Faculdade de Medicina de São José do Rio Preto
Programa de Pós-graduação em Ciências da Saúde

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FATORES PROGNÓSTICOS DOS PACIENTES COM ESCLEROSE MESIAL TEMPORAL SUBMETIDOS À CORTICOAMIGDALOHIPOCAMPECTOMIA EM CENTRO TERCIÁRIO

São José do Rio Preto
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Fatores Prognósticos dos Pacientes Com Esclerose Mesial Temporal Submetidos à Corticoamigdalohipocampectomia em Centro Terciário

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SUMÁRIO

DEDICATÓRIA

À minha mãe Ramilde Rocha

Que sempre me apoiou nas minhas escolhas.

À minha amada Milena Moreira Arruda

Que acreditou em meu potencial e deu força nos momentos difíceis.

Ao meu colega Lucas Crociati Meguins

Por ter ajudado nos meus projetos científicos.

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EPÍGRAFE

Quanto mais nos elevamos, menores parecemos aos olhos daqueles que não sabem voar. (Friedrich Nietzsche)

LISTA DE TABELAS

Artigo 3

LISTA DE ABREVIATURAS E SÍMBOLOS

AED	Antiepleptic drug
CAH	Corticoamigdalohipocampectomia / corticoamygdalohippocampectomy
DAE	Drogas antiepilépticas
EEG	Eletroencefalograma / electroencephalogram
ELT	Epilepsia do lobo temporal
FAMERP	Faculdade de Medicina de São José do Rio Preto
GTCs	Generalized tonic-clonic seizure
ILAE	International League Against Epilepsy
MTS	Mesial temporal sclerosis
MRI	Magnetic Resonance Image
PET	Positron Emission Tomography (Tomografia por emissão de pósitrons)
RME	Ressonância Magnética Nuclear do Encéfalo
SPECT	Single Photon Emission Computed Tomography (Tomografia computadorizada por emissão de fóton único)
TLE	Temporal lobe epilepsy
VEEG	Vídeo-eletroencefalograma / video-electroencephalogram

RESUMO

Introdução: A esclerose mesial temporal (EMT) é a doença mais comumente encontrada em uma série de cirurgia para epilepsia. Idade de início precoce, um histórico de convulsões febris, descargas epileptiformes no EEG, duração da epilepsia, número de crises convulsivas generalizadas, tipo de auras e gravidade dos transtornos psiquiátricos são possíveis fatores prognósticos em pacientes com EMT. **Objetivo:** O objetivo deste estudo é avaliar os resultados da investigação clínica, semiótica, psicológica, eletrofisiológica e neuroradiologica, relacionando suas descobertas com o prognóstico dos pacientes com EMT que foram submetidos à córticoamígdalohipocampectomia (CAH). **Métodos:** De 1214 pacientes avaliados para cirurgia no Centro de Epilepsia da Faculdade de Medicina de São José do Rio Preto (FAMERP), um centro terciário de epilepsia no Brasil, 400 pacientes foram submetidos a CAH para EMT. Exames e dados clínicos foram analisados e comparados com os resultados da classificação de Engel. **Resultados:** De todos os itens analisados, a ressonância magnética mostrou uma maior influência sobre o resultado dos pacientes. Sobre a avaliação clínica, os antecedentes patológicos, a idade no momento da cirurgia, a duração da epilepsia, lesões perinatais, uma história familiar de epilepsia, convulsões febris, alterações neuropsicológicas e presença de crise tônico-clônica generalizada tiveram uma significância estatística. Uma relação significativa foi encontrada entre o lado do EMT, a RME e SPECT com EEG ictal bilateral mostrando resultados piores. Os resultados cirúrgicos correlacionados com EEG ictais e interictais não mostraram diferença na análise de descargas unilateral ou bilateral, independentemente se o EEG era interictal ou ictal. Analisando-se os pacientes pelo tipo de aura, aqueles que tinham auras extratemporais tiveram pior resultado no pós-cirúrgico e na classificação de Engel. Enquanto auras mesiais, aparentemente, são bons fatores prognósticos. Pacientes sem aura também tiveram pior prognóstico. Auras simples e

múltipla não tiveram nenhuma diferença. **Conclusão:** Afim de identificar os candidatos mais apropriados para CAH, é muito importante considerar os fatores prognósticos associados com resultado favorável para o aconselhamento de pacientes na prática diária.

Palavras-chave: Epilepsia, Fatores Prognósticos, Seguimento, Cirurgia De Epilepsia, Esclerose Mesial Temporal, Corticoamigdalohipocampectomia.

ABSTRACT

Introduction: Mesial temporal sclerosis (MTS) is the most common disease encountered in an epilepsy surgery series. Early age of onset, a history of febrile convulsions, epileptiform discharges on EEG, duration of epilepsy, number of generalized seizures, type of auras and severity of psychiatric disorders are possible prognostic factors in patients with MTS. **Objetive:** The aim of this study is to assess the results of clinical research, semiotic, psychological, electrophysiological and neuroradiological, associating their findings with the prognosis of patients with MTS who underwent cortico-amygdalohippocampectomy (CAH). **Methods:** Of 1214 patients evaluated for surgery in the Epilepsy Center of Faculdade de Medicina de São Jose do Rio Preto (FAMERP), a tertiary brazilian epilepsy center, 400 underwent CAH for MTS. Exams and clinical data were analyzed and compared with Engel classification for outcome. **Results:** Of all the items analyzed, the MRI showed a greater influence on the outcome of patients and for clinical evaluation and pathological antecedents, age at surgery, the epilepsy duration, perinatal insults, a family history of epilepsy, febrile seizures, neuropsychological abnormalities and presence of generalized tonic clonic seizure had a statistical significance. A significant relationship was found between the side of MTS under MRI and on SPECT with bilateral ictal EEG showing worse results. Surgical results correlated with ictal and interictal scalp EEG patterns and there was no difference when analyzing unilateral or bilateral discharges regardless of whether it was the interictal or ictal EEG. Analyzing the patients according to the type of aura, those who had extratemporal auras had worst result in post-surgical in Engel classifcation. While mesial auras apparently are a good prognostic factor. Patients without aura also had worse prognosis. Simple and multiple aura had no difference. **Conclusion:** In order to identify

the most appropriate candidates for CAH, it is very important to consider the prognostic factors associated with favorable result for counseling these patients in daily practice.

Keywords: Epilepsy, Prognostic Factors, Follow-Up, Surgery Of Epilepsy, Mesial Tempoal Sclerosis, Cortico-Amygdalohippocampectomy.

1. INTRODUÇÃO

INTRODUÇÃO

O lobo temporal é crucial para a transferência da memória de curto prazo para a memória de longo prazo nos córtices de associação (1). Ele está envolvido principalmente com a memória episódica (informação amarrada a um tempo e lugar) e a memória declarativa (memória para fatos) para eventos, experiências e para a navegação espacial (2). Pacientes com danos aos lóbulos temporais podem tornar-se amnésicos com uma incapacidade de formar e manter novas memórias (3). O lobo temporal é a região mais epileptogênica do cérebro humano (1). A Epilepsia Do Lobo Temporal (ELT) é um grupo de doenças que predominantemente envolve desregulação da função do hipocampo causada por hiperexcitabilidade neuronal (4). A ELT é a forma mais comum de epilepsia parcial em adultos (Engel et al., 1997, (5). A Esclerose Mesial Temporal (EMT) é talvez a síndrome epiléptica que melhor a caracterizada eletroclinicamente a ELT (1). As crises são tipicamente caracterizadas por sintomas subjetivos autônomos e / ou psíquicos (mais comumente uma sensação de algo subindo do estômago), olhar fixo, ou automatismos gestuais ou oral-alimentares (6, 7). A aura pode ser isolada ou pode ser seguida por olhar fixo ou generalização secundária. Outros sintomas autonômicos vegetativos e fenômenos psíquicos, incluindo flashbacks, Déja Vù, estados de sonho, ilusões e alucinações complexas, multimodais são menos comuns (8). A EMT é a doença mais comum encontrado em séries de cirurgias de epilepsia e podem ser facilmente detectados por ressonância magnética do encéfalo (RME). A Esclerose Mesial Temporal é tanto uma consequência como uma causa de convulsões (7, 9-11). A aparência normal do hipocampo ocorre em 30% a 40% dos casos (10, 12). Entretanto quando visíveis nos exames podemos notar que a esclerose do hipocampo é uma combinação de atrofia e astrogliose da amígdala, do hipocampo, do giro para-hipocampal,

e do córtex entorrinal e frequentemente é bilateral (9, 13). Se o envolvimento do subcampo ocorre isoladamente, a EMT pode estar ausente nos resultados de exame por imagem (1). Do ponto de vista neuropatológico, a epilepsia temporal pode ser dividida em lesional e não-lesional (5). As lesionais são causas menos frequentes de epilepsia temporal e incluem gliomas, angiomas, caveromas, lesões traumáticas ou infecciosas e geralmente encontradas em séries cirúrgicas (1, 5). Estas causas secundárias podem ser vistas em 5% a 30% dos casos. Por outro lado, as não lesionais representa o subtipo mais comum e é composto por pacientes com EMT (5, 9). Há poucos relatos sobre o prognóstico e fatores prognósticos em pacientes com EMT. Alguns pacientes apresentam crises resistentes às drogas antiepilépticas (Engel et al., 1997, (11), embora tenham sido relatados que a maioria dos casos são benignos (14). Alguns autores (11, 15, 16) concordam que a resposta as drogas antiepilepticas não é boa em pacientes com epilepsia do lobo temporal. Na literatura, a taxa de remissão completa varia de 5% (16) a 42% (15). Idade precoce de início das crises, uma história de convulsões febris, descargas epileptiformes no eletroencefalograma, duração da epilepsia, número de convulsões generalizadas e severidade de distúrbios psiquiátricos são possíveis fatores prognósticos em pacientes com esclerose mesial temporal (11, 17-21). Estabelecer os mecanismos etiológicos e fisiológicos subjacentes a esta forma de epilepsia, ou seja, os fatores responsáveis pela e associada a resistência aos medicamentos, é importante para fins terapêuticos (6).

