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Ictal Fear: Semiologic Characteristics and Differential Diagnosis with Interictal Anxiety Disorders

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ABSTRACT

Introduction: Ictal fear (IF) is one of the most frequent emotional auras. It is the sole or predominant manifestation of simple partial seizures or initial expression of a complex partial seizure. It is more often experienced in patients with mesial temporal lobe epilepsy (TLE), probably associated with mesial temporal structures, like the amygdala. Anxiety disorders are very common psychiatric disorders associated with epilepsy, with a prevalence of 15 to 25%. **Objectives:** To describe three patients with IF with refractory mesial TLE, also presenting the results of EEG, imaging exams, neuropsychological, quality of life and psychiatric evaluations. **Methods and Results:** Three case reports of patients with refractory mesial TLE and IF followed up in the outpatient's clinic at the Epilepsy Section, Universidade Federal de São Paulo, Brazil, were submitted to presurgical evaluation and corticoamygdalohippocampectomy. Two patients presented ictal scalp-sphenoidal EEG onset on left side. Two patients had major depressive disorder in psychiatric evaluation. **Conclusion:** Although IF is the most frequent ictal psychological symptom, anxiety and mood disorders are very common psychiatric comorbidity in patients with epilepsy. It was concluded that differential diagnosis of interictal anxiety disorders, panic attacks and IF can be difficult, and requires careful management.

Key words: anxiety disorders, epilepsy, ictal fear, neurology, psychiatry.

RESUMO

Medo ictal: características semiológicas e diagnóstico diferencial em transtornos de ansiedade interictais

Introdução: O medo ictal (IF) é uma aura comum. Pode ser a unica manifestação de uma crise parcial simples ou o início de uma crise parcial complexa. Freqüentemente vivenciada por pacientes com epilepsia do lobo temporal mesial (TLE) é associada a comprometimento de estruturas mesiais como a amígdala. Os transtornos de ansiedade são muito comuns entre os transtornos psiquiátricos associados a epilepsia, com uma prevalência de 15 a 20%. **Objetivos:** descrever três casos de pacientes com medo ictal como manifestação de epilepsia refratária do lobo temporal mesial, apresentando também resultados do EEG, exames de imagem, avaliação neuropsicológica, de qualidade de vida e psiquiátrica. **Métodos e Resultados:** Três pacientes acompanhados no ambulatório do setor de Epilepsia da Universidade Federal de São Paulo com epilepsia refratária do lobo temporal mesial foram submetidos a avaliação pré-cirúrgica e corticoamidalahipocampectomia. Dois apresentaram EEG de superficie com eletrodos esfenoidais com início ictal do lado esquerdo e dois tinham transtorno de depressão maior segundo a avaliação psiquiátrica. **Conclusão:** Embora o medo ictal seja uma aura freqüente, é importante levar em conta os índices elevados de comorbidades psiquiátricas, como os transtornos ansiosos, nos pacientes com epilepsia. Concluiu-se que pode ser difícil o diagnóstico diferencial de transtornos de ansiedade interictal, ataques de pânico e medo ictal, exigindo um manejo cuidadoso.

Unitermos: transtorno de ansiedade, epilepsia, medo ictal, neurologia, psiquiatria.

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INTRODUCTION

Ictal fear (IF) is one of the most frequent emotional auras. It is the sole or predominant manifestation of simple partial seizures or initial expression of a complex partial seizure (CPS) that usually has a mesial temporal lobe origin[1]. It typically manifests as a sudden fearful affect at the beginning of or during an epileptic seizure, without context or any relation to a precedent causal perception or cognition. The intensity may vary from a slight trace of anxiety to a feeling of intense terror. Its duration is usually short, varying from 30 to 60 s, and it can be accompanied of other ictal signs like automatisms and impaired consciousness[1-3]. Although IF has also been reported in extratemporal epilepsies, it is more often experienced by patients with mesial temporal lobe epilepsy (TLE), with an overall prevalence of 15 to 20% in more recent studies[1,2].

There is evidence that certain structures of the brain are very important in the production of ictal anxiety symptoms. The leading role of the amygdala, as well as that of the hippocampus and the parahippocampal gyrus, in the mechanisms of inducing a fearful perception is well established by studies of electrical stimulation performed intraoperatively or during presurgical evaluation using intracranial depth electrodes. Studies using magnetic resonance imaging (MRI) have also shown a significant reduction in amygdala volumes in patients with intractable TLE and IF compared with those without this symptom[4].

