The dynamic time course of memory recovery in transient global amnesia

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Aims: To investigate the dynamic time course of transient global amnesia (TGA)—that is, the process of recovery and the interindividual variability—by testing four patients during the day of TGA itself (on three occasions) and at follow up (on two occasions).

Methods: A specially designed protocol focusing on semantic (both conceptual and autobiographical knowledge) and episodic (both anterograde and retrograde components) memory.

Results: Every patient showed marked impairment of both anterograde and retrograde episodic memory during the acute phase, with a relative preservation of personal and conceptual semantic knowledge. During the following phase, the authors observed similarities and differences among the patients’ patterns of recovery. In general, retrograde amnesia recovered before the anterograde amnesia and anterograde episodic memory was recovered gradually in every case. In contrast, shrinkage of retrograde amnesia was more heterogeneous. In two of the patients, this shrinkage followed a chronological gradient and the most remote events were recovered first. In the two other patients, it depended more on the strength of the trace, and there was no temporal gradient. For the latter, an executive deficit could account for difficulties in accessing both conceptual knowledge and autobiographical memories.

Conclusions: This profile of recovery suggests a “neocortical to medial temporal” process in every case, and the possibility of an additional frontal dysfunction in some cases. Hence, the acute phase seems to be characterised by a common episodic impairment. This variability between subjects appears in the recovery phase with two different patterns of impairment.

Transient global amnesia (TGA) is characterised by a selective disorder of memory with a sudden onset and without any accompanying neurological deficit in patients aged around 50 years or over. Neuropsychological examinations performed during the acute phase have shown that general cognitive functions and some components of memory—such as working memory, procedural memory, and priming—remain intact.1–4 The preservation of semantic memory is debatable, as some authors have reported intact conceptual knowledge,5 public knowledge,3 and autobiographical knowledge (except for current knowledge concerning the hospitalisation period such as the doctor’s name).6 In contrast, others have described an impairment of public knowledge.1–3 6 7 Episodic memory is the worst affected system in TGA, displayed by both massive anterograde amnesia (AA) and extensive retrograde amnesia (RA),4 although AA and RA may be differently impaired.1 8–10

This neuropsychological variability from case to case may be due to both interindividual differences and the stage of recovery at which the testing is carried out.11 Few studies have focused on the memory recovery process because of the methodological difficulties arising from the briefness of this disorder. TGA is a short lived syndrome (only a few hours) and neuropsychological investigations rely on specific logistics which notably require the presence of a neurologist and a neuropsychologist at the emergency unit.12 For these reasons, it is difficult to carry out more than one neuropsychological examination. Even so, a small number of patients have undergone brief examinations in two separate studies.13 14 Only Kapur et al15 have described a case of symptomatic transient amnesia which resulted from a cerebral angiography with four neuropsychological investigations during the attack. As far as AA is concerned, the results showed an improvement 8 ½ hours after the onset of TGA. Conceptual knowledge was back to normal by the time of the second evaluation, and the test of public knowledge yielded normal results at the third investigation. RA, assessed by carrying out structured interviews about personal semantic information, stretched back approximately 22 years during the first investigation and gradually shrunk, though without any fixed chronological order, as childhood memories were not recovered first. Finally, performances improved after the end of the attack. These data argue in favour of different profiles in the recovery of the conceptual, public, and personal semantic knowledge. However, these results need to be interpreted with a degree of caution, because of the different methodologies used in each task and consequently the cognitive processes involved. Furthermore, the authors could not reach any precise conclusion about the recovery of episodic memory because only the anterograde component had been assessed. Thus, although this is a very interesting study, it does not allow us to identify the relation between recovery from anterograde amnesia and that from retrograde amnesia. Moreover, these results need to be further investigated for a more complete understanding of this clinical syndrome.