Nas epilepsias por EMT fármaco-resistentes, mecanismos moleculares estão alterados, tais como os baixos níveis cerebrais de ácido gama aminobutírico (22), as alterações nos níveis de glutamato e transportadores neuronais do glutamato (23). Não existem dados disponíveis sobre os fatores prognósticos e resultados dos diferentes tipos de lesões mesiotemporal e epilepsia por EMT refratária. Lobectomia temporal anterior ainda é o padrão mais frequentemente aplicada para o tratamento cirúrgico da epilepsia do lobo temporal (24). O protótipo de uma síndrome

epiléptica cirurgicamente remediável é a epilepsia por EMT refratária. A Cortico-amigdalohipocampectomia (CAH) para EMT é uma medida muito eficaz para controlar as crises, e a probabilidade de ficar livre de crises é de aproximadamente 70 a 90% (8, 10, 25-27). No entanto, até 30% dos pacientes continuam a sofrer convulsões depois da cirurgia (8, 25-27). Portanto, determinar fatores prognósticos é muito importante em encontrar os candidatos ideais para a cirurgia. Estudos anteriores relataram diversos fatores que podem prever o resultado do controle de crises, mas a maioria são incompletos, sendo a ênfase dada a EMT e uma atenção especial focada sobre a importância de convulsões febris, etiologia da convulsão e atrofia hipocampal vista na RME (10). Radhakrishnan et al. (28) relatou os fatores prognósticos de 175 pacientes consecutivos submetidos a cirurgia e afirmou que tanto atrofia hipocampal unilateral detectada por todas as descargas epileptiformes interictais e por ressonância magnética concordantes com o local de início ictal, foram fatores prognósticos pré-cirúrgicas significativas para epilepsia do lobo temporal (26). Além disso, a determinação de fatores prognósticos para cirurgia de epilepsia é importante para o aconselhamento dos pacientes na prática diária (25). Fatores genéticos também são vistos na EMT (1). A forma familiar pode ou não ter dominância autossômica e geralmente não são relacionados com oscilação de alta frequência, embora possam ser associadas com a oscilação de alta frequência sem convulsões com parentes de primeiro grau (29). Outros marcadores genéticos, como SCN1B, parece ser um fenótipo partilhado entre os pacientes com EMT (30). O polimorfismo genético no gene ABCB1 atua como um gene de resistência a múltiplas drogas em pacientes com EMT (31). As resistências aos fármacos devem ser diagnosticadas o mais cedo possível, porque as convulsões subsequentes podem ser eliminadas cirurgicamente por lobectomia temporal anterior em uma elevada percentagem de pacientes (70-90%) e outros (aproximadamente 20%) com uma redução significativa das crises (25, 32-34).

No entanto, o resultado após a cirurgia pode ser bastante variável, e este ser influenciado por inúmeros fatores, apesar de muitos estudos sobre os preditores do desfecho pós-operatório (32). Malla et al., 1998 (35) tentou avaliar até crise pós cirúrgicas precoces como fator preditor de prognóstico. Embora a EMT seja a lesão mais comumente identificada nesses pacientes, o papel da lesão no desenvolvimento da epilepsia refratária ao tratamento clínico permanece incerto (Bia et al., 2006). A EMT é uma doença heterogênea, pois há pacientes com uma forma refratária grave, enquanto muitos outros têm um distúrbio epiléptico leves e entram em remissão com ou sem medicação antiepiléptica (5).

Clinicamente, a EMT é frequentemente associada a uma história pessoal de convulsões febris e com início das crises resistentes às drogas durante a adolescência ou na idade adulta (5, 6). Outros fatores de risco estão associados com o desenvolvimento de epilepsia, incluindo crises febris prolongadas na infância, estado de mal, infecções, traumatismo craniano, neoplasias, insultos perinatais / vascular, esclerose mesial temporal, e uma história familiar de epilepsia. Estes fatores de risco que estão a resultar em lesão cerebral a um nível molecular, que conduzem a uma alteração morfológica ou biológico ao longo de anos, resultando finalmente no desenvolvimento de epilepsia (36). Crises febris prolongadas durante a infância têm sido associadas com danos graves nas estruturas temporomesiais (29). No entanto, o papel das crises febris no desenvolvimento da EMT permanece controverso (37). Na atual classificação das epilepsias e síndromes epilépticas foram incluídas duas formas de epilepsia do lobo temporal: mesial e lateral (neocortical), mas a história de convulsões febris não é característica da forma lateral (7). Outro fator investigado é a presença de epilepsia na história familiar, incluindo epilepsia de lobo temporal (5). A maioria dos pacientes com epilepsia do lobo temporal familiar tem um curso benigno e crises refratárias foram relatados apenas em uma minoria dos pacientes (5).

Outro fator que foi avaliado para determinar prognostico pós-cirurgico dos pacientes com EMT é a aura. Uma aura é um fenômeno ictal subjetivo que pode preceder um ataque observável (38). Auras constituem uma característica fundamental da ELT e as auras típicas em pacientes com ELT por EMT são sensações epigástricas e sintomas psíquicos, que incluem medo, dismnesia (como déjà vu e jamais vu) e sensações olfativas e gustativas (39-41). Os pacientes podem relatar auras simples ou múltiplas ou, ocasionalmente, sem aura (42). No entanto, poucos são os estudos que associam a aura como o fator prognóstico, embora, sendo os primeiros sintomas de convulsões, muitos tipos de auras têm valor significativo de localizações ou lateralizatórias e até mesmo de extensão do foco epileptogênico [18].

Analise do eletroencefalograma (EEG) nestes pacientes também são feitas. Alguns autores encontraram uma relação significativa entre a ocorrência de picos nos EEG e principalmente após a cirurgia de epilepsia para epilepsia do lobo temporal (9, 43-45), outros estudos não conseguiram identificar tal associação (29). Nos EEG a EMT é frequentemente associada a picos temporais anteriores ou a ondas agudas com voltagem máxima nas regiões temporal anterior que é tipicamente achada em 90% dos pacientes (46). No entanto, um terço dos pacientes têm descarga epileptiforme interictal temporal bilateral (DEI), que se torna aparente com monitorização EEG longo prazo (47). Estudos identificaram que os melhores resultados cirúrgicos acontecem quando 100% das DEIs temporais são unilaterais e combinados com descargas ictais que permanecem regionalizadas sem propagação contralateral no EEG do couro cabeludo (48).

Em alguns estudos foram identificados como mal fator prognóstico alterações na imagens obtidas por RME (5). Há um consenso de que a RME é um indicador confiável da epilepsia do lobo temporal em pacientes com EMT (9). Exames de ressonância magnética quantitativos, ou seja, com medidas do volume do hipocampo, têm sido introduzidas e fornecem uma avaliação

objetiva do tamanho e do volume do hipocampo em pacientes com suspeita de epilepsia do lobo temporal (9). Exames funcionais podem auxiliar o VEEG e a RME como a tomografia por emissão de pósitrons (PET) e a tomografia computadorizada por emissão de fóton único (SPECT). Além disso, quando comparados, dados concordantes de estudos eletrofisiológicos e de neuroimagem funcional (PET, SPECT, RME funcional), os resultados de RM que localizam no lobo temporal mesial está associada com o pós-cirúrgico livre de crise em 70-90% dos pacientes (49). Por outro lado, a localização é um desafio quando a RME é normal, refletida em um resultado cirúrgico historicamente menos favorável (49).

Diversos fatores clínicos e principalmente de exames tem sido estudado para tentar se achar os fatores que realmente podem influenciar na indicação cirúrgica, no entanto pouco se tem estudado com relação a anamnese e auras epilépticas. Apesar, desta última informação necessitar de uma entrevista simples e sem maiores custos adicionais ao processo de seleção do paciente.

2. OBJETIVO

OBJETIVOS

O objetivo deste estudo é avaliar os achados da investigação clínica, semiológica, psicológica, eletrofisiológico e neurorradiológica e relacionar seus resultados com o prognóstico dos pacientes com Esclerose Mesial Temporal e consequentemente identificar fatores de risco que podem ser usados como fatores preditivos de um resultado pós-operatório favorável ou desfavorável.

OBJETIVOS ESPECÍFICOS

a) Avaliar os resultados da investigação clínica, semiótica, psicológico e de exames de imagem e relacionar suas descobertas com o prognóstico dos pacientes com EMT que foram submetidos à CAH e consequentemente, identificar fatores de risco que podem ser usados como preditores de um resultado pós-operatório favorável ou desfavorável.

b) Identificar as alterações do VEEG pré-operátorio dos pacientes com EMT que foram submetidos à CAH e relacionar suas descobertas com o desfecho pós-cirúrgico.

c) Analisar os tipos de auras e seu número nos pacientes com EMT que foram submetidos à CAH relacionando suas descobertas com o resulta do pós-cirúrgico.

3. ARTIGOS CIENTÍFICOS

ARTIGOS CIENTÍFICOS

Os resultados referentes aos objetivos dessa dissertação estão apresentados na forma de artigos científicos conforme a descrição abaixo:

Artigo 1

Título: Prognostic Factors in Temporal Lobe Epilepsy Surgery Due to Hippocampal Sclerosis in a Tertiary Epilepsy Center

Periódico: Acta Neurochirurgia

Status: Artigo publicado.

Artigo 2

Título: Electroencephalography and Seizure Outcome in Mesial Temporal Sclerosis after Epilepsy Surgery

Periódico: Journal of Neurosurgical Sciences

Status: Artigo sob revisão do comitê editorial.

Artigo 2

Título: Aura as a prognostic factors in anterior temporal lobe resections for mesial temporal lobe epilepsy

Periódico: Journal of Neurosurgical Sciences

Status: Artigo sob revisão do comitê editorial.

A. ARTIGO CIENTÍFICO 1

Factors predicting the outcome following surgical treatment of mesial temporal epilepsy due to mesial temporal sclerosis

Rodrigo Antonio Rocha da Cruz Adry, Lucas Crociati Meguins, Sebastião Carlos da Silva Júnior, Carlos Umberto Pereira, et al.

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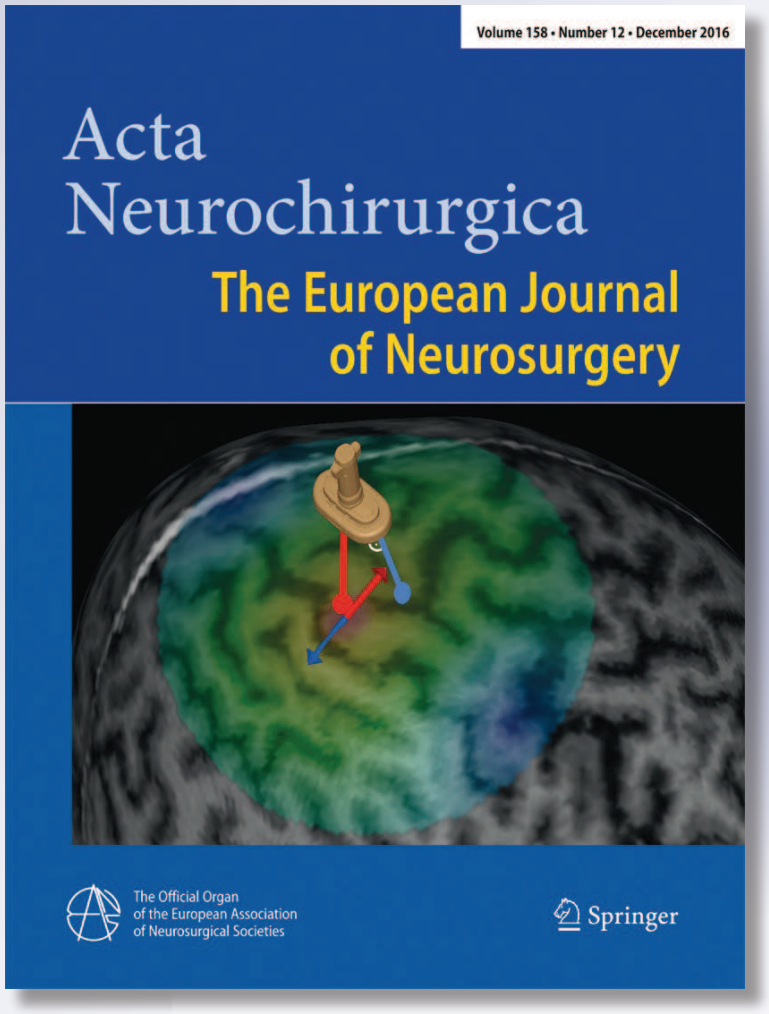