Because IF is more frequently associated with epileptic discharges from mesial temporal areas, Feichtinger et al. (2001) studied a population of patients with refractory TLE who represented a homogeneous group of good candidates for temporal lobectomy aiming to determine whether patients with IF were more likely to become seizure free after anteromesial temporal lobe resection compared with those without IF. They found that 12 (36%) out of 33 patients reported fear at the beginning of their habitual seizures. Eleven of these patients were seizure free postoperatively. In contrast, only 11 of 21 patients without IF had a favorable outcome. These results indicate the importance of diagnosing auras with IF to provide a more detailed prognosis of surgical outcome[3].

An aura of fear must be distinguished from an anxiety disorder, particularly from a panic attack, and correct identification as an epileptic aura is aided by subsequent ictal phenomena; the distinction may be difficult if the aura of fear occurs in isolation, as the onset of epilepsy[5].

The prevalence of IF in more specific populations like patients with medically intractable TLE, potentially surgical candidates, in whatever way, is not well established in the current literature. This paper describes three cases of clinically and electrographically documented medically intractable mesial TLE patients presenting IF, reporting their common findings and describing the possible underlying topography involved in this association. All patients had also had MRI and neuropsychological, quality of life and psychiatric evaluations.

CASE REPORTS AND METHODS

Three patients were investigated. All of them had complete history, seizure description by the patients and their family, neurological, psychiatrical, neuropsychological examinations and MRI study. Prolonged interictal and ictal EEG recordings of at least two seizures were carried out in all. In every case an epileptologist or a specialized nurse examined the patient during and immediately after the seizure. We tried in each patient to correlate the appearance of the fear during the events with electrical modification on EEG, image results and specialists evaluations.

RESULTS

The demographic data are summarized in Table 1. The neurological examinations were normal, except for memory loss.

The clinical description of the recorded seizures is given in Table 2. All patients reported fear and some autonomic "panic attack-like" features.

Neither of the patients presented agitation during or after seizure. The subjective sensations were different among the 3 patients. Patient 1 (A.L.) feared she was dying and felt in a unfamiliar environment with strange people. Patient 2 (C.R.) had an unpleasant fear sensation, along with "jamais vu" experience. Patient 3 (M.F.) expressed fear of delusion. Because of this she avoided having any patterned decoration at home, such as wallpaper or paintings, since these would give her the sensation of seeing "monsters." These symptoms cannot be interpreted as hallucinations because the patient keeps her judgment about this ictal experience. Patient 1 used to present her symptoms in isolation of CPS. Because of this she was considered to have pseudoseizures and did not receive adequate treatment for many years. IF was reported to begin exclusively before CPS in the other two patients. All these symptoms led to an impaired quality of life as they often avoided doing anything alone, not just because they knew fear would eventually lead to a CPS but also because they felt vulnerable with the unexpected fear sensation. Neuropsychological evaluation showed that only patient 1 had a mild mental deficiency measured through subtests of WAIS-III (IQ = 69).

Table 1. Demographic data

Patient	Sex	Hemispheric dominance	Epilepsy duration (yr)	Antecedents	Social data	Seizure frequency (monthly)	Generalised tonic-clonic seizures
A.L.	F	Left	30	unknown (adopted)	never worked	12	Yes
C.R.	F	Left	47	hyperthermic convulsion	retired	2-6	Yes
M.F.	F	Left	42	dehydration (?)	works as manicure	4	No

Table 2. Seizure description

Patient	Nunber recorded seizures	Video EEG (hours)	Aura	Autonomic disturbances	Scream speech oroalimentary automatisms	Posturing rotation movements	Postictal
A.L.	8	194	Fear	Tachycardia Hyposthesia Hyperventilation	Fear expression Scream Moviments trying to avoid something from the ceiling Oroalimentary automatisms	Right head version and arm automatisms	Not reported
C.R.	3	304	Fear Epigastric sensation Jamais vu	Tachycardia	Groaning Oroalimentary automatisms	Right arm automatisms	Fast recovery
M.F.	2	120	Fear Epigastric sensation Depersona lization	Tachycardia	Groaning Oroalimentary automatisms	Right upper body rotation	Confused (about 3 minutes)

Localization of the seizure onset was determined by clinical semiology along with interictal and ictal electrophysiological studies and MRI. The epileptogenic zone was right temporal in patient 1, and left in the other two.

Table 3. Localizations

Patient	MRI findings	Interictal scalp EEG	Ictal scalp EEG (onset)	Follow up after surgery (months)	Pathology	Volumetric measures
A.L.	Right hippocampal atrophy Hyperintense hippocampus and amygdala (T2)	Right temporal sharp waves	Right temporal	4	Mesial temporal sclerosis	Right hippocampus 1201.1 corrected 1278.8 Left hippocampus 1534.5 corrected 1664.6
C.R.	Hyperintense left hippocampus and amygdala (T2)	Left temporal slow waves	Left temporal	5	Mesial temporal sclerosis	Right hippocampus 1957.0 corrected 2295.7 Left hippocampus 975.1 corrected 1143.8
M.F.	Left hippocampal and amygdala atrophy Hyperintense left hippocampus and amygdala (T2)	Independently bilateral temporal slow waves	Left temporal	5	Mesial temporal sclerosis	Right hippocampus 1952.7 corrected 1963.0 amygdala 1379 corrected 1386.3 Left hippocampus 1060.8 corrected 1066.4 amygdala 1299.8 corrected 1306.6