The main aim of our study was to investigate the neuropsychological variability in TGA, resulting firstly from the stage of recovery at which the testing is carried out using a dynamic approach that consists of assessing the memory impairment during the acute phase of TGA and its recovery; and secondly, from case to case by examining several patients with the same methodological procedure. Assessments were carried out on three separate occasions during the attack, so as to estimate acute and early recovery phases, as well as on the following day and approximately one month later. Because of the short duration of TGA we focused on the

Abbreviations: AA, anterograde amnesia; RA, retrograde amnesia; TGA, transient global amnesia.
main memory systems which are disturbed in TGA—that is, both semantic and episodic memory. We studied several aspects of memory: conceptual knowledge, autobiographical memory (semantic and episodic components), and anterograde episodic memory. In order to compare performances between retrograde memory tests, we controlled the type of retrieval (fluency for conceptual knowledge and both semantic and episodic autobiographical memory). We have also respected the main features of the current concept of episodic memory that refer to autobiographical events located in space and time and are associated with “autonoetic awareness” in the assessment of anterograde and retrograde components of episodic memory. Therefore in every task we took into account the three essential components of episodic memory (what, where, and when) and the capacity to re-experience (autonoetic awareness) each event during both retrograde and anterograde investigations. Finally, a general cognitive assessment was provided in order to identify impairments that could have interfered with memory tasks, such as perceptual processes for anterograde and retrograde episodic memory.

**METHODS**

Four patients, satisfying the operational criteria for TGA, were included in the study. They were examined on five occasions (table 1), using a neuropsychological protocol aimed at investigating general cognitive functions, conceptual knowledge, semantic and episodic aspects of retrograde autobiographical memory, and the anterograde component of episodic memory. Three assessments were carried out during the day of TGA, one the day after, and the last about one month later. All four patients gave their consent to the study that was performed in compliance with the Declaration of Helsinki.

**General cognitive functions**

The general cognitive assessment consisted in an evaluation of orientation (Mattis Dementia Rating Scale), visuoconstructive abilities (copying of geometric figures), and working memory (digit span test). Naming and perceptual processes were assessed by means of two subtests: category naming and matching geometric figures.

**Conceptual knowledge**

Conceptual knowledge was assessed using several fluency tasks. During the day of TGA, patients carried out both a category and a letter fluency task on three occasions, each of them different. In every case, the patients were instructed to provide as many names as possible in the space of two minutes. Category fluency focused successively on animals, fruits, and furniture, whereas letter fluency referred to the letters P, R, and V respectively. The patients carried out the two first fluency tasks (animals and P letter) again the day after and two others (fruit and R letter) one month later.

**Autobiographical memory**

Two autobiographical recall tasks were designed to assess the semantic and episodic components of remote autobiographical memory from four age periods: 0–17 years, 18–30 years, more than 30 years except for the last 5 years, and the last 5 years except for the last 12 months. For each period, the patient was given 2 minutes to retrieve the maximum number of (1) items of personal semantic information (semantic recall) and (2) single, specific, autobiographical events (episodic recall). Family members were not asked to confirm the patient’s memories because two of the patients lived alone as their children had left home. Hence, semantic or episodic productions, which were produced during two or more sessions, were considered as true only when they were unchanged from one session to another. In the episodic task, when patients failed to produce any memory or produced a general memory, clues were provided. These clues were related to the patient’s age at the encoding time and concerned, for example, births, marriages, and first communications. The episodic features of the memories were tested after each assessed period by asking the patients firstly to describe all the events in detail and secondly to indicate their subjective experiences accompanying retrieval, by means of the Remember/Know procedure. This procedure allows one to distinguish autobiographical memories that patients consciously remembered—that is, epistemic memories—and those they merely knew about. “Remember” responses are based on feelings of reliving and refer to autonoetic awareness, which allows us to be conscious of the subjective time in which events occurred. “Know” responses are based only on feelings of familiarity and are an indication of the noetic awareness which characterises semantic memory. The score on each task was the total number of names in one case and the total number of episodic events in the other supplied for each time period. An episodic incident refers to a single event located in time and space with phenomenological details and associated with a Remember judgment. Furthermore, for the assessment of episodic memory, the current year was investigated using the last time period of the strictly episodic autobiographical test devised by Piolino et al. It concerned the recent past listed

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Time onset of TGA and the recovery phase and time of the neuropsychological assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Educational level</td>
</tr>
<tr>
<td>JT</td>
<td>74</td>
</tr>
<tr>
<td>GM</td>
<td>63</td>
</tr>
<tr>
<td>MJ</td>
<td>65</td>
</tr>
</tbody>
</table>