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EXPERIMENTAL RESEARCH - FUNCTIONAL

Factors predicting the outcome following surgical treatment of mesial temporal epilepsy due to mesial temporal sclerosis

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Abstract
Background Mesial temporal sclerosis (MTS) is the most common disease found in an epilepsy surgery series. Early age of onset, a history of febrile convulsions, epileptiform discharges on EEG, duration of epilepsy, number of generalized seizures and severity of psychiatric disorders are possible prognostic factors in patients with MTS.
Objective The aim of this study is to review the clinical, semiotic, psychological, electrophysiological and neuroradiological researches and relate their findings to the prognosis of patients with MTS who underwent anteromedial temporal lobectomy (ATL).
Methods Of 1,214 patients evaluated for surgery in the epilepsy Center of *Faculdade de Medicina de São Jose do Rio Preto* (FAMERP), a tertiary Brazilian epilepsy center, 400 underwent ATL for MTS. Examinations and clinical data were analyzed and compared with the Engel Outcome Classification.
Results Of all the items analyzed, the MRI showed the greatest influence on patient outcome. As for the clinical evaluation and pathological antecedents, age at surgery, epilepsy duration, perinatal insults, family history of epilepsy, febrile seizures, neuropsychological abnormalities and presence of generalized tonic-clonic seizure all had statistical significance.
Conclusion In order to identify the most appropriate candidates for ATL, it is very important to consider the prognostic factors associated with a favorable outcome for counseling patients in daily practice.

Keywords Epilepsy · Mesial temporal sclerosis · Neurosurgery · Prognostic factors

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Introduction

Epilepsy remains a common medical and neurological problem in the general population [13]. The temporal lobe is the most epileptogenic region of the human brain [31]. The mesial temporal lobe is mainly involved in episodic memory (information tied to a time and place) and declarative memory (explicit memory for facts) for experienced events and for spatial navigation [6]. Temporal lobe epilepsy is a group of disorders that predominately involves the dysregulation of the hippocampal function caused by neuronal hyperexcitability [26]. Temporal lobe epilepsy (TLE) represents the most common type of partial epilepsy [1]. Therefore, of all epilepsies, TLE is perhaps the one that is best characterized electroclinically [31].

Mesial temporal sclerosis (MTS) is the most common disease found in an epilepsy surgery series and may be readily detected by magnetic resonance imaging (MRI) of the brain. Typically, the seizures are characterized by autonomic and/or psychic subjective symptoms (most commonly a sensation of

something rising from the stomach), staring and perhaps gestural or oral-alimentary automatisms. [10, 21]

Sclerosis of the hippocampus progresses over time as both a consequence and a cause of seizures [4, 8, 10, 33, 35]. There are only a few reports concerning the prognosis and prognostic factors in patients with MTLE-HS. Some authors agree that the response to antiepileptic drugs is not good in patients with temporal lobe epilepsy [27, 30, 35]. In the literature, the rate of complete remission ranges from 5 % to 42 % [27, 30]. The prototype of a surgically remediable epileptic syndrome is medically refractory mesial temporal lobe epilepsy (MTLE) [12]. Anterior temporal lobectomy for mesial temporal sclerosis is a very effective measure to control seizures; the probability of being seizure-free is approximately 70–90 % [7, 11, 12, 22, 32]. However, 30 % of patients still experience seizures after surgery [11, 12, 22, 32]. Therefore, identifying prognostic factors is very important to find the ideal candidates for surgery.

Early age at seizure onset, a history of febrile convulsions, epileptiform discharges on the EEG, duration of epilepsy, the number of generalized seizures and severity of psychiatric disturbances are possible prognostic factors in patients with MTLE-HS [15, 17, 24, 34, 35]. Establishing the etiological and physiological mechanisms underlying this form of epilepsy—namely the factors responsible for and associated with drug resistance—is important for therapeutic purposes [21]. In addition, determining prognostic factors for epilepsy surgery is important for counseling patients in daily practice [32].

The aim of this study is to review the findings of clinical, semiotic, psychological, electrophysiological and neuroradiological researches, relate their findings to the prognosis of patients with mesial temporal sclerosis who underwent anteromedial temporal lobectomy (ATL) and consequently identify risk factors that can be used as predictors of a favorable or unfavorable postoperative outcome.

Methods

Patients selection

We performed a retrospective review of the electronic and paper-based medical record centralized database of the Center for Epilepsy Surgery, Hospital de Base, São José do Rio Preto, Faculty of Medicine at São José do Rio Preto, between 2002 and 2013. A total of 1,214 patients were evaluated for epilepsy surgery, of whom 400 underwent ATL for mesial temporal sclerosis.

Preoperative evaluation and clinical characteristics

All patients undergoing ATL for intractable epilepsy first underwent a comprehensive evaluation to confirm MTS. This assessment included magnetic resonance imaging (MRI) with a seizure protocol, inpatient continuous video-electroencephalographic monitoring (VEEG), single-photon emission computed tomography (SPECT) and neuropsychological evaluation. Each patient was discussed at a multidisciplinary epilepsy conference attended by adult and/or pediatric epileptologists, neurosurgeons, neuroradiologists and neuropsychologists. Once surgery had been offered, written informed consent was obtained.

Clinical characteristics registered for each subject included age at surgery, duration of epilepsy, age at febrile seizure onset, monthly seizure frequency and presence, status epilepticus, central nervous system infections, head trauma, neoplasms, perinatal/vascular insults, family history of epilepsy and febrile convulsion.

Surgical procedure

Anteromedial temporal lobe resection and then amygdalohippocampectomy using microsurgical techniques were performed in patients with MTS abnormalities. Briefly, after a standard frontotemporal craniotomy, the lateral temporal neocortex (from the middle of the superior temporal gyrus down to the inferior temporal gyrus) was removed while exposing the anterior temporal horn of the lateral ventricle. The extent of cortical resection from the temporal tip ranged from 4.5 to 5.0 cm depending on the side to be resected. The surgeon then extracted the amygdala and uncus subpially. Hippocampal and parahippocampal gyri were then mobilized and resected en bloc between the collateral sulcus and the choroidal fissure. Resection of the tail of the hippocampus was extended posterior to the level of the tectal plate. The pial plane between the mesial temporal structures and the ambient cistern was carefully respected.

Postoperative outcome

The postoperative evaluation was performed by a neurosurgeon or epileptologist by visiting the outpatient clinic. The operative outcomes were reviewed using the modified Engel Classification. Engel class I patients were defined as being seizure-free or having only nondisabling, simple partial seizures, or they had some disabling seizures after surgery but had been free of disabling seizures for at least 2 years, and generalized tonic-clonic seizures occurred only after the withdrawal of antiepileptic drugs. Class II patients had rare seizures (85 % reduction); class III patients had a greater than 50 % reduction in seizure frequency; class IV patients had no meaningful reduction in seizure frequency. Those achieving an Engel class I outcome were considered to have a favorable outcome, whereas those achieving classes II through IV outcomes were considered to have an unfavorable outcome. Postoperative outcomes were available for more than 2 years.

Statistical analysis

Appropriate statistical analyses were performed using SPSS statistical software. Demographic information, seizure types and frequencies were analyzed and compared with means, medians and standard deviations. Comparisons were made through Willcoxon test, chi-square test, Fisher's exact probability test and the Pearson correlation. $P < 0.05$ was considered significant.

Results

Patients' characteristics

Four hundred patients underwent anteromedial temporal lobectomy for intractable seizures due to MTE between 2003 and 2013. All patients met all inclusion criteria within at least 1 year of postsurgical follow-up. The clinical data of patients is shown in Table 1. The group of patients consisted of 218 (54.5 %) males and 182 (45.5 %) females—therefore, the genders were balanced—with a mean age of 36.72 years ranging from 1 to 75 years. Age at seizure onset ranged from 0 to 48 years with a median of 9.07 years. Seizure duration ranged from 0 to 64 years with a mean of 25.03 years. The silent interval ranged from 0 to 32 years with a mean of 2.71 years.

As for handedness, 371 (92.8 %) patients were right-handed, 20 (5 %) were left-handed, and 9 (2.3 %) patients could not be identified. The seizure frequency before ATL was 66.3 % weekly, 31.3 % monthly and 2.5 % sporadic. One hundred ninety-one patients underwent ATL on the right side and 209 on the left side. Two hundred seventeen patients presented some abnormality in neuropsychological assessment, such as memory loss and some degree of cognitive dysfunction (Table 1).

All factors considered can be found in Table 1. Seizures types were analyzed as such: generalized tonic-clonic seizure in 247 patients and complex partial seizure in 391 patients (Table 1).

Examinations

All patients were submitted to a series of examinations, namely MRI, VEEG and SPECT. All patients presented abnormalities in SPECT, and 384 patients presented abnormalities under MRI. The VEEG showed that 382 patients had abnormalities in interictal evaluation (Table 1).

Patients' outcomes

Patients' outcomes are shown in Table 2. The Engel outcomes for the overall cohort 1 year after surgery were as follows: 317 patients achieved Engel class I, 28 reached Engel class II, 20 reached Engel class III, and 35 reached Engel class IV. Considering that Engel I patients had a favorable outcome and Engel II, III and IV patients had an unfavorable outcome, there were 317 patients with a favorable outcome and 83 patients with an unfavorable outcome.

Prognostic factors

Several factors were analyzed correlating patients' Engel Classification such as gender, handedness, surgery side, seizure frequency, neuropsychological abnormalities, MRI, SPECT and VEEG abnormalities, pathological antecedents and family history, presence of generalized tonic-clonic seizure and complex partial seizure, age at seizure onset, seizure duration, age at surgery and silent interval (Tables 3 and 4). Cognitive dysfunction, VEEG alterations and abnormalities under the MRI were significant (Tables 3 and 4). The same factors were compared for patients split into two different groups according to the Engel Classification: favorable and unfavorable outcome (Tables 5 and 6).

Surgical complications

As a complication after amygdalohippocampectomy (AHC), 11 patients experienced wound infection with meningitis and were successfully treated. As for neurological complications, six patients had motor deficits due to vascular complications and five patients developed important quadrantanopia, which affected part of their daily activities. Smaller visual deficits were not regarded as a complication; rather, they were considered a predicted adverse event in temporal lobe surgery.

Discussion

TLE is the most common type of partial epilepsy, while MTS is the most common underlying pathology [1]. Although MTS is the most commonly identified lesion in these patients, the role of injury in the development of epilepsy that is refractory to clinical treatment remains uncertain. MTS is a heterogeneous disease since there are patients with a severe refractory form while many others have a mild epileptic disorder and remit with or without antiepileptic medication [1].

