Epilepsy & Behavior 60 (2016) 33–41

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Review

Isolated amygdala enlargement in temporal lobe epilepsy: A systematic review

S.M. Jessica Beh *, Mark J. Cook, Wendyl J. D'Souza

[a] The Department of Medicine, St. Vincent's Hospital Melbourne, St Vincent's PO Box 2900, Fitzroy, VIC 3065, Australia
[b] The University of Melbourne, Parkville, VIC 3010, Australia

ARTICLE INFO

Article history:
Received 19 December 2015
Revised 5 February 2016
Accepted 4 April 2016
Available online 10 May 2016

Keywords:
Amygdala enlargement
Temporal lobe epilepsy
Seizures
Amygdala volume
Amygdala volumetry

ABSTRACT

Objective: The objective of this study was to compare the seizure characteristics and treatment outcomes in patient groups with temporal lobe epilepsy (TLE) identified with isolated amygdala enlargement (AE) on magnetic resonance imaging studies.
Methods: PubMed, Embase, and the Cochrane Library were searched for relevant studies using the keywords 'amygdala enlargement', 'epilepsy', and 'seizures' in April 2015. Human studies, written in English, that investigated cohorts of patients with TLE and AE were included.
Results: Of 204 abstracts initially identified using the search strategy, 14 studies met the inclusion criteria (11 epilepsy studies and 3 psychiatry studies). Ultimately, 8 full studies on AE and TLE involving 107 unique patients were analyzed. Gender distribution consisted of 50 males and 57 females. Right amygdala enlargement was seen in 39 patients, left enlargement in 58 patients, and bilateral enlargement in 7 patients. Surgical resection was performed in 28 patients, with the most common finding being dysplasia/hamartoma or focal cortical dysplasia. Most studies involved small samples of less than 12 patients. There was a wide discrepancy in the methods used to measure amygdala volume, in both patients and controls, hindering comparisons. Most TLE with AE studies observed a later age of seizure onset (mean: 32.2 years) compared with studies involving TLE with HS (mean of mid- to late childhood). A higher frequency of complex partial seizures compared with that of convulsive seizures is seen in patients with AE (67–100% vs. 26–47%), and they have an excellent response to antiepileptic drugs (81.8%–100% of seizure-free patients). All studies that included controls also found a significant difference in frequency of seizure types between their cases and controls.
Conclusions: Reliable assessment of amygdala volume remains a critical issue hindering better understanding of the clinical management and research of this focal epilepsy syndrome. Within these limitations, the literature suggests characteristics of an older age of epilepsy onset, a greater tendency to nonconvulsive seizures, and a good response to antiepileptic drugs in this interesting group of epilepsies.

1. Introduction

The most common lesions identified in focal epilepsy are hippocampal sclerosis (40%), long-term epilepsy-associated tumors (27%), and malformations of cortical development (13%) [1]. Historically, the most common form of focal epilepsy, mesial temporal lobe epilepsy (TLE) due to hippocampal sclerosis (HS), has received the widest surgical attention. Hippocampal sclerosis can be reliably detected on routine magnetic resonance imaging (MRI) studies and is well-known for its epileptogenicity [2]. Mesial TLE due to HS is often medically resistant, and surgical resection can achieve up to 70% long-term seizure freedom in patients [3].

With improved neuroimaging and correlative presurgical techniques, clinicians are becoming increasingly aware of other potentially epileptogenic temporal lobe lesions that may also have good surgical outcome [4,5]. While seizures originating from these other causes might have been classified as 'nonlesional' or 'imaging-negative' epilepsy previously, a greater awareness of other potentially epileptogenic lesions, as well as improved imaging technology, has resulted in the identification of enlarged amygdalae in a proportion of patients (see Fig. 1).

Bower et al. retrospectively found that 64% of 'imaging-negative' cases had both significant amygdala asymmetry and amygdala enlargement

Abbreviations: TLE, temporal lobe epilepsy; AE, amygdala enlargement; HS, hippocampal sclerosis; MRI, magnetic resonance imaging; FDG-PET, [^{18}F]-fluorodeoxyglucose positron emission tomography; AMV, amygdala volume; VBM, voxel-based morphometry; AEDs, antiepileptic drugs; EEG, electroencephalography; SPECT, interictal single photon emission computed tomography; MET-PET, [^{11C}]-methionine positron emission tomography; FCD, focal cortical dysplasia; LGI1, leucine-rich, glioma-inactivated 1 (antibody); CPS, complex partial seizures; CS, convulsive seizures; IEDs, interictal epileptiform discharges.

* Corresponding author at: The Department of Medicine, St. Vincent's Hospital Melbourne, St Vincent's PO Box 2900, Fitzroy, VIC 3065, Australia. Tel.: +61 452 622 865 (mobile); fax: +61 92883065.
E-mail addresses: smjbeh@student.unimelb.edu.au (S.M.J. Beh), markcook@unimelb.edu.au (M.J. Cook), wendyl@unimelb.edu.au (W.J. D'Souza).

