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Memory for emotional material in temporal lobe epilepsy

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ABSTRACT

Several studies suggest that highly emotional information could facilitate long-term memory encoding and consolidation processes via an amygdala-hippocampal network. Our aim was to assess emotional perception and episodic memory for emotionally arousing material in patients with temporal lobe epilepsy (TLE) who are candidates for surgical treatment. We did this by using an audiovisual paradigm. Forty-six patients with medically resistant TLE (26 with left TLE and 20 with right TLE) and 19 healthy controls were assessed with a standard narrative test of emotional memory. The experimental task consisted of sequential picture slides with an accompanying narrative depicting a story that has an emotional central section. Subjects were asked to rate their emotional arousal reaction to each stimulus after the story was shown, while emotional memory (EM) was assessed a week later with a multiple choice questionnaire and a visual recognition task. Our results showed that ratings for emotional stimuli for the patients with TLE were significantly higher than for neutral stimuli ($p = 0.000$). It was also observed that patients with TLE recalled significantly less information from each slide compared with controls, with a trend to lower scores on the questionnaire task for the group with LTLE, as well as poorer performance on the visual recognition task for the group with RLTE. Emotional memory was preserved in patients with RTLE despite having generally poorer memory performance compared with controls, while it was found to be impaired in patients with LTLE.

1. Introduction

Why do we remember the events that occurred on September 11th 2001 but not what happened the day before? Why can we describe vivid details about our wedding day but barely remember a workday last year? Past studies have found that emotionally arousing events are more often retrieved than neutral or nonsignificant events [1]. Once retrieved, emotionally arousing events are frequently recalled with high accuracy and vividness [2] and sometimes involve trivial aspects like incidental sights or sounds [3].

Emotion is known to modulate declarative forms of memory [4] by improving the initial encoding of a memory trace [5] and its consolidation [6]. Prior research has shown that the hippocampal-amygdalar network fulfills an important role during these processes [7]. The modulation hypothesis states that the amygdala mediates the encoding and storage of emotionally arousing material, while the hippocampus is involved in the retrieval of the emotion-related declarative memory (EM) [8,9] and in the formation of "episodic representations of the emotional significance and interpretation of events" [7,10,11].

Both the amygdala and the hippocampus are activated during emotional events and interact actively to form long-term memories of these events [12]. Most of the research in EM has been carried out in subjects with amygdala damage [8,13,14], showing that the memory enhancement benefit is lost in patients with bilateral amygdala lesions and diminished in those with unilateral damage [15]. Patients with medial temporal lobe epilepsy (MTLE) provide a unique opportunity to systematically explore different memory processing aspects of emotional content. These patients allow us to consider the hippocampus-amygdalar involvement that could be mediated by seizure onset or by the connectivity of neural networks related to the spreading of the seizure, as well as variable changes in other cortical areas.

Previous research on emotional memory in patients with TLE yielded controversial results depending on the type of task used and if they were focused on presurgical and postsurgical patients. Thus, memory enhancement for highly emotional stimuli has been reported as reduced despite normal perception of emotional stimuli [16,17] or showing similar benefits (implying advantages or enhanced likelihood of remembering it later) as controls [18]. Most prior studies with

Abbreviations: EM, emotional memory; TLE, temporal lobe epilepsy; LTLE, left temporal lobe epilepsy; RTLE, right temporal lobe epilepsy; EZ, epileptogenic zone.

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postsurgical patients, and a few conducted in nonresected patients with TLE, have suggested that emotional memory enhancement varies depending on the association with an amygdalar lesion [19].

The present study aimed to explore the involvement of the hippocampal–amygdalar complex in emotional perception and EM in patients with TLE cleared for surgical treatment using an audiovisual story paradigm. We administered a test that has previously been used on different clinical populations [3,8,10,13,15,20] including postsurgical patients with TLE [18] but not presurgical patients with TLE.

2. Material and methods

2.1. Participants

Forty-six patients with pharmacoresistant temporal lobe epilepsy (TLE) and who were candidates for surgical treatment (between 18 and 53 years) were examined at the Epilepsy Center of the Ramos Mejia Hospital in Buenos Aires and at the National Neuroscience and Neurosurgery Center, El Cruce “Dr. Nestor Carlos Kirchner” Hospital in Florencio Varela (Argentina). Patients were matched for age, education, and sex with 19 healthy control subjects. Only patients with a full-scale IQ of >70 (WASI) and without history of psychiatric disorders or other neurological diseases were included (Table 1).

