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Epileptic auditory illusions as reliable findings in the determination of the lateralization and localization of epileptogenic zone

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ABSTRACT

Aim: The aim of this study was to investigate the types and prevalence of epileptic auditory auras (EAA) in a large population with epilepsy based on a clinical analysis, to analyze the relationship between auditory auras and the hemispheric lateralization/localization of the epileptogenic zone, and to determine whether there is a reliable EAA that could be used for the identification of the localization and lateralization of the epileptogenic zone.
Methods: The retrospective study included 1050 patients with a diagnosis of epilepsy, including 854 (81.33%) patients with focal epilepsy and 196 (18.67%) with generalized epilepsy. Medical records of 72 patients with auditory auras were singled out, and 63 of them were included in the study. The auditory auras were classified based on their clinical characteristics, and an analysis was performed to examine the relation of the type of auditory auras with the hemispheric lateralization/localization of the epileptogenic zone. Additionally, further analyses were performed to investigate whether there can be a reliable EAA that could be used for the identification of the localization and lateralization of the epileptogenic zone.
Results: Of the 1050 patients with a diagnosis of epilepsy, 63 cases of EAA were included in the study. The prevalence of EAA was 6% in the population with generalized epilepsy and 7.38% in the patients with focal epilepsy. Of the 63 patients, 58 (92.06%) were right-hand-dominant, and 5 (7.94%) were left-hand-dominant. The epileptogenic zone was mostly localized to the temporal lobe (n = 56; 88.89%). In all the 12 patients that had isolated auditory illusion or auditory illusion + elementary or complex auditory hallucinations, the epileptogenic zone was lateralized to the dominant hemisphere and even localized to the temporal lobe of the dominant hemisphere.
Significance: The prevalence of EAA in the population with generalized epilepsy can be found higher than expected if a detailed evaluation of the population with generalized epilepsy can be performed, as in specific patient groups. Our results indicated that the epileptogenic zone was lateralized to the dominant hemisphere in all the patients with isolated auditory illusion or auditory illusion + elementary or complex auditory hallucinations, which suggests that auditory illusion can be a reliable tool in the determination of the lateralization and even localization of the epileptogenic zone.

1. Introduction

Epileptic aura, also known as subjective clinical manifestation, is a retrospective sensation described by the patient after the seizure has ended, and is the signal symptom of a complex partial seizure [1]. An epileptic aura may manifest as an isolated hallucination or illusion, or a combination of both. Moreover, it may occur as the only ictal symptom of focal seizure or more often may precede other symptoms of complex partial seizure [2]. Previous studies indicated that the prevalence of epileptic auras in the population with generalized epilepsy ranges between 49% and 93% [3]. Epileptic auras are classified as ascending epigastric, experiential (déjà vu, jamais vu), fear, anxiety, olfactory, gustatory, auditory, and autonomous-vegetative sensations [2]. Dupont et al. reported the prevalence of auditory auras as 7% [4]. Moreover, it has also been shown that more than 90% of the cases of epileptic auditory auras (EAAs) are associated with the temporal lobe and both elementary and complex auditory hallucinations mostly originate from the lateral temporal lobe [2]. Auditory auras are accepted as a symptom of temporal lobe epilepsy and comprise a wide spectrum of acoustic phenomena including a tone, sound, noise, ear plugging, hearing quiet voices very loud, and hearing human voices, melodies or music [5]. On the other hand, since aura is the primary ictal symptom, it provides important information on the hemispheric localization and lateralization

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of the epileptogenic zone [6]. In this study, we aimed to investigate the types and prevalence of EAAs and the relationship between EAAs and the hemispheric localization and lateralization of the epileptogenic zone. Additionally, we also aimed to determine whether there can be a reliable EAA that could be used for the identification of the localization and lateralization of the epileptogenic zone.

