Memory for facial expressions in patients with temporal lobe epilepsy: Preliminary findings

MARICARMEN URBÁN[1,2], DAVID TREJO[1], JOSÉ M. NÚÑEZ[1], ANA L. VELASCO[1], JOSÉ D. CARRILLO-RUÍZ[1,2], FRANCISCO VELASCO[1] AND JORGE L. ARMONY[3]

[1]Hospital General de México (México); [2]Universidad Anáhuac México Norte (México); [3]McGill University (Canadá)

Abstract

Temporal Lobe Epilepsy (TLE) is associated with memory and emotional impairments. However, the majority of previous studies examined patients after the affected structures (hippocampus and amygdala) were surgically removed, so it remains unclear to what extent these deficits are associated with the illness itself or are a consequence of the surgery. Thus, the objective of this study was to compare recognition memory for facial emotional expressions in pre- and post-surgery TLE patients, and its relationship to neuropsychological and clinical variables. We observed higher memory accuracy in pre-surgical patients than in those who had undergone surgery. Moreover, there was a significant positive correlation between the task and the executive functions and memory subtests of the neuropsychological battery, as well as a negative correlation with illness duration. These preliminary results suggest a possible effect of the surgical resection on memory, and highlight the importance of an early intervention for reducing cognitive decline.

Keywords: Temporal lobe epilepsy, emotional memory, amygdala, facial expressions.

Memoria para expresiones faciales en pacientes con epilepsia del lóbulo temporal: hallazgos preliminares

Resumen

La Epilepsia del Lóbulo Temporal (ELT) está asociada a problemas emocionales y de memoria. La mayoría de los estudios previos han examinado a pacientes después de que haya habido una extirpación quirúrgica de las estructuras afectadas (hipocampo y amígdala), por lo que continúa sin estar claro qué déficits son atribuibles a la propia enfermedad y cuáles son consecuencia de la cirugía. De este modo, el objetivo de este estudio fue comparar la memoria de reconocimiento para las expresiones emocionales faciales en pacientes con ELT pre y post-quirúrgicos y su relación con la evaluación neuropsicológica y otras variables clínicas. Observamos una mejor ejecución en la memoria en los pacientes pre-quirúrgicos en comparación con los que fueron sometidos a cirugía. Además, encontramos una correlación positiva significativa entre nuestra tarea y las subtareas de funciones ejecutivas y de memoria de la batería neuropsicológica, y una correlación negativa con la duración de la enfermedad. Estos hallazgos preliminares sugieren un posible efecto de la resección quirúrgica en la memoria y destacan la importancia de una intervención quirúrgica temprana para disminuir el deterioro cognitivo.

Palabras clave: Epilepsia del lóbulo temporal, memoria emocional, amígdala, expresiones faciales.

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Author's Address: Maricarmen Urbán Ruiz-Víquez. Clínica de Epilepsia del Hospital General de México. Escuela de Psicología, Universidad Anáhuac México Norte. Dr. Balmis No.148, Col. Doctores, Delegación Cuauhtémoc, C. P. 06726, México, D. F. Tel: 2789 ·2000 Ext. 1332. maricarmen.urban@gmail.com

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Introduction

Epilepsy is a neurological syndrome characterized by the continuous presence of seizures that arise from abnormal, excessive, synchronic and intermittent electrical activity in a group of neurons during a short period of time (varying from seconds to minutes). There are two main types of epileptic seizures (Lee, 2010), classified through clinical assessments and electroencephalography (EEG): generalized, in which there is impairment of consciousness, and focalized or partial, where patients are aware of everything that happens throughout the seizure. In the latter case, seizures are originated within a specific network of brain regions. In the case of Temporal Lobe Epilepsy (TLE), seizure propagation generally begins in the amygdala and/or hippocampus and is usually, though not always, associated with unilateral abnormalities in the EEG recordings.