*Each session contains the following investigations:
Session 1: general cognitive functions, category fluency (animal), letter fluency (P letter), autobiographical recall, and anterograde component of episodic memory (version 1).
Session 2: category fluency (fruit), letter fluency (R letter), autobiographical recall, and anterograde component of episodic memory (version 2).
Session 3: category fluency (furniture), letter fluency (V letter), autobiographical recall, and anterograde component of episodic memory (version 3).
Session 4: general cognitive functions, category fluency (animal), letter fluency (P letter), autobiographical recall, and anterograde component of episodic memory (version 1).
Session 5: general cognitive functions, category fluency (fruit), letter fluency (R letter), autobiographical recall, and anterograde component of episodic memory (version 2 for JT, GM, and JQ, and version 3 for MJ).
chronologically: summer, Christmas, month, week, weekend, two days, one day, and hours before TGA. Patients were required to give details of one episodic event relating to each temporal reference and make a Remember/Know judgment for each recollection. For this time period, patients were not given any limit for producing their memories and the score was the number of episodic events.

**Anterograde component of episodic memory**

The episodic memory task was derived from Kopelman’s procedure and assessed the ability to learn facts associated with spatial and temporal features.30 This task comprised two lists of seven words belonging to 14 different categories. Each word was presented at the top or bottom of a sheet of paper. Patients were asked to learn the word (fact), its location (spatial), and its list number (temporal). Immediately after processing this information, retrieval was assessed using several forced-choice recognition tasks: recognition of the target word out of two words belonging to the same semantic category and, for correct responses, recognition of the location (top or bottom), and recognition of the temporal feature (first or second list). This procedure was repeated for all 14 target words.

During the recognition task, patients had to indicate their conscious subjective experience accompanying each response. Patient had to give either Remember responses (R) if recognition was accompanied by the retrieval of the context as a re-experiencing of the information from the learning context (such as thoughts, feelings, or perceptions), or Know responses (K) if recognition was achieved without such access. In addition, ‘Chance’ responses gave patients the possibility of signalling when their recognition judgment of an item was a matter of chance (“I guess that this item may be a target item but I do not remember or even know having seen either one or the other of these two items”).

Three different versions of this task were devised and each one was carried out successively by the patients during the episode of TGA. Each version produced three recognition scores: factual, spatial, and temporal. The recognition of spatial and temporal attributes was only carried out on target words which had been correctly identified. Accordingly, factual scores were converted into a ratio of the total number of words (that is, 14 words) and both spatial and temporal scores were turned into ratios of correct factual recognition responses. Tables show raw scores, but statistical analyses were carried out on these ratios. For each recognition task, we also obtained scores of subjective experience: Remember and Know. As these two responses refer to independent processes, we determined a Remember score and a Know score corrected according to the Yonelinas’s procedure (K/(1-R)).31 The comparisons between patients and controls were based on these scores.

**Analysis of the data**

The whole neuropsychological protocol, including the three versions of the episodic memory test, was carried out by 20 control subjects aged 45 to 75 years (9 men and 11 women, m = 59.2, σ = 9.18) with a Mattis score above 133/144 (m = 140.1; σ = 2.9). Patients’ performances were compared with normative data according to the z score method.

**RESULTS**

**Case reports**

Four women fulfilled the operational criteria of TGA,34 and had no previous medical history. JT was a retired hairdresser, GM still worked as a secretary, MJ was a retired dancing teacher, and JQ was a retired butcher. Preceding the TGA, precipitating factors were noted (emotional in three cases and physical in the latter case—a sudden change in temperature for MJ). Neurological and EEG examinations performed during the attack were normal. A brain CT scan performed a few days after the attack in three patients (JT, GM, MJ) showed no abnormalities. In every case, the first neuropsychological investigation was performed when the patients had a temporal disorientation and both AA and RA. The day after, patients had no memory impairment apart from a lacunar amnesia that concerned mainly the attack.

One month later, one patient (JQ) was still distressed by the death of her husband which had occurred a few months ago and showed depressive symptoms. Neurological examinations and the Mattis Dementia Rating Scale,39 performed about one year later were normal in every case (JT: 141/144, GM: 144, MJ: 142; JQ: 137).

**General cognitive functions**

Table 2 gives the four patients’ scores for the general cognitive assessment. During the episode, every patient showed temporal disorientation. Only one patient (JQ) had a subnormal score in the matching task. The day after, performances were back to normal apart from one patient (JQ) who still obtained a pathological score in the orientation subtest. In fact, both spatial and temporal orientations were normal but she did not remember the name of the mayor of the city where she lived. About a month later, performances were back to normal.

