



The localizing and lateralizing value of palpitation aura in patients with focal epilepsy

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ABSTRACT

The semiology of auras is essential to presurgical evaluation of patients with focal epilepsy. To assess the localizing and lateralizing value of palpitation aura in focal epilepsy, we retrospectively analyzed the demography, electroclinical, neuroimaging, surgical, pathology data, and outcomes of 114 patients with focal epilepsy and the palpitation aura occurrence in relation to epileptogenic (temporal vs extratemporal, left vs right) origin. Out of 114 patients (mean age, 23.44 ± 9.69 years), 17 (14.9%) patients experienced palpitation as the first aura. Twelve had temporal, one had parietal, one had occipital lobe, and three had multiple lobes junction onset seizures. Palpitation aura was observed more frequently in temporal epilepsy: 22.2% of temporal lobe epilepsy (TLE) and 8.3% of extratemporal lobe epilepsy (EX-TLE) exhibited palpitation aura ($p = 0.038$). However, palpitation aura had no difference between the left or right side: 16.4% with right-sided epilepsy and 13.2% with left-sided epilepsy exhibited palpitation aura ($p = 0.634$). Thus, our study suggested that palpitation was a frequent aura in patients with focal epilepsy. It is more commonly seen with temporal lobe origin, but it has no lateralizing value.

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1. Introduction

The semiology of auras is usually vital for localizing the seizure onset zone of focal epilepsy. Previous studies have shown that autonomic auras were associated with seizure onset in the insular lobe, temporal, amygdala, supplementary sensorimotor area, or anterior cingulate cortex [1–4]. These auras include cardiorespiratory (shortness of breath and palpitations), gastrointestinal (sensations of nausea, pain, or indescribable discomfort in the abdominal or periumbilical area), cutaneous sensations (feeling of warmth or cold), genitourinary (urinary urge or genital sensations), and so on [5,6]. Many of them are frequent before epileptic seizures and have a localizing and lateralizing significance [7–9]. Palpitation is a common medical symptom, which is usually caused by cardiac arrhythmias or psychiatric problems [10]. It would be considered as autonomic cardiorespiratory aura when palpitations occurred as an episode before epileptic seizures [11]. However, its clinical value in the localization and lateralization of the seizure focus has not been clear for us to date.

In the present study, we retrospectively analyzed the demography, electroclinical, neuroimaging, surgical, pathological data, and outcomes

of 114 patients with focal epilepsy to elucidate the localizing and lateralizing value of palpitation aura in focal epilepsy.

2. Methods

2.1. Patients

Medical records of 114 consecutive patients with medically refractory focal epilepsy who had resective epilepsy surgery at the Xuanwu Hospital, Capital Medical University between July 2014 and January 2015 were reviewed for the occurrence of palpitation aura. All patients underwent complete presurgical evaluations, including clinical history (medical, neurological, and neuropsychological examinations), long-term video electroencephalography (EEG) monitoring recordings (scalp and/or invasive electrodes recording), and cranial magnetic resonance imaging (MRI). Patients with at least 1 year follow-up after surgery were included in this study. Epilepsy outcome was classified according to the Engel Epilepsy Surgery Outcome Scale [12]. Patients with acute symptomatic seizures caused by intracranial infection, brain trauma, stroke, encephalitis, previous history of brain surgery, and hypoxic-ischemic encephalopathy were excluded. Patients with the cardiac, endocrine, and psychiatric disorders were also excluded. Among the 114 patients, 98 patients had Engel class I and II outcomes. Seventeen patients were identified who had palpitation aura and Engel class I and II outcomes.

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Table 1
Clinical features, MRI findings, EEG-seizure onset, surgical resection, pathological data and outcomes in patients with palpitation aura.