Approximately 25 to 50% of TLE patients do not reach a satisfactory control of their seizures with anti-epileptic medicine (Engel, Williamson, & Wieser, 1997). In these patients with pharmacologically intractable focal epilepsy, surgical removal of the brain region where seizures are generated is currently the only effective treatment option to control their seizures (Wiebe, Blume, Girvin, & Eliasziw, 2001). Surgical resection involves exposing the amygdalo-hippocampal complex and removing the damaged tissue (Wieser, Engel, Williamson, Babb, & Gloor, 1993; Wyler, 1999). The extent of the resection is determined by hemispheric language dominance and the location of the epileptic focus. In general, it has been observed that 65 to 80% of the patients remain seizure-free after surgery.

Several studies have reported that post-surgical TLE patients exhibit deficits in memory and/or emotional tasks (Adolphs, Tranel, & Damasio, 2001; Orozco-Giménez et al., 2002; Phelps, LaBar, & Spencer, 1997). This is not surprising given the established role of the hippocampal complex and amygdala in memory formation and emotional processing, respectively. However, although much less studied, there is strong evidence that patients with TLE present impairments in several cognitive functions before surgery, including, but not restricted to, memory (Drake Allegri, & Thomson, 2000; Lee, 2010), as is often reported in the clinic, where pre-surgical patients are routinely evaluated with an extensive neuropsychological battery (Kubu, Lineweaver, & Chelune, 2003) to help determine the lateralization and possible location of the epileptic focus.

These impairments in memory in pre-surgical TLE are consistent with the fact that TLE is usually associated with mesial temporal sclerosis, a general histopathological term used to describe cell loss and astrocytic gliosis in the hippocampus, amygdala and entorhinal cortex. Although hippocampal sclerosis is the most frequent alteration observed in TLE, there are significant variations among patients in the degree, pattern and regional distribution of changes (de Lanerolle et al., 2003). Thus, the memory-related deficits observed in TLE patients before surgery are likely to be due, at least in part, to structural abnormalities in medial temporal lobe regions. Remarkably, there is growing evidence that anatomical lesions in TLE patients are not restricted to the temporal lobes but can extend to other brain regions, in particular the frontal lobes (Bernhardt, Bernasconi, Concha, & Bernasconi, 2010). Such findings could help explain the clinical observation that these patients have difficulties in accomplishing tasks that require executive functions (e.g., working memory), both before and after the surgery, as such functions are thought to rely heavily on the prefrontal cortex

In contrast to memory, emotional processing has rarely been assessed in TLE patients, especially prior to surgery. This is particularly relevant given that, as

mentioned previously, the amygdala is often damaged in these patients and, furthermore, the fact that TLE is associated with elevated levels of anxiety and depression. Moreover, it is currently unknown how these processes are affected by the surgical procedure that patients undergo to alleviate their epilepsy symptoms.

Thus, the goal of the present study was to explore memory for faces depicting different emotional expressions (neutral, happiness and fear) in patients suffering from refractory TLE before and after surgery, and to relate performance in this task with other clinical and neuropsychological variables. We chose this particular task as it integrates our two processes of interest, namely memory and emotion, and it has been shown to engage both the hippocampus and amygdala (Adolphs, Tranel, & Denburg, 2000; Buchanan, Denburg, Tranel, & Adolphs, 2001; LaBar & Phelps, 1998; Richardson, Strange, & Dolan, 2004). Although our long-term goal is to test the same individuals using the same task before and after surgery, here we present preliminary findings comparing data from different groups (pre- and post-surgery).

Methods

Sixty-three patients (28 female; mean age 29 years old, range: 11-62) with Temporal Lobe Epilepsy participated in the study. Of these, 37 were tested before surgery, 18 after and 8 tested before and after. The distribution of sex, age, lateralization and surgical status is summarized in Table I. Forty-nine of these patients also completed a neuropsychological battery normalized for Mexican population that includes a wide range of tests for visual and verbal memory as well as executive functions (Ostrosky-Solis, Ardila, A., & Roselli, 1999; Ostrosky-Solis et al., 2003).