**Conceptual knowledge**

Table 3 shows that, on the day of TGA, two patients only had pathological correct response scores in the first session, whereas the other two had pathological scores in all three

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Table 2 General cognitive assessment: performances observed during TGA, the day after and at follow up (z scores, unilateral test)

<table>
<thead>
<tr>
<th></th>
<th>JT</th>
<th>GM</th>
<th>MJ</th>
<th>JQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orientation/9</td>
<td>5</td>
<td>9</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>(−17.95)*</td>
<td>(−0.23)</td>
<td>(−13.41)*</td>
<td>(−0.23)</td>
</tr>
<tr>
<td>Copying of geometric figures/12</td>
<td>6</td>
<td>7</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>(−0.76)</td>
<td>(−0.76)</td>
<td>(−0.76)</td>
<td>(−0.76)</td>
</tr>
<tr>
<td>Forward digit span</td>
<td>7</td>
<td>6</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>(−0.60)</td>
<td>(−1.45)</td>
<td>(−0.60)</td>
<td>(−0.60)</td>
</tr>
<tr>
<td>General knowledge</td>
<td>16</td>
<td>15</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>Matching figures/16</td>
<td>16</td>
<td>(−0.83)</td>
<td>16</td>
<td>(−0.83)</td>
</tr>
<tr>
<td></td>
<td>(−0.45)</td>
<td>(0.19)</td>
<td>(−0.83)</td>
<td>(0.19)</td>
</tr>
<tr>
<td>Category naming/22</td>
<td>21</td>
<td>22</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>(−1.14)</td>
<td>(−1.14)</td>
<td>(−1.14)</td>
<td>(−1.14)</td>
</tr>
</tbody>
</table>

*p<0.001; †p<0.05.

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sessions. All four patients produced a great many repetitions in both tasks. Scores were still low for two patients the day after the episode and for three patients about one month later (table 4).

**Autobiographical memory**

The performances obtained in the assessment of the semantic component of autobiographical memory are reported in tables 5 and 6. During the day of TGA, JT and GM both had pathological scores for the last five year period. The resolution of this deficit took place in the second session for one patient and in the third session for the other. Another patient, MJ, produced significantly few names concerning the earliest period in the first two sessions. She adopted a particular strategy for this period, which consisted in recollecting the context of this period—what happened at school or in the family and who was involved—before producing names of acquaintances. Moreover, unlike the other patients, this period consistently produced the lowest score, even after the episode. The next day, all the scores were back to normal.

During the acute phase of TGA, the episodic component of autobiographical memory was severely impaired for every time period (tables 7 and 8). One patient even had performances equivalent to zero. Some memories were general, lacking details as well as spatial and temporal specificity. Other memories had both spatial and temporal references but lacked details when episodic features were tested after the assessed period: “I got married on July 7th 1947 in Caen, at the church of Notre Dame. (Q: Can you tell me more?) The reception was at my parents’ house, at St Pierre Street. (Q: What did you do?) We went to the Coudray bridge in the afternoon. (Q: What for?) We may have danced.” There were also specific but false memories, as tested after the assessed period: “I danced.”

### Table 3 Conceptual knowledge: performances observed the day of TGA (z scores, unilateral test)

<table>
<thead>
<tr>
<th>Category fluency</th>
<th>JT Session 1</th>
<th>JT Session 2</th>
<th>JT Session 3</th>
<th>GM Session 1</th>
<th>GM Session 2</th>
<th>GM Session 3</th>
<th>MJ Session 1</th>
<th>MJ Session 2</th>
<th>MJ Session 3</th>
<th>JQ Session 1</th>
<th>JQ Session 2</th>
<th>JQ Session 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct responses</td>
<td>20</td>
<td>20</td>
<td>18</td>
<td>23</td>
<td>19</td>
<td>17</td>
<td>22</td>
<td>17</td>
<td>22</td>
<td>16</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Repetitions</td>
<td>–1.99**</td>
<td>–0.84*</td>
<td>–1.67</td>
<td>–1.33</td>
<td>–1.84*</td>
<td>–1.78*</td>
<td>–1.87*</td>
<td>–0.67</td>
<td>–1.43</td>
<td>–1.21*</td>
<td>–1.22*</td>
<td>–1.16*</td>
</tr>
<tr>
<td>Letter fluency</td>
<td>7</td>
<td>5</td>
<td>1</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>10</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Correct responses</td>
<td>12</td>
<td>17</td>
<td>14</td>
<td>17</td>
<td>13</td>
<td>13</td>
<td>8</td>
<td>8</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Repetitions</td>
<td>–1.57</td>
<td>–0.58</td>
<td>–1.35</td>
<td>–1.43</td>
<td>–0.67</td>
<td>–0.67</td>
<td>–0.38</td>
<td>–0.38</td>
<td>–0.19</td>
<td>–0.19</td>
<td>–0.19</td>
<td>–0.19</td>
</tr>
</tbody>
</table>