No.	Sex	Age years	Duration (years)	Seizure types	Seizure semiology	MRI lesions	EEG-monitoring	EEG-seizure onset	Surgery	Pathology	Engel class
1	F	26	12	CPS	Crossed arms, unresponsiveness	Lt temporal abnormal signal	Scalp EEG	Lt temporal (wide field)	Lesionectomy + AHE	Ganglioglioma (low grade) with FCDIIIB	I
2	F	14	9	CPS	Bilateral automatisms, unresponsiveness	Rt temporal abnormal signal and hippocampal atrophy	Scalp EEG	Rt temporal (wide field)	2/3 temporal lobe resection + AHE	FCDIIIA	I
3	F	24	17	CPS	Bilateral automatisms, unresponsiveness	Lt hippocampal abnormal signal and atrophy	Scalp EEG	Lt temporal (wide field)	2/3 temporal lobe resection + AHE	FCDIIIA	I
4	M	24	11	CPS, SGS	Contralateral clonic movements	Rt hippocampal abnormal signal	Scalp EEG	Rt temporoanterior	2/3 temporal lobe resection + AHE	FCDI	I
5	F	22	10	CPS, SGS	Bilateral automatisms, unresponsiveness	Lt hippocampal abnormal signal	Scalp EEG	Lt temporoanterior	2/3 temporal lobe resection + AHE	FCDI	I
6	M	21	20	CPS, SGS	Contralateral clonic movements	Lt hippocampal atrophy	Scalp EEG	Lt temporal (wide field)	2/3 temporal lobe resection + AHE	FCDIIIA	I
7	F	34	10	CPS, SGS	Deviation of the eyes to the left	Rt temporal abnormal signal	Scalp EEG	Rt temporal (wide field)	Lesionectomy + AHE	FCDIIIB	II
8	F	28	12	CPS	Partial loss of consciousness, goose pimples	Rt temporal tumor	Scalp EEG	Rt temporal (wide field)	Lesionectomy + AHE	FCDIIIB	II
9	M	46	16	CPS, SGS	Deviation of the eyes to the left	Normal	Scalp EEG	Rt temporal (wide field)	2/3 temporal lobe resection + AHE	FCDI	II
10	M	19	10	CPS	Bilateral automatisms, unresponsiveness	Normal	Invasive EEG Scalp EEG	Right temporobasal posterior Rt temporal (wide field)	2/3 temporal lobe resection + AHE	FCDI	I
11	F	28	4	CPS	Contralateral clonic movements	Rt hippocampal sclerosis	Invasive EEG Scalp EEG	Rt temporolateral posterior Rt temporal (wide field)	2/3 temporal lobe resection + AHE	FCDIIIA	I
12	F	32	20	CPS	Left-sided automatism	Lt hippocampal sclerosis	Scalp EEG	Lt temporal (wide field)	2/3 temporal lobe resection + AHE	FCDIIIA	I
13	F	29	15	CPS, SGS	Contralateral clonic movements	Lt frontoparietal abnormal signal	Scalp EEG	Lt parietal	Lesionectomy	FCDIIB	I
14	M	27	22	CPS, SGS	Contralateral clonic movements	Lt parietooccipital mass abnormal signal	Scalp EEG	Lt parietooccipital	Lesionectomy	FCDIIB	I
15	M	24	14	SPS, SGS	Contralateral clonic movements	Bifrontal and Rt temporal softening lesion	Scalp EEG Invasive EEG	Rt parietoposterior temporal–occipital (wide field) Rt posterior temporal–occipital junction	Right posterior temporal–occipital resection	FCDI	II
16	M	29	17	CPS, SGS	Contralateral clonic movements	Rt parietooccipital atrophy and abnormal signal	Scalp EEG	Rt occipital	Lesionectomy	Ulegyria with FCDIIId	II
17	F	23	12	CPS, SGS	Right-sided automatism	Rt temporo-parietooccipital atrophy and abnormal signal	Scalp EEG	Rt temporal–parietooccipital junction	Lesionectomy	Neuronal loss, gliosis, ulegyria	II

Sex: F, female; M, male. Seizure type: CPS, complex partial seizure; SGS, secondarily generalized seizure; SPS, simplex partial seizure. MRI, magnetic resonance imaging; Lt: left; Rt: right. AEDs, antiepileptic drugs: CBZ, carbamazepine; LEV, levetiracetam; LTG, lamotrigine; OXC, oxcarbazepine; PB, phenobarbital; PHT, phenytoin; TPM, topiramate; VPA, valproic acid. Surgery: (S)AHE: (selective) amygdalohippocampotomy. Pathology: FCD, focal cortical dysplasia; HS, hippocampal sclerosis.

This research was approved by the ethics committee of Xuanwu Hospital, Capital Medical University (China) and was performed according to the Declaration of Helsinki. All patients in this research provided their informed consent prior to their inclusion in the study.

2.2. Statistical analysis

All statistical analyses were performed with the SPSS version 17.0 (Statistical Product and Service Solutions, IBM Corporation, New York, USA). Demographic variables and relevant clinical variables were summarized descriptively to characterize the study population. Continuous prognostic variables were analyzed using the Student t-test. The chi-square or Fisher's exact tests were used for statistical comparison of dichotomous discrete variables. The level of significance was set at $p < 0.05$.

