Clinical, neuropsychological, and metabolic characteristics of transient epileptic amnesia syndrome

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SUMMARY

Objective: Transient epileptic amnesia (TEA) is a recently individualized syndrome occurring in adult patients that includes epileptic seizures with amnestic features and interictal memory disturbances.

Methods: We investigated the clinical, neuropsychological, and 18F-FDG positron emission tomography (18F-FDG-PET) features of 30 consecutive cases of TEA in our center.

Results: The mean age of onset of amnestic seizures was 59 years. Pure acute amnesia was the only epileptic manifestation in 17% of cases. Interictal electroencephalography (EEG) abnormalities were present in 57% on awake recording and in most patients in whom sleep EEG was performed (96%). Nine of 30 patients showed anterograde memory deficit and six of 30 exhibited mild executive functioning impairment. On the autobiographical memory interview (AMI), patients showed a significant deficit for the recent period of the episodic subscale. Outcome under treatment was favorable in the majority of cases. A significant improvement was noted on recollection of autobiographical memory. 18F-FDG-PET (22 cases) showed positive correlations between left mesial temporal metabolism levels and anterograde and retrograde memory scores.

Significance: TEA is an emerging epileptic syndrome that likely remains misidentified and misdiagnosed. Neurometabolic data support a dysfunction of a hippocampal-neocortical network sustaining episodic memory.

KEY WORDS: Amnesia, Epilepsy, Episodic memory, EEG, FDG-PET, Accelerated forgetting.

Partial seizures may manifest as episodes of transient amnesia, sometimes as the sole epileptic manifestation.1–8 Several terminologies have been used to designate these epileptic amnestic episodes, among which “transient epileptic amnesia” (TEA) has become the most popular.3 Introduced in 1993, this concept was further expanded to qualify a syndrome with ictal and interictal memory disturbances as core manifestations.9,10 Accordingly, TEA refers to the following: (1) a history of recurrent witnessed episodes of transient amnesia; (2) cognitive functions other than memory judged to be intact during typical episodes by a reliable witness; (3) evidence for a diagnosis of epilepsy provided by epileptiform abnormalities on electroencephalography (EEG), concurrent onset of other clinical features of epilepsy (lip-smacking, olfactory hallucinations), and/or clear response to anticonvulsant therapy or by a combination of these three factors.

Although this epileptic syndrome is becoming increasingly recognized,10–14 large homogeneous series that contribute to delineating its main characteristics remain scarce,10 and its individualization as an epileptic syndrome is therefore discussed.10 Consequently, TEA is not uniformly acknowledged as a distinct neurologic condition, and epileptic amnestic attacks probably remain
underestimated or misidentified as other transient memory disorders.

The aim of the present study was thus to increase current knowledge on TEA in light of 30 new consecutive cases diagnosed in our center. We provide a detailed account of the clinical, neurophysiologic, and neuropsychological characteristics of the patients along with brain metabolism data using 18F-FDG positron emission tomography (18F-FDG-PET) neuroimaging.

**Patients and Methods**

**Patients**

This is a retrospective study investigating patients recruited at two institutions (Timone Hospital and Henri Gastaut Hospital) in Marseille, France, during the 2007–2012 period and fulfilling diagnostic criteria for TEA. All the patients were initially seen by one neurologist in one of the institutions (OF, FB, SA). Two patients have been included in a previous neuropsychological study. Clinical characteristics of attacks, context of occurrence, possible triggering factors, and cognitive complaints were carefully assessed. All patients underwent a full neurologic examination, waking EEG, and neuropsychological assessment. In addition, sleep EEG and 18F-FDG-PET were performed in 24 and 22 patients of 30, respectively.

The detailed methodology is indicated in Data S1.

**Neuropsychological assessment**

Each patient underwent a full neuropsychological evaluation, which included a battery of tests assessing anterograde verbal and visual memory, and retrograde memory for personal events.