Psychiatric evaluations were available for all before and after surgery. Patient 1 had a history of 5 suicidal attempts, with no axis I diagnosis according to DSM IV-TR. She was given up for adoption at birth and suffered a violent home environment, running away at age 13 and getting married to her present partner. As for her complicated past history she has had psychological follow up after surgery. Patient 2 and 3 had major depressive disorders according to DSM IV-TR criteria and only patient 2 is still receiving antidepressive treatment after surgery.

All patients underwent corticoamygdalohippocampectomy. In this surgical technique 2-3 cm of left and 4-5 cm of right neocortex are ressected; most of the amygdala is aspirated, leaving 20% of amygdala tissue close to the internal capsule, while 2-3 cm of hippocampus are also removed. As for the surgery outcomes all three remain seizure free in a short follow-up and do not report any aura of fear since surgical procedure.

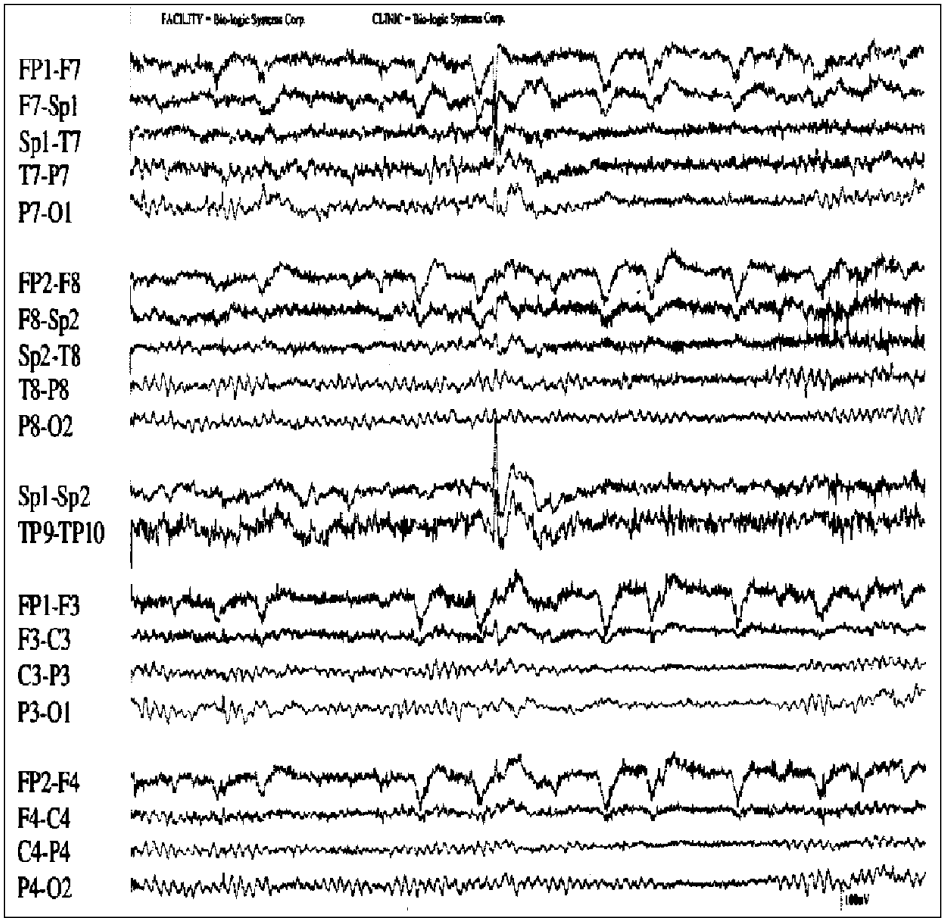
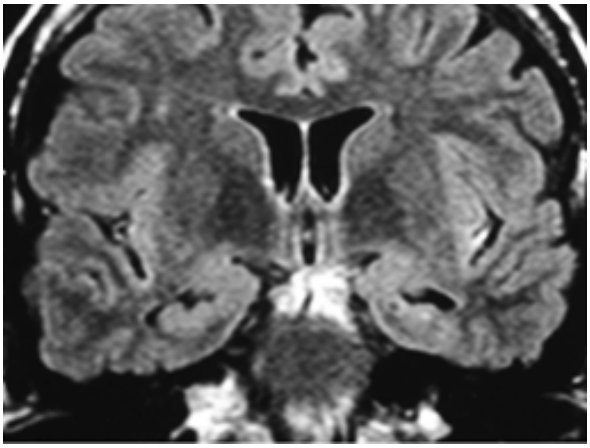


Figure 1. EEG showing interictal epileptiform discharge registered in left sphenoidal electrode (Patient 2).