http://dx.doi.org/10.1016/j.yebeh.2016.04.015
1525-5050/

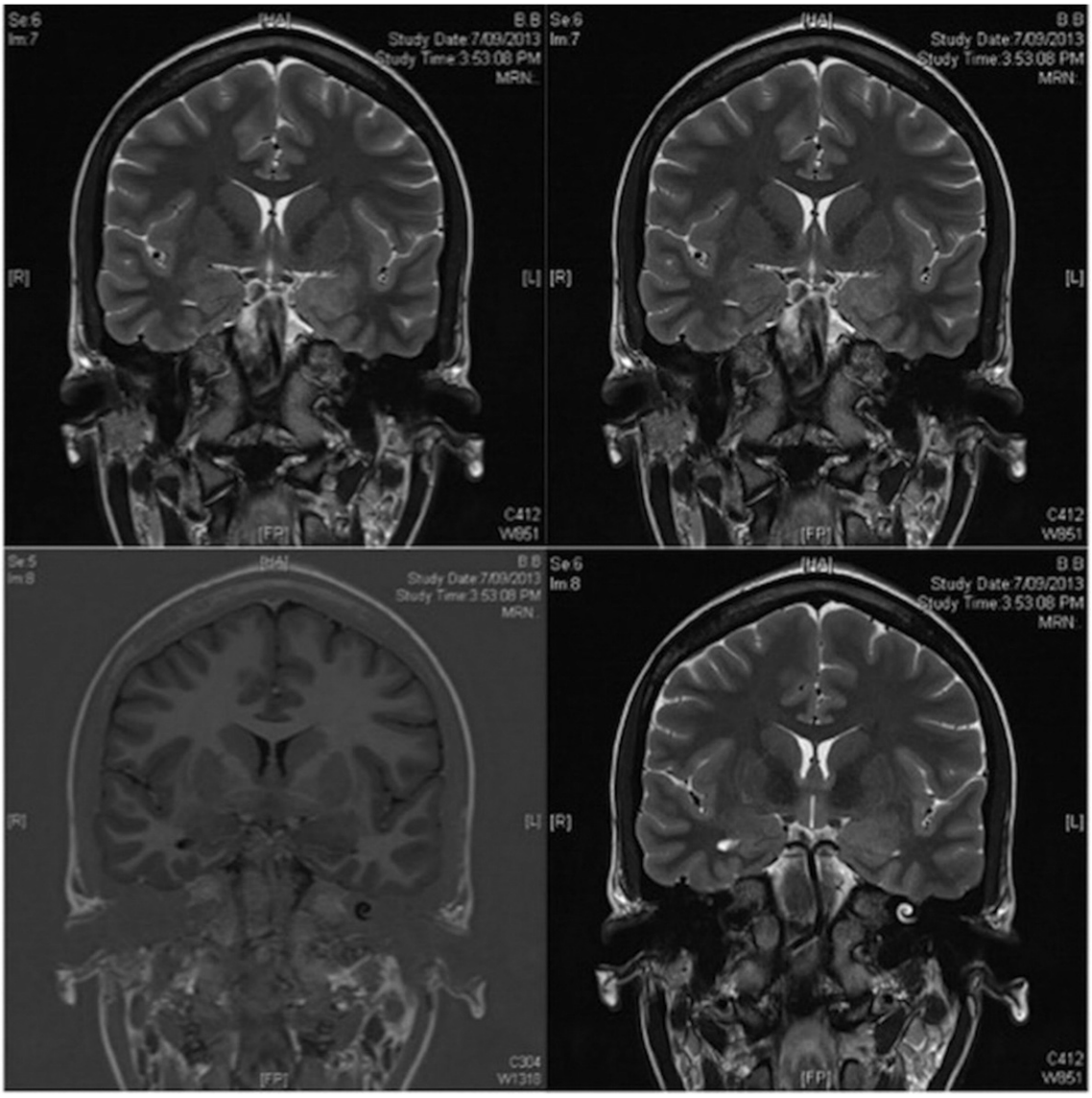

Fig. 1. Magnetic resonance imaging study demonstrating left-sided amygdala enlargement.

(AE), while Coan et al. demonstrated significant AE in 12% of previously diagnosed patients with 'nonlesional' TLE [4,6]. Because nonlesional TLE may be associated with an almost three times lower probability of seizure freedom after surgical resection compared with lesional TLE, this reclassification of newly identified AE lesions in TLE has important implications for patient management [7].

Using parcellation based on cytoarchitecture, Murphy et al. showed in 1987 that the amygdaloid complex is asymmetric in humans, while in 1992, Watson et al. attempted to establish standardized anatomical guidelines for outlining the hippocampus and amygdala on high-resolution MRI scans [8,9]. Although the technology has been available to measure amygdala volumes specifically since the early 1990s, studies linking amygdala pathology and size to seizure foci until recently have been lacking [8,9].

There are a number of clinical, electroencephalographic, radiological, and histopathological observations that have led to an increased focus on the role of the amygdala independent from HS in epilepsy in recent years. Firstly, better outcomes have been observed when the amygdala was included in surgical resection borders [10]. Secondly, studies utilizing MRI T2 relaxometry have shown that a portion of patients with 'imaging-negative' TLE have increased T2 signal in the amygdala ipsilateral to the focus detected by electroencephalography (EEG) [11]. Thirdly, [^{18}F]-fluorodeoxyglucose positron emission tomography (FDG-PET) findings of glucose hypometabolism have been isolated to the amygdala and excluding the hippocampus in some patients [12]. Finally, histopathologic abnormalities have been found in amygdala specimens resected from patients with medically resistant TLE [13].

This review pools studies on TLE and AE to provide better understanding of this imperfectly described focal epilepsy syndrome. Specific focus will be on the seizure characteristics, diagnostic investigations, treatment outcomes, and histopathological results in these cohorts of patients. We aimed to identify knowledge gaps in the literature that can guide future clinical management and research.

2. Methods

Our search strategy comprised a comprehensive literature search of PubMed, Embase, and the Cochrane Library, conducted using the terms 'amygdala enlargement', 'epilepsy', and 'seizures', either alone or in varying combinations in April 2015. Papers were excluded for the following reasons: animal studies, irrelevant topics, non-English papers, papers not involving a population with epilepsy, case reports, and those described with coexisting brain pathology. The references of included papers were also reviewed to identify any relevant papers that may