There are studies that evaluate the prognostic factors in patients with MTS; in most cases, the studies assess the factors related to resistance to drugs and patients with TLE in general. In this study the potential risk factors for an unfavorable outcome were analyzed in patients who underwent surgery for refractory epilepsy due to MTS.

When analyzing the clinical data of the patients in this present study, seizure duration and age at surgery were higher than in other reported studies, perhaps due to patients' difficulty in gaining access to a specialized

Table 1 Clinical data of 400 patients

	n (%)	Range	Mean ± SD
Sex			
Male	218 (54.5)		
Female	182 (45.5)		
Handedness			
Right	371 (92.8)		
Left	20 (5.0)		
N/A	9 (2.3)		
Age at seizure onset (years)		0–48	9.07 ± 9.24
Seizure duration (years)		0–64	25.03 ± 13.15
Age at surgery (years)		1–75	36.72 ± 13.50
Silent interval (years)		0–32	2.71 ± 5.55
			P
Seizure frequency			
Weekly	265 (66.3)		
Monthly	125 (31.3)		
Sporadic	10 (2.5)		
Pathological antecedents and family history			
Febrile seizures	63 (15.8)		
Status epilepticus	7 (1.8)		
Head trauma	16 (4.0)		
CNS infections	16 (4.0)		
Vascular insults	4 (1)		
Neoplasms	4 (1)		
Perinatal insults	31 (7.8)		
Family history	170 (42.5)		
Consanguinity of parents	4 (1)		
Psychiatric illness	25 (6.3)		
Neuropsychological assessment			
Normal	183 (45.8)		
Abnormal	217 (54.3)		
Examinations			
MRI abnormality			
Absent	16 (4)		
Present	384 (96)		
SPECT abnormality			
Absent	0 (0)		
Present	400 (100)		
VEEG interictal abnormality			
Absent	18 (4.5)		
Present	382 (95.5)		
Side of surgery			
Right	191 (47.8)		
Left	209 (52.3)		
Presence of generalized tonic-clonic seizure	247 (61.75)		
Presence of complex partial seizures	391 (97.75)		

treatment center for intractable epilepsy. This study found a significant association between handedness and the surgical results, although this relationship was not found in other studies that evaluated only the clinical seizure control [21, 32]. While evaluating several articles, some of them have found a relationship between

Table 2 Engel Classification

	n (%)
Engel I	317 (79.25)
Engel II	28 (7)
Engel III	20 (5)
Engel IV	35 (8.75)

handedness and the surgical outcome; yet, there is still no explanation for this finding. A study had previously shown that left-handed epilepsy had left-sided epileptiform discharges and neuropsychological deficits. These authors found that patients who developed epilepsy before 5 years of age used to be left-handed, unlike patients who developed epilepsy later [9]. A similar mechanism has been proposed for pathological strong right-handedness in patients with right temporal lobe refractory epilepsy [14]. These theories are based on the "pathological left-handedness hypothesis," which

Table 4 Comparison of Engel Classification and age at seizure onset, seizure duration, age at surgery and silent interval

	Engel				
	I	II	III	IV	p
Age at seizure onset (years)	9.26	6.78	10.3	8.54	0.5113
Seizure duration (years)	24.05	28.78	26.85	29.91	0.0257
Age at surgery (years)	35.92	37.5	40.75	41.05	0.0864
Silent interval (years)	2.70	1.92	3.6	2.88	0.7779

Table 3 Comparison of the Engel Classification and evaluated factors

	Engel				
	I	II	III	IV	p
Sex					
Male	179	16	8	15	0.2424
Female	138	12	12	20	
Handedness					
Right	301	24	17	29	0.0003
Left	14	3	1	2	
N/A	2	1	2	4	
Side of surgery					
Right	150	18	9	14	0.2620
Left	167	10	11	21	
Seizure frequency					
Weekly	206	14	13	32	0.0021
Monthly	105	11	6	3	
Sporadic	6	3	1	0	
Factors					
Febrile seizures	33	8	9	12	<0.0001
Status epilepticus	4	1	0	2	0.2092
Head trauma	11	3	1	1	0.2969
CNS infections	13	2	0	1	0.6412
Vascular insults	2	1	0	1	0.2924
Neoplasms	3	0	0	1	0.6340
Perinatal insults	15	4	5	7	<0.0001
Family history	133	17	19	22	<0.0001
Consanguinity of parents	3	0	1	0	0.2750
Psychiatric illness	16	2	1	6	0.0468
Neuropsychological abnormality assessment	161	11	10	35	<0.0001
Examinations					
MRI abnormality	231	27	20	35	<0.0001
VEEG interictal abnormality	302	25	20	35	0.1613
Presence of generalized tonic-clonic seizure	180	22	14	31	0.0005
Presence of complex partial seizures	315	26	17	33	<0.0001

Table 5 Comparison of outcome and evaluated factors

	Favorable outcome Engel I	Unfavorable outcome Engel II + III + IV	p
Sex			
Male	179	39	0.1556
Female	138	44	
Handedness			
Right	301	70	<0.0001
Left	14	6	
N/A	2	7	
Side of surgery			
Right	150	41	0.8304
Left	167	42	
Seizure frequency			
Weekly	206	59	0.1143
Monthly	105	20	
Sporadic	6	4	
Factors			
Febrile seizures	33	29	<0.0001
Status epilepticus	4	3	0.3246
Head trauma	11	5	0.4578
CNS infections	13	3	0.8404
Vascular insults	2	2	0.4064
Neoplasms	3	1	0.8331
Perinatal insults	15	16	<0.0001
Family history	133	58	<0.0001
Consanguinity of parents	3	1	0.8331
Psychiatric illness	16	9	0.0915
Neuropsychological abnormality assessment	161	56	0.0095
Examinations			
MRI abnormality	231	82	<0.0001
VEEG interictal abnormality	302	80	0.8888
Presence of generalized tonic-clonic seizure	180	67	0.0001
Presence of complex partial seizures	315	76	0.0001

suggests that brain damage in early life may contribute to the development of atypical handedness [25]. This idea was supported by several studies examining children with a history of bacterial meningitis, premature birth or other causes of perinatal brain injury, which found a higher incidence of atypical laterality in affected children [23]. The surgery side showed no importance in some studies [5, 7, 12, 22, 28], while other studies report a worse outcome when the left side was operated [10]; however, few studies have evaluated MTS alone. In our study, the relation between the side of surgery and the surgical result was not significant.

Table 6 Comparison of outcome and age at seizure onset, seizure duration, age at surgery and silent interval

	Favorable outcome Engel I	Unfavorable outcome Engel II + III + IV	p
Age at seizure onset (years)	9.30	8.37	0.4364
Seizure duration (years)	24.05	28.79	0.0033
Age at surgery (years)	35.92	39.78	0.0204
Silent interval (years)	2.70	2.73	0.9708

Patients with a greater seizure frequency had a worse surgical outcome when all Engel classes were analyzed; however, no association was found when patients were analyzed for a favorable versus unfavorable outcome. Nonetheless, in some studies with TLE in general and patients with MTS, the frequency did not show statistical significance [12, 28].

Regarding the pathological antecedents, the occurrence of febrile seizure, perinatal insults and family history of epilepsy were associated with a worse outcome after surgery. Studies have reported that febrile seizures would be an important prognostic factor for both clinical and surgical treatment of TLE [1]. Some authors suggest that such a phenomenon would be the cause of MTS. Vascular insults were not seen as an important factor in other studies with TLE in general like ours [2, 13], while perinatal insults and family history of epilepsy have been reported as factors associated with a worse prognosis in both patients with TLE and patients with TLE due to MTS [1, 8]. However, these factors do not appear as significant prognostic factors in some studies, especially in studies that evaluated all types of TLE [1, 7, 13, 32].

Significant neuropsychological abnormalities were also found in patients with a worse prognosis, and the most frequent changes were mental retardation and memory deficits. However, this factor may be biased, since the greater the cognitive injury, the more difficult the adherence of the patient to treatment. Some studies found that neuropsychological deficits are related to the outcome of patients with MTS, corroborating the present findings [29].

Regarding neuroimaging, MRI findings had the most significant influence on the outcome of patients, which is in accordance with other studies [12], even though another study showed the opposite [29]. However, changes in MRI can mean greater hippocampal atrophy and a more advanced and chronic disease, thus with a worse outcome due to a higher epileptogenic zone. Many studies have shown circumscribed HS on preoperative MRI as a strong predictor of remission after TLE; moreover, the prognosis for seizure freedom in MRI-negative patients is generally less good but also more variable [16]. This variability is at least partly explained by varying MRI quality, reflected in the histopathologic findings [16]. Interictal VEEG did not show an important association with the outcome, as well as studies with patients with TLE and MTS [29, 32]. When analyzing the presence of generalized tonic-clonic seizures and the presence of complex partial seizures, it was observed that both cases had a worse outcome, as in some previous studies with MTS [8]. On the other hand, since tonic-clonic seizures and complex partial seizures are often found in patients with MTS, more detailed studies on the semiotics of the seizures could better explain the kind of crisis related to the prognosis of patients. Evaluating sociodemographic characteristics, such as the age at seizure onset, seizure duration, age at surgery and silent interval, a significant association between seizure duration and a worse outcome was observed, but it was only significant when patients with a favorable outcome were compared with others with an unfavorable outcome. This may mean that early treatment for these patients is the best approach to achieve a better outcome. The longer the duration of the disease, the more likely the disease is to evolve, the more the area of sclerosis is to increase and, consequently, the more the epileptogenic zone is to grow. Similar and even opposite results have been found in other reports with general TLE and MTS [1, 5, 7, 8, 10, 12]. This result suggests that early surgery may bring greater benefit to patients with MTS.

In addition, ATL is safe and causes few post-surgical complications, the most common of which are infection, vascular injury and visual deficits. Our complication count was equal to or below the average found in the literature [3, 18, 37]. All patients underwent sterilization and antiseptic techniques with sterile materials twice and took cefuroxime prophylactically for up to 3 days. To preserve the vascular structures, the pial plane between the mesial temporal structures and the ambient cistern was carefully respected. Smaller visual deficits—not regarded as a complication, but rather as a predicted adverse event in temporal lobe surgery—are actually occurring in about 30–50 % and up to 80 % of the cases if Yasargil selective amygdalohippocampectomy is performed because of the inherent risk of injury to the Meyer loop when opening the temporal horn from the inside [19, 20]. This adverse event can be prevented to a large degree by using modern diffusion tensor imaging sequences and tractography of the Meyer loop in the navigation system [36]. However, this type of technology is not available in the public health services in Brazil, where this study was conducted.

Conclusion

In this study, the MRI findings, seizure duration, seizure frequency, perinatal insults, family history of epilepsy, febrile seizures, neuropsychological abnormalities and presence of generalized tonic-clonic seizure were all statistically associated with a worse seizure outcome in MTS patients who underwent ATL. Identifying factors that influence the outcome of surgery for epilepsy patients during pre-surgery evaluation is crucial to improve the surgical indication and better advise the patients' families as to the expected results.

