistic
sequences. This account therefore predicts lower learning with
probabilistic than with deterministic sequences (for contextual
information is degraded in the former), and lower learning in
amnesic patients than in control participants (for the latter have
more difficulty memorizing contextual information), which
is indeed what we found. This difference can also explain
why learning tends to be more explicit for healthy participants
when trained on deterministic material, for they can then
acquire distinctive episodic traces of specific contexts, which
is impossible under probabilistic conditions.

This account is also congruent with the results we obtained
on the direct tests (generation and recognition) administered
to participants after the SRT task. Both generation and recog-
nition tasks require greater reliance on memorized contextual
information than the SRT task itself. The facts that (1) healthy
participants are able to express their knowledge during genera-
tion after exposure to deterministic material and (2) the fact that
they exhibit perceptual fluency effects in the recognition task
after having been trained either with deterministic or with prob-
abilistic material are both indicative of the important role that
context plays in modulating the extent to which sequence knowl-
edge can be expressed. This stands in contrast with the generally
poor performance observed when participants are asked to
express old/new recognition judgments (contextual cuing is
more important in generation and in reacting to short sequences
in the recognition task, than in old/new recognition judgments).
Both points thus reinforce the idea that tasks on which amnesic
patients fail and those on which they perform normally may be
best distinguished by the presence, or lack thereof, of context
information (Nissen, Willingham, & Hartman, 1989). Indeed,
whereas in most procedural skill learning tasks, the stimulus
tightly constrains what response should be made, standard tests
of recall and recognition memory fail to do so. Considered
together, the graded character of our results, observed both
over different sequential materials in healthy participants, and
when comparing normal and amnesic performance across the
different tasks, suggests (1) that the extent to which learned
knowledge may be expressed depends on the amount and on the
quality of contextual information available to participants and
(2) that amnesia involves a deficit in our ability to bind together
elements of the context in such a manner that high-quality traces
associating the context with the appropriate response can be
formed.

Finally, as each amnesic patient performed the experiment
in both conditions, we were able to compare individual perfor-
mance over the two sessions. We observed that 5 weeks after the
first experiment, amnesic patients had forgotten the complex
sequential knowledge they had learned over the first session, but
they were nevertheless faster at the beginning of the second SRT
session (which involved a different sequence). This suggests
that procedural learning had been maintained over the 5 weeks
interval, and confirms the preserved learning and retention of
complex perceptual-motor skills in severe amnesia (Milner et al.,
1968; Brooks & Baddeley, 1976; Cohen & Squire, 1980);
4.2. Nature of the acquired knowledge: learning without consciousness?

Was learning implicit or explicit in our experimental situation? As discussed in Section 1, generation and recognition tasks allow us to clarify the nature of the knowledge acquired in the SRT task (see Destrebecqz & Cleeremans, 2001; Shanks et al., 2003). Healthy participants trained under deterministic conditions exhibited strong sequence learning during the SRT task, and were also to perform well on the subsequent generation task, successfully reproducing the training sequence under inclusion instructions, and successfully avoiding the reproduction of this sequence under exclusion instructions. The sequential knowledge they have acquired over training thus appears to be explicit.

In contrast, healthy participants trained under probabilistic conditions exhibited sequence learning during the SRT task, but were neither able to generate nor to recognize the sequence that whatever episodic knowledge had been acquired was by trying to recognize the next stimulus in amnesic patients. In this context, we can use the term “amnesia” to refer to a condition in which a patient is unable to learn or remember information that is important for successful performance in a task. Amnesia is a common symptom of several neurological disorders, including Alzheimer’s disease, Huntington’s disease, and traumatic brain injury.

4.3. A multiple learning systems perspective?

Our results are congruent with previous research on amnesia conducted in other fields. Thus, for example, Chun and Phelps (1999) found that amnesic patients were impaired for learning associations between repeated visual configurations and the location of a target. They suggested that amnesia results in a deficit in learning contextual information, which requires the binding of multiple spatial or temporal cues. Another experiment points to the same conclusion. Ryan et al. (2002) examined the performance of amnesic patients using eye movement monitoring to measure memory for spatial relations among objects within scenes. Amnesic patients showed a normal general facilitation when scanning familiar scenes but failed to show excessive scanning of manipulated zones in the rearranged scenes. Again, our results confirm that amnesia results in a selective deficit in memory for the relations among the constituent elements of scenes or events.

Our results are consistent with a multiple learning systems view, in which memory for stimulus relationships (“binding”) would be impaired in amnesia and result in their decreased ability to learn about novel information at a normal rate. However, thanks to other hippocampus-independent learning systems, learning would still be possible, particularly when the same contextual information is repeated (that is, without noise). This is the case for procedural learning (Milner et al., 1968; Brooks & Baddeley, 1976; Cohen & Squire, 1980; Cavaco, Anderson, Allen, Castro-Caldas, & Damasio, 2004) in general, and also, we argue, for the deterministic sequences used in this study. Further research will have to explore whether other variables, such as time available for processing, that is, the interval between participants’ responses and the onset of the next stimulus in the SRT task influence the development of episodic representations of the links between the temporal context set by previous elements of the sequence and the location of the next stimulus in amnesic patients.

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