Title
When is temporal lobe epilepsy not temporal lobe epilepsy?

Permalink
https://escholarship.org/uc/item/21t0q51n

Author
Jr, EJ

Publication Date
2016-02-01

DOI
10.1093/brain/awv374

Peer reviewed
the only mechanism of the MCT diet requires further investigation.

Michael A. Rogawski
Department of Neurology,
School of Medicine, University of
California, Davis Sacramento,
California, USA
E-mail: rogawski@ucdavis.edu
doi:10.1093/brain/awv369

References


When is temporal lobe epilepsy not temporal lobe epilepsy?

This scientific commentary refers to ‘Temporal plus epilepsy is a major determinant of temporal lobe surgery failures’, by Barba et al. (doi:10.1093/brain/awv372).

Stereotactic electroencephalography (SEEG) originated in France in the 1950s. Bancaud and Talairach, at St. Anne’s Hospital in Paris, introduced this approach to define the 3D extent of dysfunctional brain tissue surrounding intraparenchymal brain tumours, and more specifically, to define epileptogenic brain tissue in patients with pharmacoresistant epileptic seizures (Bancaud et al., 1975). The approach required a hypothesis that would enable the placement of multiple, mostly unilateral, depth electrodes to sample a reasonably limited number of regions of interest. The results then guided a tailored surgical resection. This technique was adapted by Crandall et al. (1963) at UCLA for patients with suspected mesial temporal lobe epilepsy. Crandall,
however, used a standardized, bilaterally symmetrical, depth electrode approach, designed to sample those structures known to be primarily involved in generating limbic seizures. Because French law did not allow Bancaud and Talairach to leave their electrodes in place for more than a few hours, their analyses were based on interictal activity, as well as electrically and chemically induced seizures. Crandall, therefore, was the first to perform chronic depth electrode recording, over days and weeks, in order to capture spontaneous ictal events. Because investigators at UCLA had recently developed an EEG telemetry device for NASA to record from chimpanzees orbiting in space, Crandall was also able to use this new technology to establish EEG telemetry for long-term monitoring of epileptic seizures. Data were used to determine that the epileptogenic region was contained within the area of a standardized anterior temporal resection (Falconer, 1953), which was then performed routinely. Two schools of invasive presurgical evaluation for epilepsy surgery then evolved: the French school, which performed classical SEEG, using multiple electrodes placed predominantly around a suspected unilateral lesion to guide a tailored surgical resection; and a North American school, which used more or less standardized bilateral depth electrode placem ents to inform performance of a standardized anterior temporal resection. Over the years, advanced neuroimaging made invasive EEG unnecessary in many patients with mesial temporal lobe epilepsy, and the limits of the resections were refined to include only those structures subsequently identified as most important for generation of mesial temporal seizures (Spencer et al., 1984). The paper by Barba et al. (2016) in this issue of Brain is the latest report from the French School to examine why surgery for refractory mesial temporal lobe epilepsy does not always eliminate all seizures. At least one reason appears to be the existence of ‘temporal plus’ epilepsy (TPE).

At the 1991 Palm Desert Conference, Claudio Munari, the principal disciple of Bancaud and Talairach, explained that in mesial temporal lobe epilepsy, he not only resected the structures where EEG-recorded ictal discharges began, but also those to which they propagated within 5 s, even if this included extra-temporal areas (Lüders et al., 1993). This was perhaps the first description, at least in the English literature, of TPE. It is somewhat surprising, therefore, that the epilepsy surgery programmes at Grenoble and Lyon, direct descendants of the St. Anne school, carried out classical SEEG in patients with suspected mesial temporal lobe epilepsy, identified TPE in some, but then (at least up until 2001) performed the same standardized anteromesial temporal resection routinely used in North America. This is fortuitous, however, because the results presented by Barba et al. clearly demonstrate that patients with TPE usually do not benefit from removal of mesial temporal limbic structures only. It appears that tailored resections were carried out in patients with TPE after 2001, so we can look forward to more recent data revealing whether more extensive additional extratemporal removals lead to better outcomes.