Compliance with Ethical Standards

Funding No funding was received for this research.

Conflict of Interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

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Comments

The authors present a large cohort of patients with MTLS, 400 out of 1214 patients evaluated for epilepsy surgery in the epilepsy center of Faculdade de Medicina de São Jose do Rio Preto. In their setting they have followed patients from several states of Brazil. My view is that the strength of this report is the large cohort operated on at one center, and it has taken a substantial effort to collect the data. They found the most important prognostic factor in their cohort to be the MRI finding, which is not surprising, but also factors such as age at surgery, epilepsy duration, seizure frequency, perinatal insults and other factors. They have an impressively low number of major complications, 6 out of 400, and they report separately findings of quadrantanopia, which of course is not regarded as an unexpected complication. Even if the results and conclusions of this report are not different from what we regard as important in the treatment of mesial temporal lobe sclerosis, it is still a confirmation in a large cohort of patients, and I recommend reading it.

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B. ARTIGO CIENTÍFICO 2

ARTIGO CIENTÍFICO 2

ELECTROENCEPHALOGRAPHY AND SEIZURE OUTCOME IN MESIAL TEMPORAL SCLEROSIS AFTER EPILEPSY SURGERY.

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ABSTRACT

Introduction: Epilepsy surgery is a safe and effective alternative treatment to medical therapy in patients with intractable partial epilepsy. The mesial temporal lobe epilepsy (MTE) is the most common form of partial epilepsy in adults. Therefore, of all epilepsies, mesial temporal sclerosis is perhaps the one that is best characterized electroclinically. Objetive: is to evaluate changes in interictal and ictal EEG as a prognostic factor for outcome in patients with mesial temporal sclerosis submitted to amygdalohippocampectomy. **Methods:** Of 1214 patients evaluated for surgery in the epilepsy Center of Faculdade de Medicina de São Jose do Rio Preto (FAMERP), a tertiary Brazilian epilepsy center, 400 underwent ATL for MTE. Electroencephalogram was analyzed and compared with Engel classification for outcome. **Results:** A significant relationship was found between the side of MTS under MRI and on SPECT with bilateral ictal EEG showing worse results. Surgical results correlated with ictal and interictal scalp EEG patterns and there was no difference when analyzing unilateral or bilateral discharges regardless of whether it was the interictal or ictal EEG. **Conclusion**: Identifying factors that influence the outcome of surgery for epilepsy patients during pre-surgery evaluation is crucial to improve the surgical indication and better advise the patients' families as to the expected results.

Key-Words: epilepsy, temporal lobe epilepsy, neurosurgery, prognostic factors, electroencephalogram, surgery

INTRODUCTION

Epilepsy surgery is a safe and effective alternative treatment to medical therapy in patients with intractable partial epilepsy; the most commonly performed surgical treatment for epilepsy is an anterior temporal lobectomy(1). The mesial temporal lobe epilepsy (MTLE) is the most common form of partial epilepsy in adults(2). Therefore, of all epilepsies, mesial temporal sclerosis is perhaps the one that is best characterized electroclinically(3).

Some authors found a significant relationship between the occurrence of spikes in electroencephalograms, especially after epilepsy surgery for temporal lobe epilepsy(4-7), while other studies failed to identify such an association(8). Electroencephalograms are often associated with anterior temporal spikes or sharp waves with voltage that is typically maximal in the anterior temporal regions in 90% of patients with MTLE(9). However, one-third of patients have bilateral temporal interictal epileptiform discharge (IEDs), which becomes apparent with long-term EEG monitoring(10).

Studies identified that the best surgical outcomes derive when 100% unilateral temporal IEDs are combined with ictal scalp EEGs that remain regionalized without contralateral propagation(11). Thus, the aim of this study is to evaluate changes in interictal EEG as a prognostic factor for outcome in patients with mesial temporal sclerosis submitted to amygdalohippocampectomy.

METHODS

Patients Selection

We performed a retrospective review of the centralized electronic and paper-based medical record database of the Center for Epilepsy Surgery, Hospital de Base, São José do Rio Preto — Faculty of Medicine at São José do Rio Preto between 2002 and 2013. A total of 1,214 patients were evaluated for epilepsy surgery of whom 400 underwent amygdalohippocampectomy for temporal lobe epilepsy.

Preoperative Evaluation and Clinical characteristics

All patients undergoing AHC for intractable epilepsy first underwent a comprehensive evaluation to confirm TLE. This assessment included magnetic resonance imaging (MRI) with seizure protocol, inpatient continuous video-electroencephalographic monitoring (VEEG), single-photon emission computed tomography (SPECT) and neuropsychological evaluation. Each patient was discussed at a multidisciplinary epilepsy conference attended by adult and or pediatric epileptologists, neurosurgeons, neuroradiologists, and neuropsychologists. Once surgery was offered, written informed consent was obtained.

All patients involved in the present study were submitted to non-invasive VEEG monitoring. The Stella system, Neuro Workbench software and Nihon Kohden hardware were used to record and later evaluate all the epileptic events. Every patient was analyzed by an experienced epileptologist as an integral part of patient assessment.

Mainly the result of the EEG interictal and ictal period was analyzed and the patients were split into groups according to their results. Regarding the focus patients were divided into unilateral (right or left) and bilateral. Patients with interictal abnormalities (spikes and sharp waves) were divided into two groups: abnormal unilateral or abnormal bilateral. The results of ictal EEG were evaluated when the seizure started. Again, two groups were considered: unilateral, when the seizure started or remained in one hemisphere, and bilateral, when the seizure started in both hemispheres or when discharge changed hemispheres.

Surgical Procedure

Anteromedial temporal lobe resection and then aggressive amygdalohippocampectomy using microsurgical techniques were performed in patients with MTS abnormalities. Briefly, after a standard frontotemporal craniotomy, the lateral temporal neocortex (from the superior down to the inferior temporal gyrus) was removed while exposing the anterior temporal horn of the lateral ventricle. The extent of cortical resection from the temporal tip ranged from 4.5 to 5.0 cm. The surgeon then extracted the amygdala and uncus subpially. Hippocampal and parahippocampal gyri were then mobilized and resected en bloc between the collateral sulcus and the choroidal fissure. Resection of the tail of the hippocampus was extended posterior to the level of the tectal plate. The pial plane between the mesial temporal structures and the ambient cistern was carefully respected.

Postoperative Outcome

The operative outcomes were reviewed using the modified Engel classification. Engel class I patients were defined as being seizure-free or having only nondisabling, simple partial seizures, or they had some disabling seizures after surgery but had been free of disabling seizures for at

least 2 years and generalized tonic-clonic seizures occurred only after withdrawal of antiepileptic drugs. Class II patients had rare seizures (85% reduction); class III patients had a greater than 50% reduction in seizure frequency; and class IV patients had no meaningful reduction in seizure frequency. Those achieving an Engel class I outcome were considered to have a favorable outcome whereas those achieving classes II through IV outcomes were considered to have an unfavorable outcome. Postoperative outcomes were available for more than 1 year.

Statistical Analysis

Appropriate statistical analyses were performed using SPSS statistical software. Demographic information, seizure types and frequencies were analyzed and compared with means, medians, and standard deviations. Para realizer a comparação entre duas amostras independentes, cujo os dados são categóricos, pode-se conduzir o estudo através do teste exato de Fisher, do teste qui-quadrado ou do teste do posto de Spearman. No entanto, se os dados envolvidos são contínuos utilizou-se por exemplo, o teste t. Neste trabalho, as variáveis consideradas no estudo de correlação foram os testes estatísticos utilizados foram os mencionados anteriormente. $P<0.05$ was considered significant.

RESULTS

Patients' Characteristics

Four hundred patients underwent amygdalohippocampectomy for intractable seizures due to MTS between 2003 and 2013. All patients met all inclusion criteria within at least one year of

postsurgical follow-up. The clinical data of patients is shown in Table 01, divided into overall group and 2 ictal EEG groups (unilateral and bilateral). The group of patients consisted of 218 (54.5%) men and 182 (45.5%) women, with 132 (60.8%) men and 86 (39.2%) women in the unilateral group and 86 (47%) men and 97 (53%) women in the bilateral group — there was a balance between genders —, with a mean age of 36.72 years ranging from 1 to 75 years; 35.58 years in the unilateral group and 38.08 years in the bilateral group. Age at seizure onset ranged from 0 to 48 years with a mean of 9.07 years; 8.58 years in the unilateral group and 9.66 years in the bilateral group. Seizure duration ranged from 0 to 64 years with a mean of 25.03 years; 24.08 years in the unilateral group and 26.16 years in the bilateral group. The silent interval ranged from 0 to 32 years with a mean of 2.71 years; 3.02 in the unilateral group and 2.34 years in the bilateral group.

About the handedness, 371 (92.8%) patients were right-handed, 20 (5%) were left-handed and 9 (2.3%) patients could not be identified. The seizure frequency before amygdalohippocampectomy was 66.3% weekly, 31.3% monthly and 2.5% sporadic. One hundred and ninety-one patients underwent amygdalohippocampectomy on the right side and 209 on the left. Information on both the unilateral and bilateral groups — including the p value and the side of surgery — can be seen in Table 01.

Exams

All patients were submitted to a series of exams, MRI, EEG and SPECT. All patients presented abnormalities in SPECT and 384 patients presented abnormalities under MRI. The side of MTS within each group can be seen in Table 01. As for interictal EEG, 345 patients had unilateral presentation and 55 patients had bilateral presentation (Table 01).

Patients' Outcomes

Patients' outcomes are shown in Table 2. The Engel outcomes for the overall cohort one year after surgery were as follows: 317 patients achieved Engel class I, 28 Engel class II, 20 Engel class III, 35 Engel class IV. Considering that Engel I patients had a favorable outcome and Engel II, III and IV patients had an unfavorable outcome, we have 317 patients with a favorable outcome and 83 patients with an unfavorable outcome.

Prognostic Factors

Several factors were analyzed correlating the class of Engel patients such as gender, handedness, surgery side, seizure frequency, side of MTS under MRI, side of MTS in SPECT, interictal EEG lateralization and ictal EEG lateralization, age at seizure onset, seizure duration, age at surgery and silent interval (Table 3). The same factors were compared for patients split into two different groups according to the Engel classification: favorable and unfavorable outcome (Table 4). The p value can be found in the same tables.

DISCUSSION

Mesial temporal sclerosis is the disease that best characterizes temporal lobe epilepsy, which can lead to intractable epilepsy as well as physical and social disability. More than 60% of patients with focal seizures will become seizure-free with AEDs(12). The rest of the patients may control seizures through surgery. In addition, the study of prognostic factors may help determine the best candidates for surgery or the expected seizure control. The pre and postoperative EEG has been used to determine possible factors for these patients.