All subjects gave written informed consent approved by the Institutional Ethics Committee at Ramos Mejia Hospital, which follows the guidelines of the Declaration of Helsinki.

In order to determine lateralization and localization of the epileptogenic zone (EZ), video-EEG monitoring and magnetic resonance imaging (MRI) testing were performed for each patient. A neuropsychological assessment was performed according to the EC presurgical protocol using the z-score value of −2 as the cutoff [21,22].

2.2. Experimental tasks

To assess EM, we used two similar tasks, the Heuer and Reisberg test [3] (Task A) and its modified version developed by Cahill and others [8,10,13,20] (Task B). The first stage of our procedure, which was carried out 4 to 12 months prior to surgery, consisted of baseline testing sessions where both tasks (A and B) were randomly administered among participants. The second stage was carried out only in those patients who underwent surgery and is not reported here because of ongoing testing. To avoid content-learning effects between stages, participants were tested with different tasks at baseline (e.g., Task A) and when they were operated on (e.g., Task B).

The first story (Task A) contained a set of 11 pictures about a boy who suffers a terrible car accident on his way to visit his father at work and how he has to be rushed to the operating room at the hospital. The second story (Task B) included a total of 12 photos depicting a story about a son visiting his father at his workplace, who turns out to be a surgeon assisting a victim of an accident, and the child seeing him performing the surgery. Both verbatim narratives (A and B) were translated to Spanish from a previous published version [8]. Some original pictures were replaced to make them more relevant to Argentinean culture but maintaining the same structure and grouping emotionally arousing stimuli as the original ones. The stimuli adapted were as follows: woman with child, bus stop, hospital entrance, and police station. Both tasks comprised a series of sequential picture slides and an accompanying narrative depicting a story. Each story included an emotional central segment (phase 2: slides 5–8) preceded by a section that set the scene (phase 1: slides 1–4) and followed by the repercussions of the main event (phase 3: slides 9–12). The first and third sections were neutral or nonemotional.

The slides were projected on a computer screen using E-prime version 1.0 and were shown along with the previously recorded narrative. Participants were told to pay attention to the story to rate the emotional reaction after the presentation. Memory tests were incidental since participants were unaware that they had to retrieve any kind of information.

After the slides were shown, we carried out a set of tasks [8,13]:

1 Emotional personal reaction: immediately after the presentation, each stimulus was shown once again, and participants were asked to rate their emotional arousal reaction to each of the slides on a scale from 1 to 10 (1 = none, 10 = high impact).
2 Questionnaire: EM was assessed a week after the story was shown using a multiple choice questionnaire [3,8] translated to Spanish, which asked ten questions per slide. Each question was displayed on a computer screen using E-prime version 1.0 and included four possible answers, which resulted in a chance response level of 25%. Subjects had to press the number of the response they considered correct using a keyboard in order to continue to the next question. The questionnaire was conducted a week later because the results are going to be compared with a postsurgical assessment, when the critical recovery period is over.
3 Visual recognition memory: after the questionnaire, subjects were shown the original pictures and 20 lures (e.g., pictures that showed a similar situation but in a different place) on a computer screen using E-prime version 1.0. Subjects had to indicate whether or not they had previously seen the image, using a keyboard. Response latencies to each picture were automatically recorded. Thirty-two subjects with TLE (19 with left TLE and 13 with right TLE) and eighteen control subjects participated in this task.

2.3. Statistical analysis

The group with TLE and the control group were matched for age, sex, and formal education. For each patient, the raw values of every cognitive test in the neuropsychological battery were normalized to a z-score and classified as a ‘deficit’ for values less than or equal to −2.

We compared performance on the personal emotional reaction and emotional memory tasks of the group with LTLE and the group with RTLE with that of the control group using Student's *t*-test, one-way ANOVA analysis, Bonferroni correction post hoc test, nonparametric test (Wilcoxon), and Pearson correlation coefficient r. The slight difference between Task A and Task B was adjusted to run the analysis.

All comparisons that were significant at the $p < 0.05$ level were reported. Statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS version 20).