TABLE I

Demographic and clinical characteristics of the patients. Values for years represent the mean of the group with the range in parenthesis

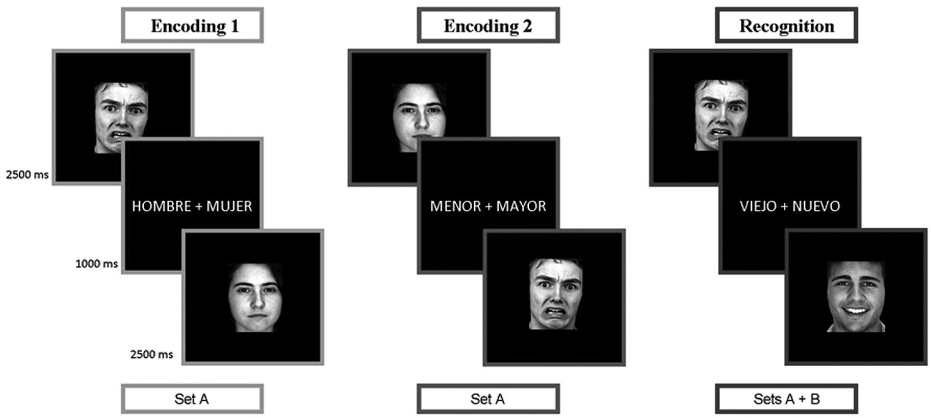
		PRE-SURGERY	POST-SURGERY	PRE- & POST-SURGERY
Sex (F/M)		18 / 19	8 /10	2 /6
Lateralization	Right	15	6	4
	Left	15	10	4
	Bilateral	2	0	0
	Undetermined	5	2	0
Age (years)		26.7 (11-62)	32.3 (15-48)	35.5 (22-48)
Education (years)		9.3 (6-16)	10.4 (8-16)	11.5 (6-16)
Age of Diagnosis (years)		11.0 (0.1-35)	12.1 (2-19)	14.2 (5-33)
Duration of Illness (years)		14.9 (0.5-37)	18.8 (1-40)	21.5 (1-40)

The emotional memory task was adapted from a previous one we conducted in healthy individuals (Sergerie, Lepage, & Armony, 2005, 2006) and in psychiatric patients (Dickie, Brunet, Akerib, & Armony, 2008; Sergerie, Armony, Menear, Sutton, & Lepage, 2010) and is illustrated in Figure 1. During the initial encoding phase, subjects were shown 48 pictures of different individuals depicting fearful, happy or neutral expressions (16 of each). Pictures

were shown twice in separate runs; during the first one subjects were instructed to indicate whether the person in the picture was male or female (sex discrimination task) and in the second run whether they thought the person was younger or older than 30 years (age discrimination task). Immediately after the completion of the encoding phase, the same pictures were presented intermixed with those from a second set of similar pictures never seen before. Subjects were asked to determine if they had seen or not the picture during the encoding session (old/new judgment). Stimuli were presented on a computer screen and responses were collected using a two-button mouse using E-PRIME software. Stimulus duration was 2.5s, with an intertrial interval of 1s, during which the answer options (male/female; younger/older; old/new) remained on the screen to help the subjects remember the task and button assignment. Pictures were presented in a pseudo-random order so that all factors of interest (emotion, sex, new/old) were equally distributed along each run. In addition, no more than 3 faces displaying the same expression were presented consecutively in order to avoid any potential mood induction effects.