This study tried to correlate the results of pre-surgical ictal and interictal EEG with surgical outcomes of patients undergoing CAH for seizure control. The study was based on the

hypothesis that patients with bilateral abnormalities in interictal EEG or ictal EEG with propagation might have a worse prognosis in seizure control; however, this association was not found. There was no significant difference in patients who had an ictal EEG bilateral lateralization, regardless of whether the interictal EEG showed unilateral or bilateral abnormalities. In a previously published study about unilateral MTS, there is no relation between the location or lateralization of seizures with post-surgical prognosis of patients.

When the ictal and the interictal EEG were analyzed through Engel classification with surgical outcomes, there was also no statistical significance. However, Schulz et al., 2000, affirmed that the switch of lateralization or bitemporal asynchrony in the ictal scalp EEG and bitemporal IED are most probably an index of bitemporal epileptogenicity in MTS and are associated with a worse outcome(11). Aguglia et al. reported that neither free- or not-free-of-seizure patients showed differences in the interictal EEG regardless of being normal or abnormal, bilateral or unilateral(2). In two different works Jeong et al. evaluated ictal and interictal EEG with respect to the side of the surgery and patients showed that discharges on the same side of the surgery did not show better results than those who had discharges on the opposite side of the surgery(13, 14). This result was similar when comparing the side of the surgery with ictal EEG and outcome according to Engel classification. Another study performed in the same country and region found similar results to those shown in our study, stating that the analysis of the location, morphology, and lateralization of ictal EEG patterns did not provide prognostic information regarding seizure-free status in patients with MTS undergoing CAH(15).

Other factors were evaluated for the patients' prognosis. A significant relationship was found between the side of MTS under MRI and on SPECT with bilateral ictal EEG showing worse

results, unlike what is presented by Monnerat et al., 2013(15). O teste de correlação apresentou um p-valor igual a 0,002398 indicando que há uma associação significativa entre o lado do MTS sobre o MRI dos pacientes submetidos a AHC e a lateralização do EEG ictal. Entretanto, o teste de correlação apresentou um p-valor igual a 0,06084 indicando que não há uma associação significativa entre o lado do MTS sobre o SPECT os pacientes submetidos a AHC e a lateralização do EEG ictal, neste exame só houve correlação quando analisado o exame individualmente sem influência do resultado do EEG. Quanto o lado da cirurgia dos pacientes submetidos a AHC e a lateralização do EEG ictal, o p-valor igual a 0,001202 indicou uma associação significativa. The surgery side showed no importance in some studies(14, 16-19), while other studies report a worse outcome when the left side was operated(20), but few studies have evaluated the MTS alone. Mas nenhum destes estudos chegou a correlacionar o EEG ictal com o lado da cirurgia. A destreza manual não teve relação quando separado de acordo com EEG ictal, apenas quando analisada isoladamente com a classificação de Engel. Although the relationship was not found in other studies that evaluated only the clinical seizure control(21, 22). Patients with a greater seizure frequency had a worse surgical outcome when all Engel classes were analyzed; however, no association was found when patients were analyzed for a favorable versus unfavorable outcome. Nonetheless, in some studies with TLE in general and patients with MTS, the frequency did not show statistical significance(14, 19).

In the present study, patients with MTS undergoing CAH did not have their surgical results correlated with ictal and interictal scalp EEG patterns and there was no difference when analyzing unilateral or bilateral discharges regardless of whether it was the interictal or ictal EEG. Therefore, the unilaterality and propagation are found in patients with MTS; however, it

does not imply surgical outcome. Nevertheless, other factors are associated, such as MTS on MRI and SPECT.

O teste de correlação apresentou um p-valor igual a 0,007643 indicando que há uma associação significativa entre o sexo dos pacientes submetidos a AHC e a lateralização do EEG ictal, sendo o sexo feminio apresentou mais alterações bilaterais e pior resultado. No entanto, esse achado não foi encontrado em outros trabalhos(15). Talvez essa correlação se deva a diferença de proproção entre os dois grupos.

CONCLUSION

In the present study, seizure frequency, side of MTS under MRI and SPECT, side of surgery, handediness, seizure frequency were statistically associated with a worse seizure outcome in MTS patients who underwent CAH, but ictal and interictal scalp EEG patterns and there was no difference. Identifying factors that influence the outcome of surgery for epilepsy patients during pre-surgery evaluation is crucial to improve the surgical indication and better advise the patients' families as to the expected results.

Table 1: Clinical data of all 400 patients with MTS underwent an AHC and divided per ictal EEG lateralization.

	Total	Unilateral	Bilateral	p
	N=400	N=217	N=183	
Sex				
Male (%)	218 (54.5)	132 (60.8)	86 (47)	0.007643
Female	182 (45.5)	85 (39.2)	97 (53)	
Handedness				
Right	371 (92.8)	204 (94)	167 (91.7)	0.1541
Left	20 (5.0)	11 (5)	9 (4.9)	
N/A	9 (2.3)	2 (1)	7 (3.9)	
Age at seizure onset in years (mean)	9.07 ± 9.24	8.58±8.89	9.66 ± 9.63	0.8098
Seizure duration in years (mean)	25.03 ± 13.15	24.08 ± 12.68	26.16 ± 13.63	0.9906
Age at surgery in years (mean)	36.72 ± 13.50	35.58 ± 12.65	38.08 ± 14.37	0.9143
Silent interval in years (mean)	2.71±5.55	3.02 ± 6.23	2.34 ± 4.61	0.8101
Seizure frequency				
Weekly	265 (66.3)	135 (62.2)	130 (71)	0.1468
Monthly	125 (31.3)	75 (34.6)	50 (27.3)	
Sporadic	10 (2.5)	7 (3.2)	3 (1.7)	
Exams				
Side of MTS under MRI				
Normal	16 (4)	14 (6.4)	2 (1.1)	0.002398
Right	122 (30.5)	70 (32.3)	54 (29.5)	
Left	165 (41.2)	95 (43.8)	73 (39.9)	
Bilateral	97 (24.3)	38 (17.5)	54 (29.5)	
Side of MTS on SPECT				
Right	102 (25.5)	64 (29.5)	38 (20.8)	0.06084
Left	166 (41.5)	87 (40.1)	79 (43.1)	
Bilateral	132 (33)	66 (30.4)	73 (38.9)	
Interictal EEG				
Unilateral	345 (86.2)	181 (83.4)	164 (89.6)	0.09889
Bilateral	55 (13.8)	36 (16.6)	19 (10.4)	
Side of surgery				
Right	191 (47.8)	87 (40.1)	104 (56.8)	0.001202
Left	209 (52.3)	130 (59.9)	79 (43.2)	

Table 2: Engel classification

	n (%)
Engel I	317 (79.25)
Engel II	28 (7)
Engel III	20 (5)
Engel IV	35 (8.75)

Table 3: Comparison of Engel Classification and evaluated factors.

	Engel				
	I	II	III	IV	p
Sex					
Male	179	16	8	15	0.2424
Female	138	12	12	20	
Handedness					
Right	301	24	17	29	0.0003
Left	14	3	1	2	
N/A	2	1	2	4	
Side of surgery					
Right	150	18	9	14	0.2620
Left	167	10	11	21	
Seizure frequency					
weekly	206	14	13	32	0.0021
monthly	105	11	6	3	
sporadic	6	3	1	0	
Exams					
Side of MTS under MRI					
Normal	13	3	0	0	0.0029
Right	105	6	4	7	
Left	141	8	6	10	
Bilateral	63	12	8	14	
Side of MTS on SPECT					
Right	85	6	4	7	0.0171
Left	142	7	7	10	
Bilateral	90	15	9	18	
Interictal EEG					
Unilateral	176	17	8	16	0.3419
Bilateral	141	11	12	19	
Ictal EEG onset					
Unilateral	179	15	10	13	0.1789
Bilateral	138	13	10	22	

Table 4: Comparison of outcome and evaluated factors.

	Favorable outcome Engel I	Unfavorable outcome Engel II + III + IV	P
Sex			
Male	179	39	0.2424
Female	138	44	
Handedness			
Right	301	70	0.000271
Left	14	6	
N/A	2	7	
Side of surgery			
Right	150	41	0.8304
Left	167	42	
Seizure frequency			
weekly	206	59	0.1085
monthly	105	20	
sporadic	6	4	
Exams			
Side of MTS under MRI			
Normal	13	3	
Right	105	17	0.0003184
Left	141	24	
Bilateral	63	34	
Side of MTS on SPECT			
Right	85	17	0.0005919
Left	142	24	
Bilateral	90	42	
Interictal EEG			
Unilateral	176	41	0.3826
Bilateral	141	42	
Ictal EEG onset			
Unilateral	179	38	0.1062
Bilateral	138	45	

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C. ARTIGO CIENTÍFICO 3

ARTIGO CIENTÍFICO 3

AURAS AS A PROGNOSTIC FACTOR IN ANTERIOR TEMPORAL LOBE RESECTIONS FOR MESIAL TEMPORAL SCLEROSIS

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ABSTRACT

Introduction: Anterior temporal lobectomy for mesial temporal sclerosis is a very effective measure to control seizures, and the probability of being seizure-free is approximately 70-90%. However, 30% of patients still experience seizures after surgery. An Aura is a subjective ictal phenomenon that may precede an observable seizure. Nevertheless, few are the studies associating the prognostic factor with aura, although, being the initial symptoms of epileptic seizures, many types of auras have significant localizing or lateralizing value. **Objetive:** This study hypothesized that the type of preoperative aura may predict the postsurgical outcome in patients with medically refractory temporal lobe epilepsy due to mesial temporal sclerosis. Methods: Of 1214 patients evaluated for surgery in the epilepsy Center of Faculdade de Medicina de São Jose do Rio Preto (FAMERP), a tertiary Brazilian epilepsy center, 400 underwent ATL for MTS. Number and type of auras was analyzed and compared with Engel classification for outcome. **Results:** Analyzing the patients by the type of aura, those who had extratemporal auras had worst result in post-surgical in Engel classifcation. While mesial auras apparently is a good prognostic factor. Patients without aura also had worse prognosis. Simple and multiple aura had no difference. **Conclusion:** In order to identify the most appropriate candidates for ATL, is very important to consider the prognostic factors associated with favorable for counseling patients in daily practice.

Key words: epilepsy, mesial temporal sclerosis, neurosurgery, prognostic factors, auras

INTRODUCTION

Epilepsy remains a common medical and neurological problem in the general population[1]. The temporal lobe is the most epileptogenic region of the human brain[2]. Mesial temporal lobe epilepsy (MTLE) is the prototype of a surgically remediable epileptic syndrome in medically refractory cases[3]. Mesial temporal sclerosis (MTS) is the most common disease found in an epilepsy surgery series and may be readily detected by magnetic resonance imaging (MRI) of the brain[4, 5]. Anterior temporal lobectomy for mesial temporal sclerosis is a very effective measure to control seizures, and the probability of being seizure-free is approximately 70-90%[3, 5-8]. However, 30% of patients still experience seizures after surgery[3, 5-8].

