NeuroImage: Clinical 11 (2016) 515–529

Contents lists available at ScienceDirect

NeuroImage: Clinical

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

Computational analysis in epilepsy neuroimaging: A survey of features and methods

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ARTICLE INFO

Article history:
Received 10 December 2015
Received in revised form 11 February 2016
Accepted 22 February 2016
Available online 23 February 2016

Keywords:
Multimodal neuroimaging
Epilepsy
Drug resistant epilepsy
Focal cortical dysplasia
Malformations of cortical development
Machine learning

ABSTRACT

Epilepsy affects 65 million people worldwide, a third of whom have seizures that are resistant to anti-epileptic medications. Some of these patients may be amenable to surgical therapy or treatment with implantable devices, but this usually requires delineation of discrete structural or functional lesion(s), which is challenging in a large percentage of these patients.

Advances in neuroimaging and machine learning allow semi-automated detection of malformations of cortical development (MCDs), a common cause of drug resistant epilepsy. A frequently asked question in the field is what techniques currently exist to assist radiologists in identifying these lesions, especially subtle forms of MCDs such as focal cortical dysplasia (FCD) Type I and low grade glial tumors. Below we introduce some of the common lesions encountered in patients with epilepsy and the common imaging findings that radiologists look for in these patients. We then review and discuss the computational techniques introduced over the past 10 years for quantifying and automatically detecting these imaging findings. Due to large variations in the accuracy and implementation of these studies, specific techniques are traditionally used at individual centers, often guided by local expertise, as well as selection bias introduced by the varying prevalence of specific patient populations in different epilepsy centers. We discuss the need for a multi-institutional study that combines features from different imaging modalities as well as computational techniques to definitively assess the utility of specific automated approaches to epilepsy imaging. We conclude that sharing and comparing these different computational techniques through a common data platform provides an opportunity to rigorously test and compare the accuracy of these tools across different patient populations and geographical locations. We propose that these kinds of tools, quantitative imaging analysis methods and open data platforms for aggregating and sharing data and algorithms, can play a vital role in reducing the cost of care, the risks of invasive treatments, and improve overall outcomes for patients with epilepsy.

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Abbreviations: FCD, focal cortical dysplasia; GM, gray matter; WM, white matter; T1W, T1-weighted MRI; T2W, T2-weighted MRI; DRE, drug resistant epilepsy; FLAIR, fluid-attenuated inversion recovery; VBM, voxel-based morphometry; SBM, surface-based morphometry; DWI, diffusion weighted imaging; DTI, diffusion tensor imaging; PET, positron emission tomography; GW, gray-white junction; HARDI, high angular resolution diffusion imaging; MEG, magnetoencephalography; MRS, magnetic resonance spectroscopy imaging; PNH, periventricular nodular heterotopia.

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http://dx.doi.org/10.1016/j.nicl.2016.02.013

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1. Introduction

Epilepsy affects 65 million people in the world and has been estimated to cost the US upwards of $12.5 billion annually, based on a 1995 epidemiology study (Schachter, 2015; Kwan et al., 2011; Begley et al., 2000). Patients with drug resistant epilepsy (DRE) account for only 20–40% of patients with epilepsy but contribute a large portion of the epilepsy-associated cost due to risk of premature death, seizure-related injuries, psychosocial dysfunction and general reduction in quality of life measures (Kwan et al., 2011).

Resective surgical therapy has been the mainstay of therapy, but surgical candidacy depends on the clinical team's ability to identify and fully delineate structural and functional lesions, such as regions of dysplastic cortex. Overall, the odds of seizure freedom after surgery for epilepsy are 2–3 times higher in cases that exhibit an identifiable lesion on histopathology or MRI (Téllez-Zenteno et al., 2010). Thus, the overall goal of neuroimaging in epilepsy is to monitor therapy and identify biomarkers of disease, candidates for surgery, and predictors of post-surgical outcomes (Bernasconi and Bernasconi, 2014).

Currently, the gold standard for outlining lesions in epilepsy patients is through identifying the epileptogenic zone, defined as the region recruited to seize on EEG, either measured on the scalp or in conjunction with invasive intracranial monitoring utilizing subdural strips, grids, depth or stereo EEG electrodes (Najm et al., 2002). The irritative zone is defined as the region near the structural or functional lesion that generates interictal epileptiform discharges identified by ECoG and fMRI (Koepp and Woermann, 2005). In these cases, the location of the epileptogenic zone, determined by electrophysiology, is compared with the irritative zone, determined by possible lesions discovered on imaging, to guide therapy. A majority of these are caused by malformations of cortical development.

1.1. Malformations of cortical development

Malformations of cortical development (MCD), which describe a variety of structural and metabolic abnormalities of brain arising during gestation, were traditionally thought to cause a significant proportion of epilepsy (~15%) (Sisodiya, 2000; Lerner et al., 2009). Some lesions remain undetected, even at high resolution MRI, and are only discovered on histopathology after resective surgery (Sisodiya, 2000). As a result, previous estimates of the incidence of MCD have been low, and now at least 25% of all cases are thought to be due to MCD lesions. Histopathology of resected lesions show that these are mostly focal cortical dysplasias (45%), gliosis (22%), and hippocampal sclerosis (13%) (Wang et al., 2013).

Table 1 shows the distribution of malformations of cortical development and their incidence. Few studies have looked at the incidence of the different possible malformations, but focal cortical dysplasias is considered to account for the majority of the cases (Wang et al., 2013; Raymond et al., 1995). Focal cortical dysplasias (FCD) are a

Table 1
Incidence of different malformations of cortical development organized by groupings (Barkovich et al., 2012). Group 1 includes malformations due to abnormal cell proliferation, Group 2 includes malformations due to abnormal cell proliferation, and Group 3 includes malformations due to abnormal cortical organization. These incidence data are adapted from Papayannis et al. (2012).

Group I (49%)	
Focal cortical dysplasia (Type I and II)	48%
Focal cortical dysplasia + glioneural tumors	14%
Dual or triple pathology: focal cortical dysplasia + tumors + hippocampal sclerosis	14%
Glioneural tumors	10%
Tuberous sclerosis	10%
Hemimegalencephaly	1%
Focal hemimegalencephaly versus possible focal cortical dysplasia	3%
Group II (40%)	
Periventricular nodular heterotopia	55%
Subcortical heterotopia	18%
Mixed forms of heterotopia	10%
Dual pathology: periventricular nodular heterotopia + hippocampal sclerosis	13%
Double cortex or subcortical band heterotopia	5%
Group III (11%)	
Schizencephaly	37%
Polymicrogyria (bilateral)	26%
Polymicrogyria (unilateral)	37%