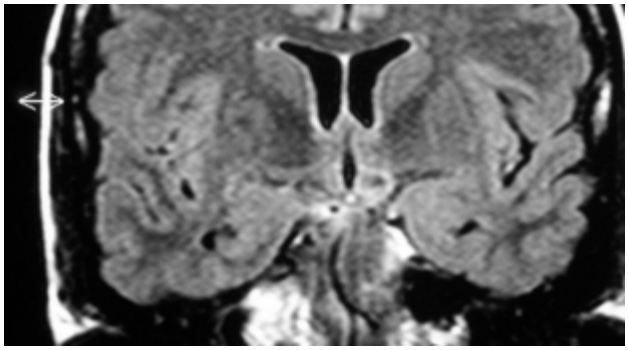


Figure 2. MRI coronal Flair showing atrophy/hyperintense left hippocampus and amygdala.

DISCUSSION

This study aimed to contribute providing more information about the presence of IF in TLE and also to point out clinical similarities and differences with panic disorder (PD), through the description of three cases of clinically and electrographically documented medically intractable TLE patients. The possible underlying topography involved in this association is commented based on other studies in the current literature.

IF can range from mild anxiety to intense terror, out of proportion to, and separable from the understandable apprehension that accompanies the beginning of a seizure. In some cases, it resembles a real-life experience such as suddenly finding a stranger standing close behind, and may also be associated with an unpleasant psychic hallucination of past events. IF may be accompanied by symptoms and signs of autonomic activation (mydriasis, piloerection, tachycardia, and hyperventilation)[5]. Also it may coexist with other auras as was seen in patients 2 (epigastric aura and jamais vu) and 3 (epigastric aura and depersonalization).

Anxiety and mood disorders are the most common psychiatric comorbidity in patients with epilepsy. Population-based studies have estimated the prevalence of anxiety in epilepsy patients to range between 15 and 25%. These prevalence rates can be even higher in studies carried out in hospital-derived populations[1]. The various forms of anxiety disorders (generalized anxiety disorder, PD, phobias, obsessive-compulsive disorder and posttraumatic stress disorder) can present interictally with the same clinical features seen in the general population; however, the peri-ictal presentations of anxiety symptoms often differ from interictal manifestations.

Panic attacks, as well as epileptic seizures, may be described as paroxysmal events. They are characterized by discrete periods of intense fear or emotional discomfort, accompanied by a range of somatic symptoms (palpitation, trembling, shortness of breath, sweating) and psychological symptoms (depersonalization, fear of losing control or dying). The clinical diagnosis is characterized by panic attacks, avoidance of situations in which previous attacks have occurred and worrying the possibility of future attacks[6]. The differential diagnosis of panic attacks and IF can be difficult requiring careful differential diagnosis. Table 4 shows the main differences between them.

It has been reported that women with PD are more likely to report depression, anxiety, or agoraphobic avoidance than men[7]. The National Comorbidity Survey, a large American epidemiologic study, found that besides being more frequent in females, panic attacks have a peak of onset in older women than in men. On the other hand, PD also has an important association with years of education being noted that people with less than 12 years of schooling were up to ten times more likely to have PD[8]. We found no data, however, suggesting the association of IF to gender prevalence, sociodemographic characteristics or to specific psychiatric aspects.

MRI studies had already shown a significant reduction in amygdala volumes in patients with intractable mesial TLE and IF compared with those without this symptom[9]. Recent data suggests that IF with coordinated behavior and autonomic features may be part of or interfere with a complex information processing network involving orbito-prefrontal, anterior cingulate and temporal limbic cortices[10].

Frequently, patients fail to recognize and report associated ictal event symptoms, which often results in its misdiagnosis and treatment as a PD[1,2].

Table 4. Differential diagnosis of panic attacks versus focal seizure with ictal fear*

	Primary panic attack	**Focal seizure with ictal fear**
Consciousness	Alert	Alert but may progress to impaired
Duration	5-10 minutes	0.5-2 minutes, but may vary
Déjà vu hallucinations	Very rare	More than 5%
Automatisms	Very infrequent	Common, progressing to complex partial seizure
Depressive symptons	Commonly associated	Uncommon
Anticipatory anxiety	Very common	Uncommon
Interictal EEG	Normal	Often abnormal
Ictal EEG	Normal	Usually abnormal
MRI of temporal structures	Usually normal	Often abnormal

* Modified from Beyenburg S, Mitchell AJ, Schmidt D, Elger CE, Reuber M[2] (2005).

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