3. Results

3.1. All included patients characteristics

Among the 114 patients with focal epilepsy (male = 69; female = 45), there were 54 cases (47.4%) of temporal lobe epilepsy (TLE), 18 cases (15.8%) of frontal lobe epilepsy (FLE), 2 cases (1.8%) of parietal lobe epilepsy (PLE), 3 cases (2.6%) of occipital lobe epilepsy (OLE), and 37 cases (32.5%) of multiple lobes junction epilepsy (MLJE). There were 61 cases (53.5%) with epilepsy onset from the right hemisphere and 53 cases (46.5%) from the left hemisphere. The mean age of the patients was 23.44 ± 9.69 years (range: 3–48 years, median: 23.0 years), the mean duration of the epilepsy was 12.57 ± 7.48 years (range: 11 months–32 years, median: 11.0 years). Seventeen (14.9%) patients experienced palpitation aura as the first aura (Table 1).

3.2. Differences of palpitation aura between epilepsies arising from different lobes

The relationship of palpitation aura with the 5 types of lobar epilepsy was investigated by the Fisher's exact test (Table 2). Twelve (22.2%) of the 54 patients with TLE, 1 (50%) of the 2 patients with PLE, 1 (33.3%) of the 3 subjects with OLE, and 3 (8.1%) of the 37 patients with MLJE reported having palpitation auras while none of 18 subjects with FLE reported palpitation auras. The difference was statistically significant ($p = 0.021$). However, because of fewer cases of PLE and OLE in this study, we compared the localizing and lateralizing value of palpitation aura between patients with TLE and extratemporal lobe epilepsy (EX-TLE) in the study.

3.3. Characteristics of patients with TLE and those with EX-TLE

The mean age of patients with TLE was 25.20 ± 8.84 years (male = 29, female = 25) whereas the mean age of patients with EX-TLE was 21.85 ± 10.20 years (male = 40, female = 20), and the mean duration of the patients with TLE and EX-TLE was 12.20 ± 6.65 years and 12.90 ± 8.20 years, respectively. There were no significant difference in age ($t = 1.866, p = 0.065$), duration ($t = -0.495, p = 0.622$), gender distribution (chi-square = 1.999, $p = 0.157$), and the distribution of palpitation aura and other auras (chi-square = 0.230, $p = 0.631$) between patients with TLE and EX-TLE (Table 3).

Table 2
Differences of palpitation aura characteristics among lobar epilepsies.

Aura		TLE (n = 54)	FLE (n = 18)	PLE (n = 2)	OLE (n = 3)	MLJE (n = 37)	p value*
Palpitation	+	12(22.2%)	0(0%)	1(50%)	1(33.3%)	3(8.1%)	$p = 0.021$
	-	42	18	1	2	34	

TLE, temporal lobe epilepsy; FLE, frontal lobe epilepsy; PLE, parietal lobe epilepsy; OLE, occipital lobe epilepsy; MLJE, multiple lobes junction epilepsy. +: present, -: absent.

* Results of the Fisher's exact test comparing the presence/absence of palpitation aura across the five types of lobar epilepsy.

Table 3
Characteristics of patients with TLE and EX-TLE ($\bar{x} \pm S$).

	TLE (n = 54)	EX-TLE (n = 60)	p value
Age (years)	25.20 ± 8.84	21.85 ± 10.20	$p = 0.065$
Duration (years)	12.20 ± 6.65	12.90 ± 8.20	$p = 0.622$
Gender	Female	25	$p = 0.157$
	Male	29	
Aura	Palpitation	12	$p = 0.631$
	Other auras	36	

TLE, temporal lobe epilepsy; EX-TLE, extratemporal lobe epilepsy.

3.4. Comparison of palpitation aura between patients with TLE and EX-TLE

We compared palpitation auras between patients with TLE and EX-TLE with the chi-square or Fisher's exact test. Palpitation aura was significantly more common in patients with TLE than those with EX-TLE ($p = 0.038$) (Table 4).

3.5. The lateralization of palpitation value between the patients with right-sided and left-sided epilepsy

Palpitation aura was compared between the subjects with right-sided epilepsy and those with left-sided epilepsy by the chi-square or Fisher's exact test (Table 4). Although there was no statistical significance ($p = 0.634$), there was a trend that palpitation aura was more common in patients with right-sided epilepsy (Table 4).

4. Discussion

The symptomatology of auras and seizures is a reflection of activation of specific brain regions and often helps to localize the seizure onset zone for epilepsy surgery. They provided important information for both lateralization and localization of seizure onset [5]. Autonomic auras have recently been studied more intensely, which include cardiorespiratory, gastrointestinal, genitourinary, and cutaneous symptoms. These auras frequently occur in patients with TLE [1,4,13,14]. Among them, palpitation is a frequent autonomic cardiorespiratory aura [15]. However, there are limited published data addressing the localizing and lateralizing value of palpitation aura [11]. Therefore, we investigated the localizing and lateralizing value of palpitation aura in focal epilepsy in this study.