2. Material and methods

The present study was conducted at the Fırat University Medical School Hospital Epilepsy Unit that provides medical treatment and follow-up care for patients with epilepsy. Moreover, in this unit, vagus nerve stimulation (VNS) insertion is also available for patients with treatment-resistant epilepsy (in coordination with the neurosurgery department) and a clinical portfolio is created for each patient, involving extensive details on the clinical findings and medical records of the patients. The patients applying to this unit are often followed up at the outpatient clinic but may also be referred to the inpatient clinic as needed. At regular intervals, video-electroencephalography (EEG), cranial magnetic resonance imaging (MRI) scanning, complete blood count (CBC), and biochemical analysis are performed for each patient. In addition, advanced imaging techniques such as single photon emission computerized tomography (SPECT) and video-EEG monitoring are also performed as required. Video-electroencephalography is performed routinely using bipolar and reference montage formats with 21 electrodes of the international 10–20 system. Cranial MRI scanning is performed with the standard epilepsy protocol on a 1.5-Tesla MRI device. This protocol is based on the oblique coronal plan perpendicular to hippocampal axis for the visualization of temporal lobe abnormalities as well as coronal and sagittal T1- and T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences.

The retrospective study reviewed the medical records of 1050 patients with epilepsy that presented to our epilepsy unit over the 10-year period between 2008 and 2018. Medical records of 72 patients with auditory auras were singled out. Of these, 9 patients with otorhinolaryngological diseases that may lead to hearing disorders and psychiatric disorders were excluded from the study. As a result, 63 patients with a diagnosis of EAAs were included in the study. The study investigated the type and prevalence of EAAs detected in our patients, the relationship between EAAs and the hemispheric lateralization/localization of the epileptogenic zone, and the localization and characteristics of the lesions shown on cranial MRI, if any. Additionally, further analyses were performed to investigate whether there can be a reliable EAA that could be used for the identification of the localization and lateralization of the epileptogenic zone. On the other hand, hemispheric dominance was determined based on the common fact that the left hemisphere of the brain is dominant in individuals with right-hand dominance and the right hemisphere of the brain is dominant in individuals with left-hand dominance. The study protocol was approved by the institutional ethics committee, and all the participants gave informed consent before enrolling in the study.

Chi-square test was used to evaluate the significance of the localization/lateralization values of the EAAs. A p value of <0.05 was considered significant.

3. Results

The retrospective study included 1050 patients with a diagnosis of epilepsy, including 854 (81.33%) patients with focal epilepsy and 196 (18.67%) with generalized epilepsy. Of these, 72 patients were with a diagnosis of auditory auras, of which 9 patients were excluded, including 3 patients with Meniere's disease and 6 patients with schizophrenia and psychosis. As a result, 63 cases of EAAs were included in the study, comprising 43 (68.25%) women and 20 (31.75%) men with a mean age of 30.56 ± 10.71 (range, 14–65) years. The average age at the first unprovoked seizure was 22.10 ± 11.85 (range, 1–64) years. The prevalence of EAAs was 6% in the population with generalized epilepsy and 7.38% in the patients with focal epilepsy.

The clinical spectrum of EAAs in our patients was established as follows:

1. *Elementary auditory hallucination* that could not be described clearly by the patient, resembling a sound or noise that could not be attributed to a specific living being or object, e.g., a tingling, humming, buzzing, crackling, or rattling sound or noise.
2. *Complex auditory hallucination* that could be clearly described by the patient, resembling a sound or noise attributable to a specific living being or object, e.g., the sound or noise of a crying child, a helicopter, a crying woman, crowd of people, and birds.
3. *Auditory illusion* that resulted in a different perception of the sounds in the environment by the patient, i.e., the perception that sounds were louder, lower, absent, fainter, more distinct, nearer or farther away, sounds that were echoing, changing in quality, or a combination of all these variations.
4. *Combined EAAs* that consisted of more than one aura occurring one after another during the seizure:
   a. Elementary auditory hallucination + Complex auditory hallucination
   b. Elementary auditory hallucination + Auditory illusion
   c. Complex auditory hallucination + Auditory illusion

Distribution of the patients according to the classification abovementioned is presented in Table 1.

The patients with complex auditory hallucinations stated that they experienced the same sound during each seizure, which resembled the sound or noise of a crying child, a helicopter, a crying woman, crowd of people, and birds. In a similar way, the patients with elementary *auditory hallucinations* also stated that they experienced the same sound during each seizure, which they could not describe clearly, e.g., a tingling, humming, buzzing, crackling, or rattling sound or noise.

Of the 63 patients included in the study, 58 (92.06%) were right-hand-dominant and 5 (7.94%) were left-hand-dominant. All the 5 patients with left-hand-dominance were present with elementary auditory hallucinations, among whom the epileptogenic zone was lateralized to the left hemisphere in 4 and in the right hemisphere in 1 patient.

Table 1
Types and prevalence of epileptic auditory auras.