3. Results

3.1. Emotional personal reaction

A paired samples *t*-test indicated that, as expected, subjects with TLE and control subjects endorsed significantly higher subjective ratings in highly emotional compared with neutral stimuli: for phase 2 versus phase 1: TLE − $t(44) = -10.72$, $p = 0.000$; controls − $t(18) = -8.98$, $p = 0.000$ and for phase 2 versus phase 3: TLE − $t(44) = 7.96$, $p = 0.000$; controls − $t(18) = 6.68$ $p = 0.000$. We observed that patients with TLE tended to assign higher scores compared with controls in each phase, with a statistically significant difference in phase 1 ($t(57.91) = 2.43$; $p = 0.018$) and phase 2 ($t(62) = 2.57$; $p = 0.013$) (Fig. 1). There was no effect of EZ side in any phase. When subjects' ratings for each picture were analyzed, results did not show relevant differences between subjects with TLE and control subjects, with no effect of EZ side.

3.2. Questionnaire of emotional memory

Patients with TLE retrieved significantly less information for each stimulus (highly emotional and neutral) compared with the control group ($p < 0.05$; Student's *t*-test). The group with LTLE obtained lower

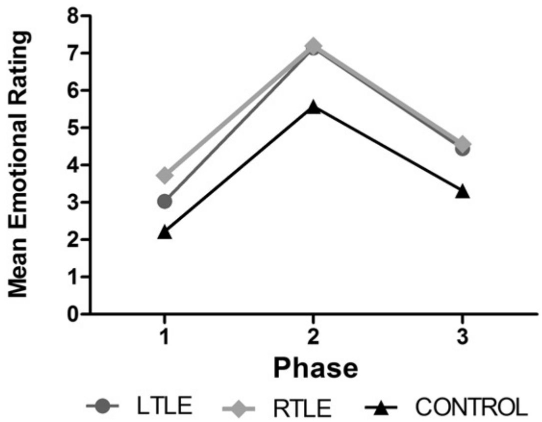

Fig. 1. Emotional reaction ratings. Mean per phase (phase 1: slides 1–4; phase 2: slides 5–8; and phase 3: slides 9–12).

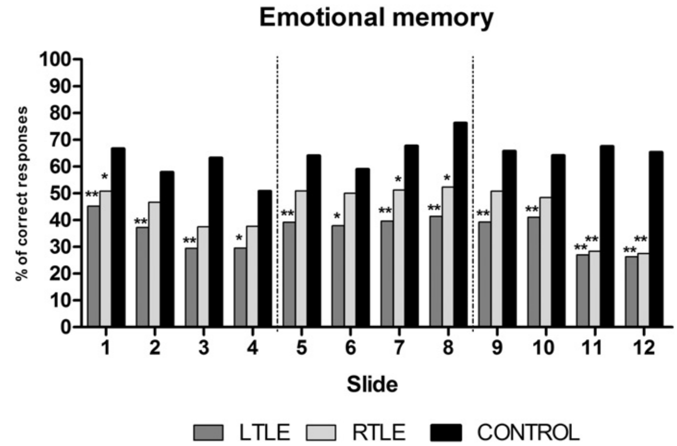

Fig. 2. Percentage of correct responses per slide on a week delayed multiple choice questionnaire. Statistical differences are between the group with LTLE/RTLE and the control group. *$p < 0.05$; **$p < 0.01$.

scores compared with the group with RTLE for each stimulus with no statistically significant differences (Fig. 2).

Comparisons performed using a two-tailed Student's *t*-test showed that patients with TLE recalled significantly less information for each phase compared with the control patients (Table 2), and no differences were found between the group with LTLE and the group with RTLE.

A paired sample Student *t*-test showed that emotional stimuli (phase 2) induced memory enhancement compared with the neutral stimuli in subjects with TLE (versus phase 1: $t(45) = -2.20$, $p = 0.033$; versus phase 3: $t(45) = 3.75$, $p = 0.000$; two-tailed test) as well as in controls (phase 2 versus phase 1: $t(18) = -3.00$, $p = 0.008$). In the group with RTLE, the proportion of correct responses for emotional stimuli was significantly higher than for neutral ones (phase 2 versus phase 1: $p = 0.034$; phase 2 versus phase 3: $p = 0.002$; Wilcoxon test) (Fig. 3). Subjects with LTLE also displayed higher scores during phase 2, but unlike the group with RTLE, the difference was not statistically significant when compared with the other phases (versus phase 1: $p = 0.353$; versus phase 3: $p = 0.067$; Wilcoxon test) (Fig. 3).