Anterograde memory was evaluated using the logical memory from Wechsler Memory Scale III (WMS-III; immediate and 30-min delayed recall); the Rey-Osterrieth Complex Figure (ROCF) test (immediate and 30 min delayed recall); and the RL-RI 16, a French adaptation of the Free and Cued Selective Reminding Test (immediate and 30 min delayed recall). Autobiographical memory was tested with the autobiographical memory interview (AMI). Autobiographical memory for the last 5 years and the last 12 months was assessed using a semi-structured questionnaire (TEMPau task). In addition, long-term consolidation was examined in a subset of patients referred to as accelerated long-term forgetting (ALF) subgroup, who exhibited the following: (1) normal performance on standard anterograde memory tests; (2) autobiographical memory deficit; and (3) subjective complaint of accelerated forgetting. Sixteen ALF patients (mean age 62.81, standard deviation ± 9.14) were individualized, and performances were compared to those obtained from a group of 14 healthy age-matched controls (mean age 64.28 ± 4.5). The experimental protocol was established according to a previous study from our group that showed dissociation of long-term consolidation between context-rich and context-free (single item) memory in patients with temporal lobe epilepsy (TLE). Context-rich memory tasks consisted of two tests—the logical memory subtest of the WMS-III and the ROCF—composed of several isolated elements (words, drawings) embedded within a context (words are linked together within a narrative context, parts of the figure are linked together within a spatial context). Context-free memory tasks included three single-item recognition memory tests (for details of procedures, please refer Tramoni et al.). Recognition was then tested at 1 h and 6-week delays in a two forced-choice procedure. Performance of TEA patients was compared with that obtained by control subjects using the nonparametric Mann-Whitney U test.

**Interictal 18F-FDG-PET study**

Interictal brain metabolism was studied in 22 of 30 patients (mean age 63.2 ± 8.0 years), according to the same protocol for 22 age-matched healthy controls (mean age 62.5 ± 10.7 years). PET scan was performed using an integrated PET/computerized tomography (CT) camera (Discovery ST; GE Healthcare, Waukesha, WI, U.S.A.) using 150 MBq of 18F-FDG that was injected intravenously in an awake and resting state, with eyes closed, in a quiet environment. Whole-brain statistical analysis was performed at voxel-level using SPMS software (Welcome Department of Cognitive Neurology, University College, London, United Kingdom). Significant regions of hypometabolism in the patients were sought in comparison to healthy subjects.

**Results**

**Clinical and EEG data**

The clinical characteristics of the patients are indicated in Table S1.

This series included 18 men (60%). The mean age of onset of amnestic attacks was 59 years (range 43–77 years), whereas the mean age at the time of diagnosis was 62 years (i.e., diagnostic delay of 3 years on average, several weeks to 13 years). The first consultation was motivated by memory complaints in 16 patients (53%), and only 7 patients (23%) were referred directly for investigation of epilepsy. Most patients had no history of neurologic disorder prior to the onset of amnestic attacks. In fifteen patients (50%), a negative emotional life event (illness, death of a relative, retirement, and so on) had occurred soon before the beginning of symptoms. Ten patients (33%) had a past or current history of depression. Nine patients (30%) had an autoimmune disorder or biologic abnormalities (Table S1). A history of seizures was found in a first-degree relative in three patients (10%), one of them having been diagnosed as TEA.

**Amnestic attacks and seizures**

Seven patients (23%) experienced attacks that lasted <5 min, 11 patients (37%) had attacks from 5 to 10 min in
duration, and 4 patients (13%) from 30 to 60 min. For the remaining eight patients (27%), attacks could exceed 1 h. Regarding the frequency of seizure, 13 patients (43%) experienced from 1 to 10 attacks per year, 13 patients (43%) experienced 1–10 attacks per month, and 3 patients (10%) experienced 1–10 attacks per week. Only one patient reported attacks that occurred several times a day. In all cases, attacks occurred during the daytime, but in five patients (17%) they also occurred at night. Attacks on awakening were present in 23% of cases (seven patients). Pure acute amnesia was the sole epileptic manifestation in five cases (17%). During these episodes, patients typically exhibited an appropriate behavior while pursuing their ongoing activity and, afterwards they had little or no recollection of the episode. They were occasionally perplexed and anxious (11 patients, 37%), with repetitive questioning (six patients, 20%) or confused, having incoherent speech, and time and/or space disorientation (13 patients, 43%). Afterwards, 10 patients (33%) could provide a partial account of the episode, whereas for the remaining 20 patients (67%), amnesia of the episode was complete.