* p<0.05; † p<0.01; ‡ p<0.001.

### Table 4 Conceptual knowledge: performances observed the day after and at follow up (z scores, unilateral test)

<table>
<thead>
<tr>
<th>Category fluency</th>
<th>JT Session 4</th>
<th>JT Session 5</th>
<th>GM Session 4</th>
<th>GM Session 5</th>
<th>MJ Session 4</th>
<th>MJ Session 5</th>
<th>JQ Session 4</th>
<th>JQ Session 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct responses</td>
<td>29</td>
<td>19</td>
<td>28</td>
<td>25</td>
<td>20</td>
<td>20</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td>Repetitions</td>
<td>–1.00</td>
<td>–0.4</td>
<td>–1.11</td>
<td>–0.71</td>
<td>–1.99*</td>
<td>–0.15</td>
<td>–1.88*</td>
<td>–0.81</td>
</tr>
<tr>
<td>Letter fluency</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Correct responses</td>
<td>–1.02</td>
<td>–2.53*</td>
<td>–2.53*</td>
<td>–0.59</td>
<td>–1.70</td>
<td>–1.84*</td>
<td>–2.52*</td>
<td>–2.39*</td>
</tr>
<tr>
<td>Repetitions</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* p<0.05.

### Table 5 Autobiographical recall: semantic component. Performances observed the day of TGA (z scores, unilateral test)

<table>
<thead>
<tr>
<th>Age group</th>
<th>JT Session 1</th>
<th>JT Session 2</th>
<th>JT Session 3</th>
<th>GM Session 1</th>
<th>GM Session 2</th>
<th>GM Session 3</th>
<th>MJ Session 1</th>
<th>MJ Session 2</th>
<th>MJ Session 3</th>
<th>JQ Session 1</th>
<th>JQ Session 2</th>
<th>JQ Session 3</th>
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<tr>
<td>0–17 years old</td>
<td>11</td>
<td>16</td>
<td>18</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>18–30 years old</td>
<td>10</td>
<td>12</td>
<td>13</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>&gt;30 years old</td>
<td>17</td>
<td>15</td>
<td>16</td>
<td>13</td>
<td>13</td>
<td>13</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Last five years</td>
<td>2</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>12</td>
<td>10</td>
<td>6</td>
<td>3</td>
<td>7</td>
</tr>
</tbody>
</table>

* p<0.05.
year for JT and GM. The second was patchier, as it did not follow a chronological order. Instead, memories were negative emotional events, such as events related to death or war, or were produced in response to clues, such as births, first communions, and marriages.

The next day, three patients’ scores were back to normal. The last patient was still unable to recollect all episodic events for the current year, but a month later, her performances were also normal.

**Anterograde component of episodic memory**

Table 9 shows results collected during the day of TGA. We have only reported factual scores and the Remember/Know judgments, as the patients were so amnesic that spatial and temporal data were not informative.

The first session was characterised by pathological scores in factual recognition and for each patient every score was based on a Chance judgment. In the second session, recognition scores were back to normal for one patient but Remember and Know judgments were still flawed (there was a floor effect in controls and therefore Know scores equalled zero they were not pathological). However, Know scores seemed to improve before Remember scores (session 2 for JT and JQ, session 3 for GM and MJ). Therefore, patients may have used first their semantic memory and finally their episodic memory, with the capacity to re-experience the experimental event. The day of TGA, memory recovery was effective only for JT at the third session. The other patients obtained pathological scores either in judgments or in both judgments and recognition tasks, even though there was a clear improvement.