3.3. Visual recognition memory

A one-way ANOVA showed a main effect of group on visual recognition memory for target pictures ($F(2, 46) = 7.235$, $p = 0.002$). A post hoc analysis (Bonferroni) revealed that both the group with LTLE ($M = 8.24$, $SD = 2.66$) and the group with RTLE ($M = 8.64$, $SD = 1.45$) recognized significantly less target stimuli compared with controls ($M = 10.50$, $SD = 1.10$). The most shocking stimulus (slide 8) was correctly recognized for all subjects in the group with RTLE and for 89.5% of the subjects with LTLE (Fig. 4). It was also found that patients with RTLE displayed higher false recognition of lures compared with controls ($F(2, 46) = 8.92$, $p = 0.000$). No differences between the group with RTLE and the group with LTLE were found.

Response latency during visual recognition of new stimuli was statistically longer in patients with RTLE ($F(2, 46) = 7.66$, $p = 0.001$) than in controls. No differences were observed between patients with LTLE and controls or between patients with RTLE and patients with LTLE.

Table 1
Demographic, clinical, and neuropsychological variables of subjects.

	Subjects with LTLE	Subjects with RTLE	Controls
N	26	20	19
Age	35.12 (9.63)	32.05 (8.92)	30.32 (8.72)
Education	12.42 (3.53)	12.10 (2,93)	14.05 (3.34)
Age at seizure onset (years)	14.50 (9.78)	9.75 (6.71)	NA
Duration of epilepsy (years)	20.62 (12.82)	22.25 (12.59)	NA
Sex: male/female	14/12	10/10	9/10
Handedness: left/right	3/23	6/14	2/17
MRI	HS: 17 O: 6 N: 3	HS: 14 O: 4 N: 2	NA
IQ (WASI)*	93.88 (13.34)	86.05 (11.19)	103.68 (11.06)
RAVLT-delayed z-score	−1.29 (1.14)	−1.09 (1.24)	NA
RCFT-delayed z-score	−1.08 (1.28)	−1.77 (1.35)	NA

Values are mean (SD) or n. HS: hippocampal sclerosis. O: other lesions (tumor, DNET, sequelar lesion, and dysplasia). N: normal/no lesion. IQ: intelligence quotient. WASI: Wechsler Abbreviated Scale of Intelligence. RAVLT: Rey Auditory Verbal Learning Test. RCFT: Rey Complex Figure Test.
* $p < 0.05$.

4. Discussion

This study explored EM performance of patients with TLE with unilateral medial temporal damage. Our findings showed that subjects with TLE endorsed higher subjective ratings to those stimuli that portrayed emotionally arousing scenes like surgery at a hospital or a damaged limb compared with those that represent neutral situations. This finding is consistent with studies that have described preserved emotional perception judgment in patients with TLE [14] but is in contrast to those showing that this process would be impaired in these patients, particularly after temporal lobectomy [23]. These different findings could be related to the heterogeneity of lesions and damage extension within the groups with TLE assessed. We also observed a tendency to assign higher ratings to each stimulus, including the neutral ones, in patients with TLE compared with controls, even though we did not compare the ability to rate another type of scenes that are not related to health issues. This outcome could be associated with diverse factors like stress due to chronic illness, their condition of being surgical candidates, and the impact of the hospital environment in their everyday lives.

Despite a generally poor performance on memory tasks in patients with TLE compared with control subjects, EM was preserved in patients

Table 2
Questionnaire of emotional memory. Mean proportion of correct responses per phase for the group with TLE and for the control group.

Phase	Group with TLE Mean (SD)	Control group Mean (SD)	Group with TLE versus control group (sig)
1	0.38 (0.16)	0.59 (0.15)	$p = 0.000$
2 − emotional	0.44 (0.21)	0.67 (0.12)	$p = 0.000$
3	0.36 (0.17)	0.65 (0.14)	$p = 0.000$

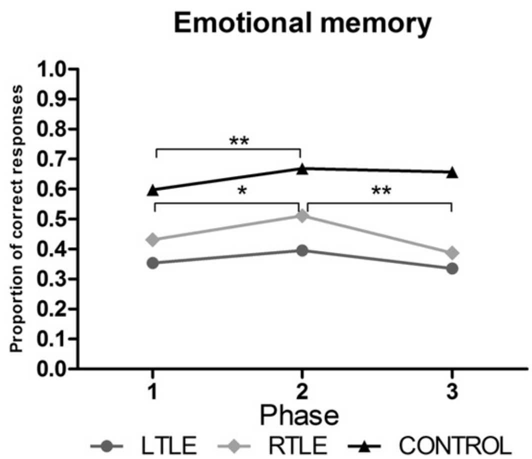

Fig. 3. Proportion of correct mean responses per phase on a multiple choice questionnaire. Intragroup significant differences between emotional and neutral phases. $^*p < 0.05$; $^{**}p < 0.01$.

