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Orbitofrontal epilepsy: Case series and review of literature

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ABSTRACT

Background: Orbitofrontal epilepsy (OFE) is less known and is poorly characterized in comparison with temporal lobe epilepsy, partly because it is rare and possibly because it is unrecognized and therefore underestimated.
Objective: This paper aimed to better characterize seizure semiology, presurgical findings, and surgical outcomes in patients with OFE.
Methods: We retrospectively reviewed all confidently established OFE cases from six Canadian epilepsy monitoring units between 1988 and 2014, and in the literature between 1972 and 2017. Inclusion criteria were identification of an epileptogenic lesion localized in the OFC or if the patient was seizure-free after surgical removal of the OFC in nonlesional cases.
Results: Sixteen cases were identified from our databases. Fifty percent had predominantly sleep-related seizures; 56% had no aura (the remaining had nonspecific or vegetative auras), and 62.5% featured hypermotor (mostly hyperkinetic) behaviors. Interictal epileptiform discharges over frontal and temporal derivations always allowed lateralization. Magnetic resonance imaging (MRI) identified an orbitofrontal lesion in 8/16, positron emission tomography (PET) identified a hypometabolism extending outside the orbital cortex in 4/9, ictal single-photon emission computed tomography (SPECT) identified an orbital hyperperfusion in 1/5, magnetoencephalography (MEG) identified lateral orbital sources in 2/4, and intracranial electroencephalography (EEG) identified an orbitofrontal onset in 9/10. Fourteen patients underwent surgery, all reaching a favorable outcome (71.4% Engel 1; 28.6% Engel 2; mean FU = 5.6 years). Pre- and postoperative neuropsychological assessments revealed heterogeneous findings. Our review of literature identified 71 possible cases of OFE, 32 with confident focus localization. Extracted data from these cumulated cases supported observations made from our case series.
Conclusions: Orbitofrontal epilepsy should be suspected with sleep-related, hyperkinetic seizures with no specific aura, and frontotemporal interictal discharges. Several patients have nonmotor seizures with or without auras which may resemble temporal lobe seizures. Postoperative seizure outcome was favorable, but there is inherent bias as we only included patients with a seizure-free outcome if the MRI was negative. A larger study is required to address identified gaps in knowledge such as identifying discriminative features between medial and lateral OFE, evaluating the value of more recent diagnostic tools, and assessing the neuropsychological outcome of orbital epilepsy surgery.

1. Introduction

The orbitofrontal cortex (OFC) rests on the roof of the orbit and comprises the orbital gyri and the gyrus rectus. Although it is most commonly subdivided into a medial and lateral portion, this complex structure can be divided into as many as 20 different architectonic areas which are interrelated by an elaborate set of connections and networks [1]. The OFC receives inputs from the gustatory, olfactory, visceral, somatosensory, auditory, and visual sensory areas, with direct reciprocal connections with other limbic structures such as the amygdala, hippocampus, and cingulate cortex [2–4]. It contains the secondary taste cortex and the secondary and tertiary olfactory cortical areas, and is thought to be involved

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in monitoring the reward value of reinforcers, in evaluating punishers, in learning and reversing stimulus-reinforcement associations, and in decision making [5–7].

Epileptic seizures arising from the OFC are less well characterized in comparison with other types of epilepsy (e.g., medial temporal lobe epilepsy), partly because orbitofrontal epilepsy (OFE) is rare and possibly because it is unrecognized and therefore underestimated. Most of the available literature reports anecdotal cases, with the largest reports including up to eight patients [8–10]. Heterogeneous and relatively nonspecific clinical presentations have been reported including cephalic and various vegetative auras and nonmotor and motor manifestations [11,12]. Moreover, outcomes of OFE surgery in patients with drug-resistant seizures remain uncertain, especially in terms of neuropsychological impairments. Because of its rare occurrence, a collaborative effort among several large surgical centers would be required to yield a sufficient number of cases in order to find patterns in semiology, electrophysiology, imagery, and cognitive profile in OFE and to document the outcomes of epilepsy surgery in the OFC territory [13].