Performances were normal, or close to normal, for two patients in the following sessions. Conversely, the assessment revealed mild impairment in the other two cases (table 10).

In summary, these results showed that the acute phase of TGA is mainly characterised by a massive impairment of both retrograde and anterograde episodic memory. Retrograde amnesia seemed to recover before AA in every case. As far as
AA is concerned, recovery operated gradually from feelings of familiarity to a recollection process including autonocetic consciousness. However, the rate at which these memory functions recovered was different in each patient; more rapidly for two patients and slower for the other two (fig 1). This slowness could reflect an additional impairment of executive functions for these two patients.

**DISCUSSION**

This is the first prospective study to highlight the variability that depends on the dynamic feature of TGA—that is, the recovery of memory processes, and the individual variability using improved experimental designs and original test instruments. Patients were submitted to repeated neuropsychological investigations using as many versions as possible of the cognitive tasks (category fluency, letter fluency, and anterograde episodic memory) (table 1). Our findings are discussed in two parts: (1) the pattern of disturbance that characterises the acute phase of TGA and (2) the recovery phase and differences noted between patients tested at the same stage of recovery.

**Acute phase of TGA: a common pattern of disturbance**

The acute phase was characterised by a massive impairment of both anterograde and retrograde episodic memory. Our findings about AA underline the usefulness of taking the state of awareness into account when assessing episodic memory. Our patients were able to give correct responses during the acute phase, but none of them gave either Remember or Know responses. Every forced choice recognition response was based on a guessing process (Chance response); that was the reason patients obtained about 50% of correct responses in the first session. The absence of both Know and Remember responses suggested that they had massive and global anterograde amnesia (as expected by Manns et al[34]). Concerning remote memory, patients either had no deficit in autobiographical semantic knowledge or else the perturbation was restricted purely to recent information. However, as can be seen, this component was back to normal during the recovery phase. Only one patient, MJ, had difficulty recalling people’s names in the first time period. However, for this time period, she tried to recollect the context before recalling the names—what happened at school or in the family and who was involved. The retrieval strategy used by this patient does not allow us to infer any real impairment of semantic memory during TGA. Consequently, the preservation of the semantic component stands in clear contrast to the massive deficit of the episodic component whatever the time period tested. This deficit of episodic memory during the acute phase has been reported by several authors[35,36] using different methodologies. However, our results point to a clear cut dissociation between the two aspects of autobiographical memory (episodic and semantic). The episodic/semantic distinction is well documented in the permanent amnestic syndrome and in neurodegenerative diseases with cases which manifest an isolated impairment of an episodic component[37,38] or the reverse pattern—that is, an isolated disturbance of the semantic component.[39,40] These observations are in line with current models of retrograde amnesia which have taken into account this dichotomy.[37-40] Nonetheless, two different alternative interpretations can be formulated. Firstly, this dissociation between episodic and semantic components of remote memory may in fact reflect differences in the degree of rehearsal of the kind of

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<th>JT</th>
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*p<0.001; t<0.05; t<0.001.

Table 10 Anterograde component of episodic memory: performances observed the day after and at follow up (z scores, bilateral test)

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*p<0.05.

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information these two tasks referred to—that is, semantic information (the names of acquaintances) is more rehearsed than episodic information (personal events). If so, our patients should have produced some repeated personal events such as flashbulb memories: “rehearsal underlies the formation of the highly detailed and stable memories that are characteristic of “flashbulb” events.”3 However, they did not recall any episodic memory, even flashbulb ones. In contrast, some personal events were general and composed of semantic features. Secondly, given the importance of visual imagery in episodic autobiographical memory, the massive impairment of episodic memory in TGA may have resulted from an impairment of perceptual memory.16 However, impairment of episodic memory in TGA may have resulted from a dissociation of episodic/semantic in autobiographical memory.39 This model postulates a differential role of the medial temporal lobe in the consolidation of episodic and semantic information respectively. Although this region is temporary implicated in semantic recall, it is essential for remembering episodic memories whatever their remoteness. Therefore, the episodic disorder observed in our study may result from a transient disruption of either the retrieval process, affecting every time period and subserved by a transient and massive dysfunction of the medial temporal lobe,29 or a transient disruption of the frontal network37–39 or of the neocortical sites which store episodic fragments.37–39 Remote personal semantic information could be dependent on other temporal cortical systems that may be spared in TGA. One exception is the names of acquaintances made in the last few years that have not yet been consolidated and are still dependent on the medial temporal lobe.