Twenty-four patients (80%) reported additional epileptic phenomena such as autonomic changes (seven patients), fear and strong anxiety (seven patients), rising epigastric sensation (seven patients), myoclonic jerks (six patients), déjà vu (five patients), oral alimentary automatisms (four patients), language disturbance (three patients), prolonged state of unconsciousness (two patients), olfactory hallucinations (two patients), and hyperthermia (one patient). Secondary generalized tonic–clonic seizures occurred in three patients (10%).

Interictal EEG abnormalities were present in 17 patients (57%) on awake recording and in most patients who performed sleep EEG (23/24: 96%). Activation of epileptiform activity during sleep was found in 20 patients (83%). Fully normal sleep EEG was observed in only one patient.

Interictal epileptiform features were various and included focal spikes, sharp waves, spike-waves, or theta activity. Abnormal activity was recorded predominantly by temporal electrodes: bilaterally in 16 patients (53%), right-sided in 7 (23%), and left sided in 6 (20%).

In one patient, a seizure was recorded during video-EEG monitoring. EEG showed ictal rhythmic theta discharges alternating between left and right temporal derivations.

### Interictal memory disturbances

**Standard neuropsychological assessment**

Neuropsychological assessment was completed in all 30 patients with TEA (Table 1). In comparison to normative data, group analysis demonstrated no significant deficit on any aspect of the battery. Nevertheless, important between-subject variability was noted, as 9 of 30 patients showed anterograde memory deficit, whereas 6 of 30 exhibited mild executive functioning impairment.