Typically, the seizures are characterized by autonomic and/or psychic subjective symptoms (most commonly a sensation of something rising from the stomach), staring, or also gestural or oral-alimentary automatisms[4, 5]. An Aura is a subjective ictal phenomenon that may precede an observable seizure[9]. Auras constitute a cardinal feature of temporal lobe epilepsy (TLE), which is the most common type of focal epilepsy in adults[10]. Typical auras in TLE-HS patients are epigastric sensations and psychic symptoms, which include fear, dysmnesia (such as déjà vu and jamais vu), and olfactory and gustatory sensations[11-13]. The patients may report single or multiple auras or occasionally, no aura at all[14].

Early age at seizure onset, a history of febrile convulsions, epileptiform discharges on the EEG, duration of epilepsy, number of generalized seizures and severity of psychiatric disturbances are possible prognostic factors in patients with MTE[15-17]. Nevertheless, few are the studies associating the prognostic factor with aura, although, being the initial symptoms of epileptic

seizures, many types of auras have significant localizing or lateralizing value[18]. Therefore, identifying prognostic factors is very important to find the ideal candidates for surgery.

This is a retrospective study to analyze the clinical data of a homogeneous group of patients with MTS. This study hypothesized that the type of preoperative aura may predict the postsurgical outcome in patients with medically refractory temporal lobe epilepsy due to mesial temporal sclerosis.

PATIENTS AND METHODS

Patients Selection

We performed a retrospective review of the centralized electronic and paper-based medical record database of the Center for Epilepsy Surgery, Hospital de Base, São José do Rio Preto — Faculty of Medicine at São José do Rio Preto — between 2002 and 2013. A total of 1,214 patients were evaluated for epilepsy surgery, 400 of whom underwent amygdalohippocampectomy for mesial temporal sclerosis.

Preoperative Evaluation and Clinical characteristics

All patients undergoing AHC for intractable epilepsy first underwent a comprehensive evaluation to confirm MTS. This assessment included magnetic resonance imaging (MRI) with seizure protocol, inpatient continuous video-electroencephalographic monitoring (VEEG), single-photon emission computed tomography (SPECT) and neuropsychological evaluation. Each patient was discussed at a multidisciplinary epilepsy conference attended by adult and

pediatric epileptologists, neurosurgeons, neuroradiologists, and neuropsychologists. Once surgery was offered, a written informed consent was obtained.

Clinical characteristics registered for each subject included age at surgery, the duration of epilepsy, age at febrile seizure onset, and febrile convulsion.

Surgical Procedure

Anteromedial temporal lobe resection and then aggressive amygdalohippocampectomy using microsurgical techniques were performed in patients with MTS abnormalities. Briefly, after a standard frontotemporal craniotomy, the lateral temporal neocortex (from the superior down to the inferior temporal gyrus) was removed while exposing the anterior temporal horn of the lateral ventricle. The extent of cortical resection from the temporal tip ranged from 4.5 to 5.0 cm. The surgeon then extracted the amygdala and uncus subpially. Hippocampal and parahippocampal gyri were then mobilized and resected en bloc between the collateral sulcus and the choroidal fissure. Resection of the tail of the hippocampus was extended posterior to the level of the tectal plate. The pial plane between the mesial temporal structures and the ambient cistern was carefully respected.

Postoperative Outcome

The operative outcomes were reviewed using the modified Engel classification. Engel class I patients were defined as being seizure-free or having only nondisabling, simple partial seizures, or they had some disabling seizures after surgery but had been free of disabling seizures for at least 2 years and generalized tonic-clonic seizures occurred only after the withdrawal of antiepileptic drugs. Class II patients had rare seizures (85% reduction); class III patients had a greater than 50% reduction in seizure frequency; and class IV patients had no meaningful

reduction in seizure frequency. Those achieving an Engel class I outcome were considered to have a favorable outcome whereas those achieving classes II through IV outcomes were considered to have an unfavorable outcome. Postoperative outcomes were available for more than 1 year.

Information on the type and number of auras were obtained through interviews with patients. Auras were grouped following the Classification of Epileptic Seizures of the International League Against Epilepsy[19] and, according to their most frequent anatomical localization[20], they were divided into four groups: (1) mesial temporal lobe auras, which included psychic symptoms such as dysmnesic, cognitive and affective auras, autonomic auras such as epigastric sensation with or without other autonomic signs or symptoms, olfactory and gustatory sensations; (2) lateral temporal lobe auras, including vertiginous and auditory auras; (3) extratemporal auras, which included somatosensory, visual and dysphasic auras; and (4) unspecific auras, including a vague feeling of discomfort, whole body auras, and cephalic sensation. Patients were also classified in two groups according to the presence and number of auras: (1) absent or single aura and (2) multiple auras.

Statistical Analysis

Appropriate statistical analyses were performed using SPSS statistical software. Demographic information, seizure types and frequencies were analyzed and compared with means, medians, and standard deviations. Quando se quer realizar a comparação entre duas amostras independentes, cujo os dados são categóricos, pode-se conduzir o estudo através do teste exato de Fisher, do teste qui-quadrado ou do teste do posto de Spearman. É neste sentido que o estudo de correlação deste trabalho é realizado. $P<0.05$ was considered significant.

RESULTS

Patients' Characteristics

Four hundred patients underwent amygdalohippocampectomy for intractable seizures due to MTE between 2003 and 2013. All patients met all inclusion criteria within at least one year of postsurgical follow-up. The clinical data of patients is shown in Table 01. The group of patients consisted of 218 (54.5%) men and 182 (45.5%) women — there was a balance between genders —, with a mean age of 36.72 years ranging from 1 to 75 years. Age at seizure onset ranged from 0 to 48 years with a median of 9.07 years. Seizure duration ranged from 0 to 64 years with a mean of 25.03 years. The silent interval ranged from 0 to 32 years with a mean of 2.71 years. About their handedness, 371 (92.8%) patients were right-handed, 20 (5%) were left-handed and 9 (2.3%) patients could not be identified. The seizure frequency before amygdalohippocampectomy was 66.3% weekly, 31.3% monthly and 2.5% sporadic. One hundred and ninety-one patients underwent amygdalohippocampectomy on the right side and 209 on the left (Table 01).

Patients' Outcomes

Patients' outcomes are shown in Table 2. The Engel outcomes for the overall cohort one year after surgery were as follows: 317 patients achieved Engel class I, 28 Engel class II, 20 Engel class III, 35 Engel class IV. Engel I patients were considered to have had a favorable outcome whereas Engel II, III and IV patients were said to have had an unfavorable outcome; therefore, 317 patients had a favorable outcome while 83 patients had an unfavorable outcome.

Type of Aura

Several types of aura were analyzed: psychic symptoms, such as dysmnesic aura (7.5%), cognitive aura (1.8%) and affective aura (4.5%), epigastric sensation with other autonomic signs

(3.3%) and without other autonomic signs (19%); autonomic (31.8%) , olfactory sensation (2.5%) and gustatory sensation (1.8%), vertiginous sensation (5.8%) and auditory aura (2%), somatosensory aura (5.3%), visual aura (4.8%) and dysphasic aura (0.5%), vague feeling of discomfort (3.5%), whole body auras (3.5%) and cephalic sensation (6.5%) (Tables 3 and 4). Of all patients, 84 presented no aura (21%). After identifying the types of aura, a correlation with the Engel classification indicated that somatosensory, visual, auditory, and dysphasic patients, as well as those with no aura, showed statistical significance (Table 3).

The auras were split into four different groups according to their probable anatomical localization such as mesial temporal lobe (80.04%), lateral temporal lobe (5.96%), extratemporal lobe (9.40%) and unspecific (7.56%). Then, they were compared with the Engel classification: favorable and unfavorable outcome (Table 4), featuring a statistical significance indicating worse outcome in patients with surgical mesial aura and extratemporal aura ($6{,}725 \times 10^{-15}$). The patients with mesial aura had a better surgical outcome, while the patients with extratemporal aura had a worse outcome (Table 4).

In addition, groups were divided according to the absence of aura, if the patient had only one aura, and if they experienced multiple auras. Then, they were compared with the Engel classification (Table 5). Values were significant and the outcome was worse for patients who had no aura (0.005335).

DISCUSSION

Patients with partial epilepsy may report multiple types of aura during their seizures and the significance of the occurrence of multiple auras in the same patient is not known [21]. This

study aimed to correlate the types of aura and their anatomical localizations with the postoperative prognosis of patients after corticoamygdalohippocampectomy.

An aura or multiple auras have different prevalence in the literature ranging from 0.4% to 60%, varying according to the methods used to identify them [14, 21-24]. Widdess-Walsh et al. [21] found a multiple-aura prevalence of 0.4% in patients submitted to VEEG; however, in these centers, medication is usually discontinued in order to provoke seizures, which may favor generalized seizures, making it difficult to identify the auras. The main method to identify a patient's aura would be anamnesis, which can be influenced by the patient's level of formal education. In this study, 79% of the patients presented an aura, 35.5% presented only one type of aura and 43.5% presented multiple auras.

The mechanism that triggers several types of aura is not yet clear; seizures are believed to be focal without deepening or spreading collaterally, thus preserving the patients' conscience and allowing them to be aware of their aura[25]. Based on this theory, we might conclude that patients with multiple auras could present worse postoperative results, since having a greater number of auras means that they would have a greater initial seizure area. However, this work showed that there is no statistical significance when the number of auras are correlated with the Engel classification, except when the patient presents no aura at all. The work of Widdess-Walsh et al.[21] and the work of Ferrai-Marinho et al.[14] also concluded that the presence of multiple auras did not have a relationship with the operative outcome. Apenas quando o paciente não apresenta nenhum tipo de aura, neste caso, o paciente apresenta o prognóstico pós-cirurgico pior.

Some studies suggest that in the case of temporal lobe epilepsies, patients with more extensive lesions have worse postoperative results[26]. However, imaging exams many times do not

detect the exact size of lesions and can miss those of microscopic dimension. An alternative to determine the size of lesions would be assessing their auras. Auras with extratemporal characteristics could indicate symptomatogenic zones beyond the temporal region, therefore, a worse postoperative outcome is expected in these cases. Although previous studies show that cortical areas are silent and their symptoms only show when discharges start to spread through neighboring areas[18], other studies show that the seizure onset spot influences the type of aura[27]. In this study, when groups of patients were compared for mesial, lateral, extratemporal or unspecific aura with a favorable or unfavorable outcome based on Engel classification, the group with extratemporal aura showed a worse postoperative result when compared to the group with mesial aura; $p<0.0001$ was considered significant. Other localizations did not show any difference. Other studies confirm this hypothesis.

In the study of Erickson et al. [28], 81 patients with refractory TLE were evaluated after surgery. The authors concluded that the occurrence of somatosensory auras – be they unilateral or bilateral – should not contraindicate surgery when complementary exams show a unilateral seizure focus. However, when the group of patients with contralateral symptoms was analyzed, half of them had seizures after surgery.