Recovery phase: two different patterns of shrinkage in RA

The recovery of memory functions is a heterogeneous process. One patient was no longer showing any real memory impairment by the end of the day of the TGA attack, whereas other patients suffered from significant memory disturbance throughout the day and performances returned to normal one day, or one month, later. Moreover, the recovery profile shown by our patients reinforces the hypothesis proposed by Hodges and Ward3 and validated by Eustache et al.44 for similar results in one amnesic patient, Jon.44 This phenomenon was clearly observed in one patient, JT. Although AA and RA were not studied using strictly matched procedures, the shrinkage of RA mainly seemed to take place before the recovery from AA either the day of the TGA attack (JT and GM) or the day after (MJ and JQ) as previously reported.13–15

Concerning the anterograde episodic task, patients gradually started using familiarity (Know responses) and thereafter reliving (Remember responses) processes. As such, patients may have used semantic memory and thereafter episodic memory, with its capacity to re-experience the original event.17–19 Moreover, recognition tests can be successfully performed using only semantic memory (see reference 44 for similar results in one amnesic patient, Jon).18 This phenomenon was clearly observed in one patient, JT. Although she obtained correct performances in recognition tasks, her judgments showed that the recovery process was not yet complete. As for the subclinical memory deficit at follow up, one of the two patients had one subnormal retrieval score, which contrasted with the preservation of autonoetic awareness, whereas the other patient’s performance was poorer relative to the preceding session. In this latter patient, however, symptoms of depression may have interfered with the neuropsychological evaluation.

Contrary to AA, two patterns of recovery of RA were observed. The pattern of shrinkage of RA was characterised in two patients by the recovery of all periods except the most recent one. The memories returned in chronological order (the distant memories before the recent ones), in accordance with Ribot’s Law,45 which suggests a moderate impairment focused on the medial temporal lobe. According to Nadel and Moscovitch’s theory, remote memories are widely distributed across the brain and could be less affected by a mild dysfunction of the hippocampal region.17–19 In contrast, the shrinkage of RA in the two other cases did not follow a chronological gradient. It was rather patchy and seemed to
relies on the strength of the traces—that is, the richness of the encoding experience, emotional valence, meaningfulness, or number of retrievals.13 The stronger the memories, the easier they were to recall. This profile suggests a transient disruption of the recollection of phenomenological details of episodic memories, probably caused by a transient disruption of the frontal networks.17 Thus, in addition to a putative dysfunction of the medial temporal lobe, these patients may demonstrate a dysfunction of the frontal regions. Furthermore, Greene et al.19 have shown in Alzheimer’s disease that the production of personal events in an autobiographical recall task was correlated with letter fluency. The verbal fluency tasks carried out during TGA, notably the letter fluency task, showed low correct response scores in these two patients, which could indicate some disturbance of the process of access to the semantic store—that is, an executive process.7 47 48 However, the repetitions observed in every case may well have resulted from the massive impairment of episodic memory5 5 rather than from an executive deficit per se.49

Moreover, the shrinkage of RA before AA provides arguments for the hypothesis that neocortical areas (which play a role in the storage and recollection of remote episodic memories) recover first, and are subsequently followed by a recovery in the medial temporal lobe. In their study of one patient presenting symptomatic transient amnesia, Kapur et al.50 proposed a similar hypothesis focused on the “lateral-to-medial” role of the temporal lobe (see reference 50 for the same phenomenon in epilepsy).51 The disruption of the hippocampus throughout the TGA attack could also explain the presence of lacunar amnesia covering the entire day of the TGA attack, as well as the preceding hours in many cases.

CONCLUSIONS
In conclusion, this study provides evidence that the core symptom of TGA is a massive impairment of episodic memory, followed by varied patterns of recovery—quick in some cases, slower in others. Hence, the individual variability mainly appears in the recovery phase. Nevertheless several elements, such as the resolution of RA before AA, argue in favor of a “neocortical to medial temporal” process, as noted by several authors.5 5 42 41 52 Other neuroanatomical regions, such as the frontal lobe, may be involved where patients show an associated deficit of executive functions.5 53–56 Further studies combining neuroimaging and neuropsychological examinations need to be performed to confirm this supposition.

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