### Table 1. Neuropsychological profile of patients with TEA (n = 30)

<table>
<thead>
<tr>
<th>Neuropsychological measure</th>
<th>Mean scores of TEA patients (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Retrograde memory scores (AMI)</strong></td>
<td></td>
</tr>
<tr>
<td>Semantic subscale</td>
<td></td>
</tr>
<tr>
<td>Childhood (cutoff = 11)</td>
<td>17.29 (3.3)</td>
</tr>
<tr>
<td>Adulthood (cutoff = 14)</td>
<td>18.2 (2.3)</td>
</tr>
<tr>
<td>Recent period (cutoff = 17)</td>
<td>20 (1.4)</td>
</tr>
<tr>
<td><strong>Episodic subscale</strong></td>
<td></td>
</tr>
<tr>
<td>Childhood (cutoff = 3)</td>
<td>5.4 (2.4)</td>
</tr>
<tr>
<td>Adulthood (cutoff = 3)</td>
<td>5.1 (2.2)</td>
</tr>
<tr>
<td>Recent period (cutoff = 5)</td>
<td>5.7 (2.5)</td>
</tr>
<tr>
<td>WMS-III story recall subtest&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Immediate</td>
<td>11.0 (2.86)</td>
</tr>
<tr>
<td>Delayed</td>
<td>10.9 (2.86)</td>
</tr>
<tr>
<td>Rey figure delayed recall (36)</td>
<td>19.6 (6.88)</td>
</tr>
<tr>
<td>RL-RI16</td>
<td></td>
</tr>
<tr>
<td>Free delayed recall (16)</td>
<td>9.5 (3.6)</td>
</tr>
<tr>
<td>Total (free + cued) delayed recall (16)</td>
<td>14.6 (2.76)</td>
</tr>
<tr>
<td><strong>Language/semantic memory scores</strong></td>
<td></td>
</tr>
<tr>
<td>Picture naming (80)</td>
<td>79.5 (1.05)</td>
</tr>
<tr>
<td>Pyramid and palm tree test (52)</td>
<td>51.4 (0.7)</td>
</tr>
<tr>
<td>WAIS-III information subtest&lt;sup&gt;b&lt;/sup&gt;</td>
<td>12.1 (3.44)</td>
</tr>
<tr>
<td><strong>Executive function scores</strong></td>
<td></td>
</tr>
<tr>
<td>Trail making test A (time in seconds)</td>
<td>46.3 (18.3)</td>
</tr>
<tr>
<td>Trail making test B (time in seconds)</td>
<td>118.0 (59.19)</td>
</tr>
<tr>
<td>Letter fluency (words/2 min)</td>
<td>20.8 (8.76)</td>
</tr>
<tr>
<td>Category fluency (words/2 min)</td>
<td>31.2 (10.27)</td>
</tr>
<tr>
<td>WCST categories completed (6)</td>
<td>5.4 (1.25)</td>
</tr>
<tr>
<td>WCST total errors</td>
<td>6.4 (5.63)</td>
</tr>
<tr>
<td>Stroop interference procedure (time in s)</td>
<td>74.7 (22.23)</td>
</tr>
<tr>
<td>WAIS-III digit span subtest&lt;sup&gt;c&lt;/sup&gt;</td>
<td>9.4 (2.99)</td>
</tr>
<tr>
<td><strong>Visuospatial perception score</strong></td>
<td></td>
</tr>
<tr>
<td>Rey figure copy (36)</td>
<td>23.6 (4.01)</td>
</tr>
<tr>
<td>Benton face perception (54)</td>
<td>46.2 (4.02)</td>
</tr>
<tr>
<td>Benton line orientation (30)</td>
<td>34.2 (2.88)</td>
</tr>
<tr>
<td>Praxis (29)</td>
<td>28.6 (0.4)</td>
</tr>
</tbody>
</table>

Numbers in brackets in the first column refer to maximum scores. Scaled scores: *m = 10 ± 3.

**Autobiographical memory**

Table 1 shows the mean scores according to period of life of patients at the AMI. On the semantic subscale, only one patient scored below cutoff for each time period. This is in sharp contrast to performance on the episodic subscale, with five patients scoring below cutoff for childhood and adulthood periods and 11 patients for the recent period.

Figure 1A indicates the mean scores according to period of life for patients compared with normative data at the TEMPau task. Results demonstrated a significant loss covering the last 5 years (24/30 patients had z-score < −1.14) and the 12 last months (13/30 patients had z-score < −1.14). For the recent period, the collected episodes had occurred mainly in the several weeks prior to assessment, in agreement with the patients’ reports.
Long-term consolidation in the ALF subgroup

Performances of ALF patients and controls at recognizing single items and elements that compose stories and the ROCF are shown in Figure 1B–D (1 h and 6-week delays). No significant difference was found between the two groups in recognition of single items at 1 h (p = 0.185) and at 6-week delays (p = 0.481; Fig. 1B).

Although no significant difference was found between the two groups in recognizing stories (p = 0.085) and the ROCF (p = 0.481) at the 1-h time point, a group effect was found at the 6-week time point (p < 0.01; Fig. 1C,D).

Antiepileptic medication and clinical outcome

The mean duration of follow-up was 2.8 years (range 3 months to 12 years; Table S1). Antiepileptic drugs were introduced after the completion of the first neuropsychological evaluation and always after imaging and EEG (including sleep EEG) investigations. Antiepileptic drugs were used in 28 patients (93%), usually based on monotherapy (26 patients, 93%), but six patients required a combination of two drugs. Lamotrigine was the most used drug (96%). Outcome under treatment was considered to be favorable in the majority of cases for whom follow-up data were available (26 cases, follow-up [FU] > 6 months). Seizure freedom was observed in 19 (73%) of 26 cases, whereas a significant reduction in seizure frequency (>50%) was observed in the remaining cases (27%).