2. Methods

Using admission databases, we retrospectively identified all consecutive patients with OFE who had been investigated between 1988 and 2014 at one of six Canadian epilepsy monitoring units: CHUM — Notre-Dame Hospital (Montréal, QC), Montreal Neurological Hospital and Institute (Montréal, QC), Hôpital Sainte-Justine (Montréal, QC), Hôpital de l'Enfant-Jésus (Québec, QC), Dalhousie University (Halifax, NS), and London Health Sciences Center (London, ON). Orbitofrontal epilepsy was deemed confirmed if there was an epileptogenic lesion localized in the OFC or if the patient was seizure-free after surgical removal of the OFC in cases of nonlesional OFE. Clinical charts were reviewed to collect information on demographic characteristics (age, gender), disease-related factors (age-of-seizure onset, relevant past medical history), seizure semiology, imaging and neurophysiological findings [video-electroencephalography (VEEG), magnetic resonance imaging (MRI), positron emission tomography (PET), ictal single photon computed tomography (SPECT), magnetoencephalography (MEG), and intracranial EEG], neuropsychological assessments, as well as surgical treatment and outcome.

We then performed an exhaustive review of the literature to identify all well-documented case reports of OFE. We searched the Medline database (since inception until May 2017) using the terms "orbitofrontal epilepsy" and "orbital frontal epilepsy" limited to publications in English. We screened the titles and abstracts of all search results to identify potentially relevant studies. We also searched additional references and book chapters that were cited in relevant reports, to identify additional cases which might have been missed. Potentially relevant studies were reviewed in full text to identify confident cases of OFE, confirmed by an OFC lesion on CT/MRI or seizure control after a neurosurgical resection restricted to the OFC.

Institutional review board approval was obtained from each institution involved.

3. Results

3.1. Our case series

We compiled a total of 16 cases with OFE (9 women; mean age at admission: 32.9 years, range: 8–51 years). Clinical features of our case series are summarized in Table 1. Mean age at disease onset was 13.9 years (SD = 8.8, range = 2–37). Past medical history included head trauma in one case (Pt. 6).

Auras were reported by seven (43.8%) patients: a state of increased awareness or lucidity and the feeling of being a third-party observer (Pt. 2), a nonspecific ill feeling (Pt. 3), nausea and a rising epigastric sensation (Pt. 8), a feeling of sea sinking in the stomach and loud noise in

Table 1
Summary of clinical features of our patients with orbitofrontal epilepsy.

Pt.	Age (years)		Sex	Handedness	PMH	Aura	Gestural motor behavior	Vocalization	Oro-alimentary automatisms	Nonmotor	Other	Sleep-related
	O	Adm										
1	2	30	M	R	ADHD	−	Hyperkinetic integrated	Swearing	−	−	Facial expression of fear	−
2	9	27	Fe	R		+	Stereotypies nonintegrated	Groans	−	−	Laughter, pouting	+
3	18	48	M	R	Depression	+	−	−	−	+	−	−
4	9	51	Fe	R	NF1	−	Nonintegrated	Grunting	−	−	−	+
5	19	49	Fe	R	N/A	−	Hyperkinetic integrated	−	−	−	−	−
6	37	40	M	R	Head trauma, ADHD	−	−	−	−	+	−	−
7	10	13	Fe	L	N/A	−	Stereotypies integrated	−	−	−	−	−
8	10	27	Fe	R		+	Hyperkinetic nonintegrated	−	−	−	−	+
9	4	8	M	R	N/A	+	Wandering	−	+	−	−	−
10	7	16	Fe	L	ADHD	−	Dystonic	−	−	−	−	−
11	20	27	Fe	R	Decompression of optic nerve due to fibrous dysplasia of sphenoidal bone with cyst	+	−	−	−	+	−	+
12	17	49	M	R	Infantile spasms, L SAH followed a few years later by an ant T resection	+	−	Grunting	−	+	−	+
13	12	26	Fe	A	N/A	−	−	−	−	+	Laughter and crying without mirth	+
14	17	38	M	L	N/A	−	Nonintegrated	−	−	−	Ictal pouting, laughter	+
15	7	37	M	R	Neonatal seizures	+	Stereotypies nonintegrated	Grunting	−	−	−	+
16	25	40	Fe	R	N/A	−	−	−	−	+	−	−

Abbreviations: Pt. = patient; O = onset of epilepsy; Adm = admission for work-up; M = male; Fe = female; R = right; L = left; A = ambidextrous; PMH = past medical history; ADHD = attention-deficit and hyperactivity disorder; N/A = not available; NF1 = neurofibromatosis type 1; SAH = selective amygdalo-hippocampectomy; F = frontal; T = temporal. Note: A "+" sign denotes the presence of a characteristic, a "−" sign denotes its absence, and a "+/−"sign denotes that it is sometimes present, sometimes absent.

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