Auras that are generally associated to other brain lobes are also found in TLE patients. Bien et al. [29] found elementary hallucinations, illusions and loss of eyesight reported in all patients with occipital lobe epilepsy, as well as in patients with temporal, occipitotemporal and anteromedial seizures. In our study, some patients showed visual auras and, when the operative outcome was assessed on the type of aura, such patients presented an unfavorable surgical result. In the study of Ferrai-Marinho et al. [14], 27 of 205 (14%) patients reported visual auras

throughout life; these patients presented worse postsurgical prognosis according to this study's results.

Other studies show evidences suggesting that TLE does not affect only the hippocampus, but other brain structures as well [30-32]. Therefore, patients with these characteristics could have extratemporal auras, thus indicating a worse surgical outcome in the control of seizures[14, 28, 32, 33].

CONCLUSION

Seizure semiology may help identify ideal candidates to good operative outcome among MTS patients. The extratemporal cortex symptoms as origin of the epileptogenic focus suggest that operative outcomes will not be satisfactory, thus becoming a predictive factor of worse prognosis. Therefore, MTS patients with symptoms and clinical signs that suggest extratemporal involvement must be carefully assessed so that a sufficient are is desiccated to eliminate the epileptogenic focus during surgery and alert both patients and their families that the seizures may not be totally controlled.

Table 1: Clinical data of 400 patients

	n (%)	Range	Mean ± S.D.
Sex			
Male	218 (54.5)		
Female	182 (45.5)		
Age at seizure onset (year)		0-48	9.07 ± 9.24
Seizure duration (year)		0-64	25.03 ± 13.15
Age at surgery (year)		1-75	36.72 ± 13.50
Silent interval (year)		0-32	2.71±5.55
			P
Seizure frequency			
weekly	265 (66.3)		
monthly	125 (31.3)		
sporadic	10 (2.5)		
Side of surgery			
Right	191 (47.8)		
Left	209 (52.3)		

Table 2: Engel classification

	n (%)
Engel I	317 (79.25)
Engel II	28 (7)
Engel III	20 (5)
Engel IV	35 (8.75)

Table 3. Comparison of outcome and types of aura.

Aura type		Favorable outcome	Unfavorable outcome	**Total**	**p-valor**
Somatosensory	Presente	10 (3,2%)	11 (13,3%)	21 (5,3%)	0,0007
	Ausente	307 (96,8%)	72 (86,7%)	379 (94,8%)	
Visual	Presente	5 (4,4%)	5 (6,0%)	19 (4,8%)	0,0361
	Ausente	317 (95,6%)	78 (94,0%)	381 (95,3%)	
Auditory	Presente	5 (1.58%)	3 (3,6%)	8 (2,0%)	0,3710
	Ausente	312 (98,42%)	80 (96,4%)	392 (98,0%)	
Vertiginous	Presente	19 (6,0%)	4 (4,8%)	23 (5,8%)	0,7972
	Ausente	298 (94,0%)	79 (95,2%)	377 (94,3%)	
Olfactory	Presente	7 (2,2%)	3 (3,6%)	10 (2,5%)	0,4393
	Ausente	310 (97,8%)	80 (96,4%)	390 (97,5%)	
Gustatory	Presente	6 (1,9%)	1 (1,2%)	7 (1,8%)	1
	Ausente	311 (98,1%)	82 (98,8%)	393 (98,3%)	
Whole body auras	Presente	4 (1,3%)	1 (1,2%)	5 (1,3%)	1
	Ausente	313 (98,7%)	82 (98,8%)	395 (98,8%)	
Vague feeling of discomfort	Presente	11 (3,5%)	3 (3,6%)	14 (3,5%)	1
	Ausente	306 (96,5%)	80 (96,4%)	386 (96,5%)	
Cephalic Sensation	Presente	21 (6,6%)	5 (6,0%)	26 (6,5%)	
	Ausente	296 (93,4%)	78 (94,0%)	374 (93,5%)	1
Cognitive	Presente	5 (1,6%)	2 (2,4%)	7 (1,8%)	
	Ausente	312 (98,4%)	81 (97,6%)	393 (98,3%)	0,6383
Epigastric sensation	Presente	9 (2,8%)	4 (4,8%)	13 (3,3%)	
	Ausente	308 (97,2%)	79 (95,2%)	387 (96,8%)	0,5768
Autonomic (not epigastric)	Presente	70 (22,1%)	6 (7,2%)	76 (19,0%)	
	Ausente	247 (77,9%)	77 (92,8%)	324 (81,0%)	0,0036
Autonomic	Presente	112 (35,3%)	15 (18,1%)	127 (31,8%)	
	Ausente	205 (64,7%)	68 (81,9%)	273 (68,3%)	0,0041
Affective (no fear)	Presente	13 (4,1%)	5 (6,0%)	18 (4,5%)	
	Ausente	304 (95,9%)	78 (94,0%)	382 (95,5%)	0,6491
Fear	Presente	34 (10,7%)	6 (7,2%)	40 (10,0%)	
	Ausente	283 (89,3%)	77 (92,8%)	360 (90,0%)	0,4594
Affective	Presente	41 (12,9%)	7 (8,4%)	48 (12,0%)	
	Ausente	276 (87,1%)	76 (91,6%)	352 (88,0%)	0,3506
Dysphasic	Presente	9 (2.84%)	2 (2,4%)	2 (0,5%)	
	Ausente	308 (97%)	81 (97,6%)	398 (99,5%)	1
Psychic	Presente	30 (9,5%)	9 (10,8%)	39 (9,8%)	
	Ausente	287 (90,5%)	74 (89,2%)	361 (90,3%)	0,8655
Psychic other	Presente	2 (0,6%)	2 (2,4%)	4 (1,0%)	
	Ausente	315 (99,4%)	81 (97,6%)	396 (99,0%)	0,1917
Psychic dysmnestic	Presente	24 (7,6%)	6 (7,2%)	30 (7,5%)	
	Ausente	293 (92,4%)	77 (92,8%)	370 (92,5%)	1
No aura	Presente	56 (17,7%)	28 (33,7%)	84 (21,0%)	
	Ausente	261 (82,3%)	55 (66,3%)	316 (79,0%)	0,0023
Total		**317 (100%)**	**83 (100%)**	**400 (100%)**	-

Table 4. Comparison of outcome and anatomical types of aura.

Aura types	Favorable outcome	Unfavorable outcome	Total	P value
Mesial temporal	323 (84.78)	26 (47.27)	349 (80.04)	$6{,}725x10^{-15}$
Lateral temporal	19 (4.98)	7 (12.72)	26 (5.96)	
Extratemporal	24 (6.29)	17 (30.90)	41 (9.40)	
Unspecific	15 (3.93)	18 (32.72)	33 (7.56)	
Total	381	55	436	

Table 5. Comparison of outcome and numbers of auras

Aura	Favorable outcome	Unfavorable outcome	total	P value
Absent	56 (17.66)	28 (33.73)	84 (21)	0,005335
Single	142 (44.79)	32 (38.55)	174 (43.5)	
Multiple	119 (37.53)	23 (27.71)	142 (35.5)	
Total	317	83	400	

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4. CONCLUSÕES

CONCLUSÕES

1. No presente estudo, alterações na RME, tempo de doença, frequência das crises, lesões perinatais, história familiar de epilepsia, convulsões febris, alterações neuropsicológicas e presença de crise tônico-clônicas generalizadas foram estatisticamente associadas a um pior resultado pós-cirúrgico em pacientes com EMT submetidos à CAH. Identificar fatores que influenciam o resultado cirúrgico dos pacientes com epilepsia durante a avaliação pré-operatória é crucial para melhorar a indicação cirúrgica e o aconselhamento das famílias e dos pacientes quanto aos resultados esperados.
2. O lado do EMT no RME (a esquerda), lado da dominância manual (a esquerda) e a frequência de crises foram estatisticamente associados a um resultado cirúrgico pior em pacientes que se submeteram à CAH para EMT. Mas ao se analisar os padrões do EEG realizado sob o couro cabeludo na fase ictal e interictal não houve diferença estatisticamente significativa. Ou seja, não houve diferença na análise se as descargas eram unilaterais ou bilaterais, independentemente, se o EEG era interictal e ictal. Portanto, a unilateralidade e propagação são encontradas em pacientes com MTS; no entanto, isso não implica no resultado cirúrgico.
3. A semiologia da crise convulsiva pode ajudar a identificar os candidatos ideais para um bom resultado pós-operatório entre pacientes com EMT. Os sintomas de córtex extra temporal como origem do foco epileptogênico sugerem que os resultados pós-operatórios não serão satisfatórios, tornando-se um fator preditivo

de pior prognóstico. Portanto, os pacientes com EMT com auras e sinais clínicos que sugerem o envolvimento extra temporal, além de pacientes que não apresentam auras devem ser cuidadosamente avaliados para que na CAH uma ressecção completa seja feita afim de eliminar o foco epiléptico durante a cirurgia e alertar os pacientes e suas famílias que as crises convulsivas podem não ser totalmente controladas. Pacientes com auras com características totalmente mesiais apresentam melhor resultado. Entre pacientes com múltiplas auras e apenas uma aura não há diferença estatisticamente significante, apenas quando o paciente não possui nenhuma aura podendo estar relacionado a uma maior área da zona epileptogênica e com uma generalização mais rápida.

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6. ANEXOS

FACULDADE DE MEDICINA DE SÃO JOSÉ DO RIO PRETO
DEPARTAMENTO DE CIÊNCIAS NEUROLÓGICAS
CENTRO DE CIRURGIA DA EPILEPSIA DO HOSPITAL DE BASE

AVALIAÇÃO NEUROFISIOLÓGICA

IDENTIFICAÇÃO

Nome:	**Lateralidade:**
Prontuário:	**Naturalidade:**
Idade:	**Procedência:**
Sexo:	**Estado Civil:**
Cor:	

HISTÓRIA DA MOLÉSTIA ATUAL

ANTECEDENTE PESSOAL

ANTECEDENTE FAMILIAR

MEDICAÇÕES EM USO

MEDICAÇÕES JÁ UTILIZADAS

EXAME FÍSICO GERAL

EXAME NEUROLÓGICO

EXAMES COMPLEMENTARES

MVEP (Monitorização por Vídeo-Eletroencefalograma Prolongado):

RESSONÂNCIA MAGNÉTICA:

AVALIAÇÃO NEUROPSICOLÓGICA:

Resultados das funções cognitivas avaliadas especificamente

Função	Testes Utilizados	Pontuação Esperada	Pontuação Obtida	Resultados
Atenção	Dígitos (WAIS-III)			
	Trilhas B			
Visuoconstrução	Cubos (WAIS-III)			
Linguagem	BNT			
	Fluência Verbal (FAS)			
	Vocabulário (WAIS-III)			
	Fluência Animais			
Memória e				

Aprendizagem	Histórias - WMS			
	Reprodução Visual			
	Figura de Rey			
QI Total	WAIS-R			

Conclusão:

SPECT-basal

DIAGNÓSTICO:

CONCLUSÃO DA AVALIAÇÃO NEUROFISIOLÓGICA

_____ _____

NEUROLOGISTA CHEFE RESIDENTE / NEUROLOGIA

São José do Rio Preto, ____ / ____ / _____.