With regard to memory complaints, 12 patients were evaluated 1 year after treatment initiation. All patients reported a subjective improvement in their memory abilities. Nevertheless, statistical analysis yielded no significant improvement when comparing standard neuropsychological measures obtained before and after treatment. However, a significant improvement was noted in the recollection of autobiographical memory for the last 5-year and last 12-month periods (p = 0.01; nonparametric Wilcoxon test; Fig. 2).

Neuroimaging data

Magnetic resonance imaging

In most cases, magnetic resonance imaging (MRI) revealed no morphologic change (21 cases, 70%) or nonspecific abnormalities (Table S1).

18F-FDG-PET

In comparison with healthy subjects, patients with TEA showed significant hypometabolism (22 cases, 75.86%) within bilateral middle frontal gyri (BA6), and within left
medial, superior, precentral, and paracentral gyri (BA6, BA31; p < 0.05, corrected; Table 2 and Fig. 3A). With use of medial temporal mask, additional hypometabolism was found within the right posterior parahippocampus (BA36) and left uncus (BA28; p < 0.005, uncorrected; Table 2 and Fig. 3B,C).

To explore further the neural basis of memory disturbances, we performed additional correlation analyses between cognitive scores and the five significant clusters of decreased metabolism. Only medial temporal clusters were found to correlate with cognitive measures. In particular, we observed positive correlations between the left uncus metabolism level and the following:

- standard anterograde memory scores: immediate (p = 0.01) and delayed recall (p = 0.02) of the ROCF, delayed recall of the RL-R116 (p = 0.005),
- long-term anterograde memory scores: 6 week-delay word recognition (p = 0.016),
- retrograde memory scores: total AMI (p = 0.035) and episodic AMI scores (p = 0.016).

We also observed positive correlations between the right parahippocampal metabolism and place recognition (1 h delay; p < 0.01) and story recognition (6-week delay; p < 0.05).

## Discussion

**Electroclinical presentation**

To date, only one large series of TEA, which included 50 patients, has been published. As reported previously, TEA occurs in middle-age individuals, usually between 50 and 60 years of age, with a male predominance. The etiology underlying TEA remains poorly understood. An autoimmune context was found in a particularly high proportion of our patient series (30%). Although a chance association between unrelated conditions cannot be excluded, this observation raises interesting issues about potential pathophysiologic mechanisms.

Amnestic attacks were the main ictal manifestations. They occurred on waking in only 23% of our patient series. This contrasts with the frequent occurrence of transient amnesia upon waking previously reported in TEA (74% of cases in the series of Butler et al.). Only 23% of the patients of this current series were referred to an epileptologist after the first epileptic event. The diagnosis of epilepsy remains particularly difficult when pure acute amnesia is the sole manifestation of seizure. This occurred in 17% of our cases. During typical amnestic seizure, there is no confusion or altered consciousness. These manifestations share several characteristics with other transient amnestic states, such as transient global amnesia (TGA), including the inability to form new memories (anterograde amnesia) along with variable

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Table 2. PET hypometabolism in patients with TLE, in comparison to healthy subjects