FIGURE 1

Schematic of the recognition memory task. During encoding, 64 pictures of different individuals depicting fearful, happy or neutral expressions were presented in two contiguous sessions (Set A). During the first one (Encoding 1) participants indicated the sex of the person shown (Man/Woman) and during the second one (Encoding 2) whether the person was younger or older than 30 years of age (Younger/Older). During the Recognition phase, the same pictures, together with an equivalent set of new pictures (Set B), were shown and participants were instructed to determine whether the pictures had been previously presented or not (Old/New)



Memory accuracy scores for each expression, calculated as hit minus false alarm rates, were entered in a repeated measures ANOVA. The effects of surgical status (pre vs. post) and lateralization (left vs. right) were explored in between-groups comparisons. In addition, regression analyses were conducted between memory accuracy in the task and the neuropsychological variables measuring overall memory and executive functions, as well as duration of the illness, given its clinical importance.

Results

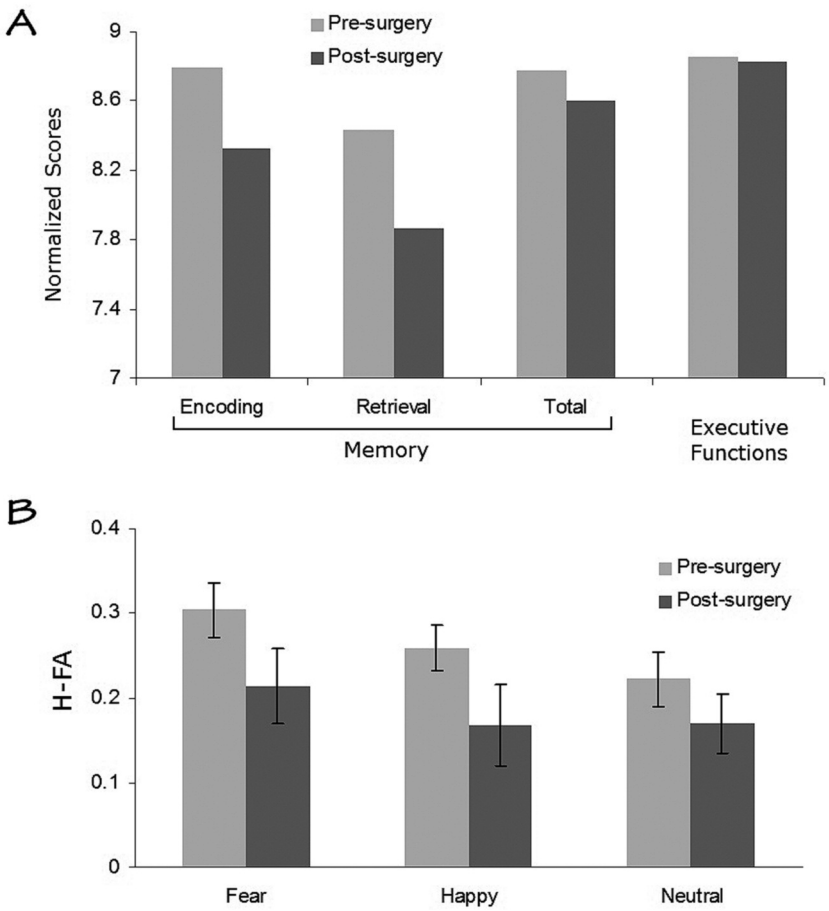
During the encoding phase, subjects responded in all trials, and accuracy in the sex discrimination task was very high (96%; accuracy for the age discrimination task was not meaningful as there were not correct or incorrect responses), indicating that participants understood the instructions and could perform the tasks without difficulty. Similarly, overall memory performance

during the recognition phase was very good, significantly above chance for the three expressions (p's < 0.001).

Results from the neuropsychological battery and the face memory task are summarized in Figure 2. We observed a trend for a main effect of emotional expression on recognition memory accuracy (p = 0.056). Planned comparisons confirmed that the direction of this effect was as expected, namely that memory for fearful faces was better than for neutral ones (p = 0.04) with no differences between happy and neutral (p = 0.38) or happy and fear (p = 0.11).