In the present study, we retrospectively analyzed the medical records of 114 consecutive patients with medically refractory focal epilepsy and investigated the localizing and lateralizing values of palpitation aura in the patients. We found that palpitation aura was more frequent in temporal epilepsy (12 of 54 patients, 22.2%) than extratemporal epilepsy (5 of 60 patients, 8.3%, $p = 0.0038$) and was also more common in patients with epilepsy onset from the right hemisphere (10 of 61 patients, 16.4%) than those from the left hemisphere (7 of 53 patients, 13.2%), although the difference between them was not statistically significant ($p = 0.634$).

As early as 1875, Lane reported three cases of adult patients with epilepsy with palpitation aura [16], and from then on, palpitation aura was recognized gradually in the epileptic seizure [17,18]. Besides, it was also reported in children with TLE [19]. Therefore, it should be considered as

Table 4
Localization and lateralization value of palpitation aura in 114 subjects with focal epilepsy.

Aura		Localization value			Lateralization value		
		TLE (n = 54)	EX-TLE (n = 60)	p value*	Right (n = 61)	Left (n = 53)	p value*
Palpitation	+	12(22.2%)	5(8.3%)	p = 0.038	10(16.4%)	7(13.2%)	p = 0.634
	–	42	55		51	46	

TLE, temporal lobe epilepsy; EX-TLE, extratemporal lobe epilepsy. +: present, -: absent.

* Results of the chi-square test comparing the presence/absence of palpitation aura between subjects with TLE and those of EX-TLE, with right-sided epilepsy and those with left-sided one respectively.

autonomic cardiac aura when palpitations are episodic, and the cardiac, endocrine, and psychiatric disorders are excluded [11]. In this study, the incidence of palpitation aura in our patients with epilepsy was 14.9%, which suggested that palpitation aura is not rare in epilepsy. We further analyzed palpitation auras by epileptogenic zone localization and found that the incidence of palpitation aura is as high as 22.2% in TLE but only 8.3% in EX-TLE. Thus, we can conclude that palpitation aura favors a temporal epileptogenic focus.

In EX-TLE, palpitation aura was reported in FLE [20]. However, none of our 18 FLE had a palpitation aura. The reason may be related to the strict inclusion criteria of our study, because we only included patients who first experienced epileptic palpitation aura during the events and excluded the patients with late palpitation symptom. In the present study, 5 patients with EX-TLE had palpitation aura. Among them, one patient had parietal epilepsy, one patient had occipital epilepsy, and three patients had epilepsy that involved multiple lobes.

It is reported that the mechanism of autonomic auras is related to the activation of the central autonomic network and followed by other ictal symptoms or may be the predominant perception of seizure [1]. Previous study suggested that seizures originating from the temporal lobe could result in cardiac arrhythmias, such as tachycardia and bradycardia, which caused by overactivity of sympathetic and parasympathetic, respectively [21]. Sinus tachycardia, which may be associated with palpitations, is the most common cardiac consequence of epileptic seizures and may occur in up to 80% of seizures [22]. Ictal bradycardia, ictal asystole, and ictal atrioventricular (AV)-conduction block predominantly occurred during seizures in patients with TLE. Sinus tachycardia, ictal bradycardia, ictal asystole and AV-conduction block have been suggested as potential mechanisms for sudden unexpected death in epilepsy (SUDEP) [23,24]. Thus, we should pay more attention to cardiac symptoms including palpitation aura in our clinical practice.

The present study has several limitations. First, there is no objective assessment of palpitation aura in the present study. Usually, palpitation is a subjective perception. It can be caused by cardiac arrhythmias, psychiatric problems, neurological problems, or miscellaneous causes such as thyrotoxicosis, anemia, medications, or caffeine [25]. Tachycardia is the most common cause of palpitation. Many patients have palpitation with normal sinus rhythm. A minority of patients have palpitation with bradycardia [25,26]. However, the relationship between palpitation aura in seizures and heart rate remains unclear. Unfortunately, only 5 patients recorded palpitation auras with the electrocardiogram (ECG) recordings in the present study, and there was no significant difference in heart rate between before and during auras. Future study could be conducted to investigate the relationship between the palpitation aura and heart rate. Second, all studies of seizure semiology are limited by the possibility that the studied behavior reflects seizure propagation rather than the zone of seizure onset. Intracranial EEG recordings can help localize the epileptogenic zone and identify the seizure propagation pattern. Unfortunately, only 2 patients with palpitation aura underwent intracranial recordings in the present study. In future study, intracranial EEG recordings could be performed in more patients with palpitation aura to confirm the origin of the palpitation aura.

In conclusion, the present study demonstrated that palpitation aura favors a temporal epileptogenic zone. However, palpitation seems to have no lateralizing value although it was more common in subjects with right-sided epilepsy than in those with left-sided epilepsy.

Declaration of Competing Interest

We declare that there are no conflicts of interest regarding the publication of this study.

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