with TLE as a whole, showing a benefit for highly emotional stimuli compared with neutral ones. Our findings are congruent with those that showed a preserved emotional benefit when comparing recall for emotional versus neutral stories in patients with TLE who had undergone temporal lobectomy [18]. Even though some authors found that EM was reduced despite preserved emotional perception in TLE before [16] and after temporal lobectomy [17], those studies used a variety of stimuli, and there could be sample differences. Nevertheless, regarding laterality, this emotional benefit seems to vanish for the group with LTLE as there was no significant difference between the emotional and neutral phases. This lack of an effect suggests an impaired EM in this group as seen in previous studies [13,14], where a deficit in EM was also observed in patients with left medial temporal lobe damage despite normal emotional judgment.

One point that deserves attention is the ability to maintain high performance in the last phase, which was observed in controls but not in patients with TLE. This finding suggests that the emotional stimuli per se would reinforce the consolidation and retrieval of additional information and that patients with TLE do not obtain this added benefit.

Additionally, we found a trend toward lower scores on the questionnaire task, which includes verbal and visual information, for the group with LTLE, while the group with RTLE showed poorer performance on the visual recognition task (longer reaction times and higher false alarms). Previous studies described a modality-specific

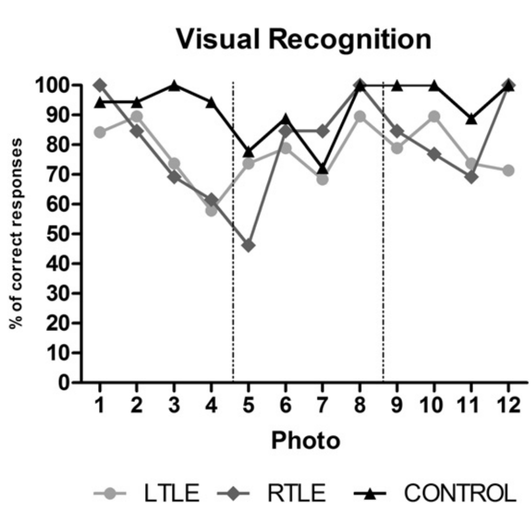

Fig. 4. Percentage of subjects by group with a correct recognition of target stimulus on visual recognition task.

amygdala modulation pattern whereby they found that patients with LTLE had poorer performance in recalling emotional stories if encoding was related to verbal material [14,18,24], while patients with RTLE showed more difficulty with recalling emotional visual-related or pictorial stimuli [14,25]. Nonetheless, other authors did not find differences related to EZ laterality [17,26].

Taking into account that in our sample the amygdala would be undamaged, but not the hippocampus, our findings are compatible with previous reports from Hamann et al. [27] where a double dissociation between EM and other memory systems was described. The authors reported that in patients with amnesia, regardless of etiology and lesion, and with mild-to-moderate verbal memory deficits, the emotional enhancing effect was unaltered during a recalled story. Conversely, declarative memory for an emotional story was selectively disrupted in patients with bilateral amygdala damage and spared hippocampus [8,28]. Even though patients with LTLE showed a trend toward an improved performance during the emotional phase, this difference was not significant when compared with the neutral phases. We could not attribute these findings to a material-specific memory deficit or to amygdala alterations within this group.

We assumed that our sample had no amygdalar lesions as MRI studies did not demonstrate any signal change, and this fact is consistent with normal emotional perception and a preserved emotional modulation for memory. However, we cannot reject amygdalar involvement as we did not perform additional analyses like MRI-based volumetry, which has been shown to be useful in detecting lesions in apparently normal structural MRI images [29,30].

Our results suggest that patients with TLE have preserved emotional perception and discrete enhancement of memory for emotional stimuli during a baseline assessment mainly observed in RTLE. Future work will analyze postsurgical performance of participants that have undergone anterior temporal lobectomy and compare it with the results of the present report.

Conflicts of interest

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.

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