The pressing question addressed by Barba et al., and countless other surgical series, as well as two randomized controlled trials (Wiebe et al., 2001; Engel et al., 2012), is: why does standard anteromesial temporal resection fail to control seizures in a significant number of patients who appear to have unilateral mesial temporal lobe epilepsy? A simple-minded answer to this question is that focal epilepsy is usually not focal, but rather, large areas of brain, often including subcortical and contralateral brain structures, are epileptogenically abnormal, and necessary to support the generation of consistently localized spontaneous ictal events. Surgical treatment therefore does not usually remove the entire area of abnormality, but rather a critical mass necessary and sufficient for spontaneous seizure generation, commonly referred to as the epileptogenic region or zone (Lüders et al., 1993). There is no diagnostic test that accurately delineates the extent of the epileptogenic region, so its boundaries can only be approximated by a variety of studies, including neuroimaging, scalp EEG, invasive EEG when necessary, and neuropsychological testing.

For mesial temporal lobe epilepsy, there is usually a common pathological substrate, hippocampal sclerosis, but this does not indicate a singular disease—there are, in fact, multiple types of hippocampal sclerosis, ranging from the classical form with a characteristic histological pattern of CA2 sparing, often associated with a history of prolonged febrile seizures, to more diffuse patterns that include atrophy of CA2, as well as the contralateral hippocampus (Mathern et al., 1997; Ogren et al., 2009; Blümcke et al., 2013) (Fig. 1). There also can be various degrees of extrahippocampal atrophy, including parahippocampal structures, ipsilateral and bilateral neocortex, and thalamus (Lin et al., 2007). The presence of hippocampal sclerosis, diagnosed by hippocampal cell counts and Timm’s stain, can be missed by MRI and even routine histopathology (Mathern et al., 1997).

Disregarding the situation where the standardized anteromesial temporal lobe resection was inadequate, leaving a large hippocampal remnant, three other common explanations for failure of this procedure to eliminate all seizures can be offered:

(i) The epileptogenic region is extratemporal in an area of ‘silent cortex’ that preferentially projects to mesial temporal structures, or there is more than one epileptogenic region, one of which is extratemporal (e.g. dual pathology), or there is an epileptogenic region in the contralateral temporal lobe. These are rarely the cause of surgical failures today, owing to high-resolution MRI, PET, and SEEG in patients where the clinical history and ictal semiology raise suspicion of extratemporal or bilateral epileptogenic regions.
(ii) The epileptogenic region involves more extensive temporal lobe tissue than is usually included in the standardized anteromesial temporal resection. This could result from the progressive nature of mesial temporal lobe epilepsy (Cendes et al., 2005), and could explain why the seizure-free outcome was 85% for patients with complete data in the Early Randomized Surgical Epilepsy Trial (ERSET), who were operated on within 2 years of pharmacoresistance (Engel et al., 2012), whereas only 60–70% of patients were seizure-free in most surgical series, including the Western Ontario randomized controlled trial (Wiebe et al., 2001), where patients typically had had epilepsy for an average of >20 years (Berg et al., 2003).

(iii) The epileptogenic region includes extratemporal structures, the condition of TPE. In some patients this could be an extension of the progressive nature of classical mesial temporal lobe epilepsy, while in others it likely represents different epileptogenic processes, involving more than the temporal lobe from the start.

The presence of different types of hippocampal sclerosis strongly suggests that there are multiple disease processes that can present as mesial temporal lobe epilepsy. Improved surgical outcomes will result from further elucidation of the various epileptogenic mechanisms and their aetiologies, which ultimately manifest clinically as mesial temporal lobe epilepsy.

Jerome Engel, Jr.  
Departments of Neurology, Neurobiology and Psychiatry and Biobehavioral Sciences and the Brain Research Institute, David Geffen School of Medicine at UCLA, Los Angeles, California, USA  
E-mail: engel@ucla.edu

doi:10.1093/brain/awv374

**Funding**  
Original research reported by the author was supported in part by Grants NS02808, NS15654, NS33310, and NS80818.
Habitual and goal-directed behaviours and Tourette syndrome

This scientific commentary refers to ‘Enhanced habit formation in Gilles de la Tourette syndrome’, by Delorme et al. (doi:10.1093/brain/awv307).

Tourette syndrome is characterized by the presence of tics, which have a fluctuating, waxing and waning course, and are typically exacerbated by stress, anxiety, excitement, anger or fatigue. Tics are known to diminish when an individual is absorbed in an activity, concentrating, focused or pleased. Studies have also shown that tics can occur during sleep, although understandably patients fail to report their presence. Further, many individuals with tics, especially older children and adults, describe a sensory phenomenon (premonitory urge), such as a tension, impulse, tingle, or feeling located in the relevant body part, prior to the tic. Although it has been suggested that tics should