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Cluster p(FWE-cor)</th>
<th>Cluster k</th>
<th>Peak p(FDR-cor)</th>
<th>Peak T</th>
<th>Peak p(unc)</th>
<th>Tailairach coordinates x</th>
<th>y</th>
<th>z</th>
<th>Localization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole-brain</td>
<td>0.045</td>
<td>482</td>
<td>0.040</td>
<td>5.22</td>
<td>&lt;0.001</td>
<td>36 -5 50</td>
<td></td>
<td></td>
<td>Right middle frontal gyrus (BA6)</td>
</tr>
<tr>
<td></td>
<td>0.000</td>
<td>1,588</td>
<td>0.040</td>
<td>5.03</td>
<td>&lt;0.001</td>
<td>34 10 53</td>
<td></td>
<td></td>
<td>Right middle frontal gyrus (BA6)</td>
</tr>
<tr>
<td></td>
<td>0.040</td>
<td>4.32</td>
<td></td>
<td>&lt;0.001</td>
<td>31 0 39</td>
<td>Left precentral gyrus (BA6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.040</td>
<td>4.88</td>
<td></td>
<td>&lt;0.001</td>
<td>44 4 48</td>
<td>Left middle frontal gyrus (BA6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.040</td>
<td>4.85</td>
<td></td>
<td>&lt;0.001</td>
<td>36 3 48</td>
<td>Left middle frontal gyrus (BA6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.040</td>
<td>4.68</td>
<td></td>
<td>&lt;0.001</td>
<td>36 3 48</td>
<td>Left middle frontal gyrus (BA6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTL mask</td>
<td>0.255</td>
<td>117</td>
<td>0.284</td>
<td>3.23</td>
<td>0.001</td>
<td>28 -39 -5</td>
<td></td>
<td></td>
<td>Right parahippocampal gyrus (BA36)</td>
</tr>
<tr>
<td></td>
<td>0.426</td>
<td>35</td>
<td>0.284</td>
<td>2.86</td>
<td>0.003</td>
<td>36 -36 -12</td>
<td></td>
<td></td>
<td>Right parahippocampal gyrus (BA36)</td>
</tr>
</tbody>
</table>

Results from SPM8 are listed in decreasing order of peak T-score value within each cluster. Cor, corrected; unc, uncorrected; FWE, family-wise error; FDR, false discovery rate. k value represents the number of significant voxels in the particular cluster. x, y, and z are the Tailairach coordinates (mm).
amnesia for recent events (retrograde amnesia). Repetitive questioning is classically less observed in TEA attacks than in TGA, interpreted as a consequence of partial rather than global anterograde amnesia. This feature has been reported, however, in about 50% of patients of the series of Butler et al. and was present in 20% of our cases.

The diagnosis of epileptic seizures is dramatically facilitated when TLE seizure symptoms are also present, such as déjà vu, automatisms, epigastric and olfactory auras. They were found in >80% of our patients but were not systematically associated with amnestic episodes.

Interictal EEG abnormalities usually reported in TEA include background slowing and epileptiform discharges, involving one or both hemispheres, over temporal or fronto-temporal electrodes. However, awake EEG revealed no abnormal activity in up to 31% of patients in the series of Butler et al. and 43% of the current study. Sleep EEG recording was particularly useful in this context showing epileptiform abnormalities in about 96% of our patient series.

Interictal memory disturbances
Interictal memory impairment was the main manifestation for seeking medical attention in about half of our patients. This observation is consistent with those of previous reports in which memory complaints preceded the full-blown syndrome by several years. Most of our patients performed within normal range on standardized memory measures, as mentioned in previous reports.

The combination of accelerated long-term forgetting (ALF) and remote autobiographical memory loss constitute the most characteristic features of interictal memory deficit in TEA. This pattern of ALF and autobiographical memory loss has also been described in other types of temporal lobe epilepsy (TLE). Several pathophysiologic factors could contribute to the occurrence of ALF, including the role of seizures, of interictal EEG abnormalities, and associated structural lesions.

However, in the current study, this typical association (ALF and autobiographical memory loss) was observed in only 16 of 30 patients. Retrograde memory loss typically involves the episodic component of autobiographical memory, whereas semantic knowledge of life events is impeded to a lesser extent. In some patients, the childhood and most recent periods were less affected, conferring a peculiar U-shape profile to the memory loss.

ALF, which is the excessively rapid loss of newly acquired memories over a period of days or weeks, has also been documented in previous studies that focus on patients with TEA. ALF may not be global but material-specific, that is, selective to certain material kinds such as episodic memory. In a recent study, we documented this hypothesis and demonstrated dissociated long-term consolidation of contextually bound experiences (including episodic memory, impaired) and context-free information (semantic knowledge and single item, preserved). The present study replicates these findings in the subgroup of patients (16/30; “ALF subgroup”) showing intact recognition of single items at 6-week delay, whereas recognition of complex material...
such as stories and ROCF at the same time point was impaired.