FIGURE 2

(A) Normalized scores for the memory and executive functions tests of the Neuropsychological battery Neuropsi. The possible range is between 1 and 19, with 7-9 corresponding to normal-low level of performance. (B) Accuracy, measured as hit minus false alarm rates, for the emotional face memory task



Results from the regression analyses revealed a significant positive correlation between overall memory accuracy in the face recognition task and performance in the subtests of the neuropsychological battery related to executive functions (r = 0.51; p<0.001) and memory (r = 0.44; p = 0.01).

In terms of clinical variables, we found a small but significant better memory accuracy in pre- compared to post-surgical patients (pre: 0.26, post: 0.18; p < 0.05). Interestingly, there was a significant negative correlation between performance in the face recognition memory task and the duration of the illness

(r = -0.48, p<0.001), especially for fearful (r = -0.42, p = 0.002) and happy (r = -0.36, p = 0.01) faces, with a smaller effect for neutral stimuli (r = -0.27, p = 0.06). Contrary to our hypotheses, we did not find any significant effects of lateralization of the epileptic focus on any of the variables.

Discussion

Here we present preliminary results from a research project that seeks to explore emotional processing in patients suffering from temporal lobe epilepsy (TLE). Specifically, we tested TLE patients on a recognition memory task involving faces displaying fearful, happy or neutral expressions. Our results confirmed the influence of emotional expression, particularly fear, on memory performance, consistent with our previous studies (Sergerie et al., 2005, 2006), although the effect was relatively small and did not reach the standard threshold of statistical significance. Although significantly above chance for all expressions, our subjects' performance was lower than previously observed in healthy controls (Sergerie et al., 2005) and psychiatric populations (Dickie et al, 2008; Sergerie et al., 2010) and therefore the small difference between conditions could have been partly due a floor effect.

Our main finding was that of a difference in overall memory performance between pre-surgical and post-surgical subjects. Specifically, individuals that had undergone surgical resection of part of their medial temporal lobe, including the hippocampus, exhibited a slightly lower memory accuracy compared to those who had not yet been operated. It is important to emphasize, though, that although the difference was statistically significant, the effect size was quite small and unlikely to have an impact on the patients' everyday lives. Furthermore, post-surgical patients still performed significantly above chance in the memory task, ruling out any indication of obvious memory impairments. A related result, with important clinical relevance, was the significant negative correlation between memory performance and duration of the illness. This finding highlights the detrimental effects of epilepsy on cognitive functions (Drake et al., 2000) and, therefore, the need to treat it as early as possible. Indeed, neuroanatomical studies have shown that TLE affects brain structures beyond the temporal lobes, particularly the prefrontal cortex (Bernhardt et al., 2010), critical for executive functions such as decision making (Sulman, 2000). In agreement with this, we observed a significant correlation between performance in our task and the executive functions subtest of the neuropsychological battery.

Contrary to our expectations, we did not see an influence of lateralization of the epilepsy focus on memory performance or any of the other variables measured. Although we do not have an explanation for this lack of effect, it is important to keep in mind that, even in the case of unilateral TLE, it is fairly common to observe damage to the amygdala and/or hippocampus in the contralateral hemisphere. Quantifying the amount of sclerosis in both hemispheres, as well as testing subjects on different tasks involving verbal and non-verbal material should help clarify this intriguing issue.

There are several limitations that need to be considered when interpreting the preliminary findings reported here. Although the pre- and post-surgical groups did not differ on demographic or clinical variables, we cannot rule out that he observed differences in memory are due, at least in part, to other factors. To circumvent this potential confound, we are currently testing the same subjects before and after surgery. This strategy will allow us to directly assess, in a more powerful and strict within-subjects design, the direct effects of surgery

on memory and other cognitive processes. Another limitation is the absence of specific information on the exact location and extent of the medial temporal sclerosis before surgery, as well as that of those of the tissue removed during resection. Future studies should include this information, which can be obtained non-invasively using magnetic resonance imaging.

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