**Treatment responsiveness**

Most of our patients experienced a complete resolution of amnesic attacks or a markedly reduced frequency (as reported in previous studies).\(^9,10,14,31,32\) Subjective memory improvement is often reported after treatment initiation.\(^9,10,14\) as in the current study. However, direct comparison between pretreatment and posttreatment memory performance has been undertaken on rare occasions. In a recent study focusing on three patients with TEA, cognitive functions were assessed before and 6 months after initiation of antiepileptic therapy. A persistent decline in remote autobiographical memory despite full resolution of amnestic seizures was demonstrated.\(^33\) Here, we found no significant improvement on standard neuropsychological measures obtained before treatment and 1 year following treatment initiation. Although ALF was not formally reassessed at the 1-year time-point, recollection of autobiographical events was found to improve. Of interest, autobiographical memory improvement was significant only for the most recent period, suggesting that reduced ALF may have, at least partly, contributed to this recovery.

**Neuroanatomic correlates**

Although the precise anatomic substrates of TEA remain to be established, several lines of evidence suggest a strong implication of the medial temporal lobe (MTL). In addition, mild metabolic hippocampal changes have been reported in a group study combining 18F-FDG-PET and magnetic resonance spectroscopy imaging.\(^15\) In a volumetric study, there was mild volume reduction in both hippocampal bodies.\(^34\) These authors also found a positive correlation between hippocampal volume and performance on visual memory performance but no correlation with ALF or autobiographical memory scores.\(^34\) This leads to the suggestion that ALF and autobiographical memory impairment could result from a diffuse anatomic dysfunction rather than from focal MTL damage. Our PET findings do not support this view, as correlation analysis showed that medial temporal clusters and the parahippocampal cortex (PHC) correlated not only with verbal and visual anterograde memory performance but also with long-term anterograde memory (6-week delay word and story recognition) and retrograde memory (total AMI and episodic AMI) scores. This result is in agreement with a recent study that has investigated patients with TEA using a functional MRI (fMRI) anterograde memory paradigm. In comparison with controls, patients showed reduced activation of the posterior parahippocampal gyrus (pPHG) and a reduced effective connectivity between the right pPHG and the right middle temporal gyrus.\(^35\)

However, dysfunction may encompass medial temporal regions in comparison with controls. These data are coherent with the known architecture of the episodic memory network. fMRI studies have demonstrated that, in addition to temporal and retrosplenial/cingulate cortices, prefrontal regions are associated with autobiographical recollection.\(^36,37\) In addition to recollection, prefrontal cortices may also participate in consolidation processes via the early tagging of information to ensure the progressive hippocampal-driven rewiring of cortical networks that support remote memory storage.\(^38\)

Taken together, interictal memory impairment in TEA is probably sustained by neural dysfunction that impedes the hippocampal–neocortical interplay necessary to form and stabilize new memory traces, but also to recollect remote experiences.\(^39\)

**Conclusion**

The present series largely confirms previous reports including seizure occurrence in middle-age subjects that comprise amnestic features and other TLE symptoms. Impaired remote autobiographical memory and ALF, which were frequently the main cause of seeking medical attention, were also noted. Additional features include the frequent occurrence of depression and association with autoimmune disorders, raising interesting issues regarding putative pathophysiologic mechanisms. Furthermore, neurometabolic data support a dysfunction of a hippocampal–neocortical network sustaining episodic memory.

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**Disclosure**

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

**References**


**Supporting Information**

Additional Supporting Information may be found in the online version of this article:

**Data S1.** Neuropsychological testing and Interictal F18-FDG-PET study (detailed methodology).

**Table S1.** Clinical data in patients with TEA (n = 30).

**Table S2.** EEG data in patients with TEA (n = 30). WE, waking EEG.