Epilepsy Research (2014) 108, 1286—1298

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

Recent seizure activity alters motor organization in frontal lobe epilepsy as revealed by task-based fMRI

Kristine E. Woodward[a,e,f], Ismael Gaxiola-Valdez[e,f], David Mainprize[f], Matthew Grossi[f], Bradley G. Goodyear[c,d,e,f], Paolo Federico[a,b,c,e,f,*]

[a] Department of Neuroscience, University of Calgary, 2500 University Drive NW, Calgary, AB, Canada T2N 1N4
[b] Department of Clinical Neuroscience, University of Calgary, 2500 University Drive NW, Calgary, AB, Canada T2N 1N4
[c] Department of Radiology, University of Calgary, 2500 University Drive NW, Calgary, AB, Canada T2N 1N4
[d] Department of Psychiatry, University of Calgary, 2500 University Drive NW, Calgary, AB, Canada T2N 1N4
[e] Hotchkiss Brain Institute, University of Calgary, 2500 University Drive NW, Calgary, AB, Canada T2N 1N4
[f] Seaman Family MR Research Center, University of Calgary, 2500 University Drive NW, Calgary, AB, Canada T2N 1N4

Received 6 February 2014; received in revised form 26 May 2014; accepted 13 June 2014
Available online 6 July 2014

KEYWORDS
Connectivity;
Motor coordination;
BOLD;
Frontal lobe epilepsy;
fMRI

Summary
Purpose: Patients with frontal lobe epilepsy (FLE) commonly demonstrate motor impairments, suggesting that frontal lobe seizures affect motor function. However, the underlying mechanisms of these deficits are not known, nor has any study systematically examined motor organization in these patients. We therefore examined cortical motor organization in a group of adult patients with FLE, using task-based fMRI.
Methods: Eleven right FLE patients, six left FLE patients, and ten control subjects underwent task-based fMRI. Two tasks were performed using the right and left hands separately, and both hands together. The first task was a finger-tapping task and the second task was a more complex coordination task. Functional MR data were compared between patient groups and controls. A laterality index of brain activation was also calculated between the epileptic and healthy hemisphere to determine hemispheric dominance during task performance to explore its relationship with a variety of patient-specific epilepsy factors.

* Corresponding author at: Departments of Clinical Neurosciences and Radiology, University of Calgary, Room C1214a, Foothills Medical Centre, 1403 29th Street NW, Calgary, AB, Canada T2N 2T9. Tel.: +1 403 944 4091; fax: +1 403 283 2270.
E-mail addresses: kwoodwar@ucalgary.ca (K.E. Woodward), igaxiola@ucalgary.ca (I. Gaxiola-Valdez), dgmainpr@gmail.com (D. Mainprize), mvgrossi@ucalgary.ca (M. Grossi), goodyear@ucalgary.ca (B.G. Goodyear), pfederic@ucalgary.ca (P. Federico).

http://dx.doi.org/10.1016/j.eplepsyres.2014.06.015

Results: Overall, right FLE patients demonstrated decreased BOLD activity in the epileptic hemisphere and increased BOLD activity in the healthy hemisphere compared to controls ($p < 0.05$). The comparison of left FLE patients to controls provided less conclusive differences, possibly due to the low number of left FLE patients studied. Laterality indices of the coordination task were positively correlated to the number of months since the last seizure in both patient groups (right FLE: $r_s = 0.779$, left FLE: $r_s = 0.943$). Patients that had experienced a recent seizure relied more on the sensorimotor cortex of the healthy hemisphere during task performance, compared to those that were relatively seizure free ($p < 0.05$).
Significance: Patients with FLE exhibited changes in motor BOLD activity that was dependent on the duration of seizure freedom. These results demonstrate the presence of seizure-related alteration of cortical motor organization in FLE, which may underlie the motor deficits seen in these patients.

Introduction

Frontal lobe epilepsy (FLE) is the second most common form of focal epilepsy (Tellez-Zenteno et al., 2005). For most types of frontal lobe seizures, motor symptoms occur during the ictal period; however, patients with FLE exhibit deficits in motor control, coordination, and planning during daily activities, suggesting that seizures also affect motor function during interictal periods (Exner et al., 2002; Helmstaedter et al., 1996). This is further demonstrated by poorer performance on tests of psychomotor speed, coordination, motor planning, and motor sequencing in FLE patients when compared to patients with temporal lobe epilepsy (Helmstaedter et al., 1996; Upton and Thompson, 1996). Despite these findings, the mechanisms underlying motor deficits in FLE remain unknown.

Few studies have investigated the cortical organization of motor function in FLE patients. Direct cortical stimulation and transcranial magnetic stimulation studies have revealed alterations in motor organization, but with variable results (Branco et al., 2003; Hamer et al., 2005; Labyt et al., 2007). A limitation of these studies was poor spatial resolution compared to other available imaging techniques, namely functional MRI (fMRI). Not only does fMRI provide high spatial resolution, but it is also non-invasive with no known risks, and is therefore a mainstay in the study of brain organization. Several case studies of patients with epilepsy have demonstrated changes in cortical motor organization using task-based fMRI (Macdonell et al., 1999; Moo et al., 2002; Stoeckel et al., 2002). An intracortical microstimulation study of rats also showed that repeated seizure activity near the sensorimotor cortex leads to impaired interictal motor performance, along with alterations of motor cortex maps (Henry et al., 2008). Additionally, we recently examined the effects of FLE on cortical motor networks as examined using resting-state fMRI and found that increased seizure burden was correlated with decreases in functional connectivity within the motor network (Woodward et al., 2014). These studies suggest that frontal lobe seizures can induce changes in motor cortex organization, and that these changes may be related to interictal motor deficits.

The organization of cortical motor function has also been shown to change over time in epilepsy patients and animal models of epilepsy. In a case study of FLE, fMRI scans taken before and after multiple subpial transections of right motor cortex showed increased motor activation in the unaffected hemisphere seven weeks post surgery, and a return to pre-surgical activation 13 weeks after surgery (Moo et al., 2002). A study using the pilocarpine rat model of epilepsy also demonstrated variable patterns of motor cortex organization, with larger cortical motor representations 48 h following a seizure, and a return to control patterns one and three weeks later (Young et al., 2009). These studies suggest that motor organization may be affected by individual epilepsy factors, such as recent seizures or surgical procedures.

To date, no fMRI studies have examined motor organization in a group of adult patients with FLE, largely because brain activation is strongly dependent on seizure focus location, seizure frequency, age at epilepsy diagnosis, and other factors (Muller et al., 1997; Upton and Thompson, 1997). We therefore studied motor organization in FLE patients, as well as the effect of individual clinical factors on this organization. Patterns of brain activation also depend on lesion type (Janszky et al., 2003), functional deficit zone as measured by FDG-PET (Gaillard et al., 2011), and EEG findings of interictal activity (Janszky et al., 2006). These data were not available for all patients in the present study, so these factors were not investigated. We hypothesized that FLE would be associated with decreased activation in the epileptic hemisphere and increased activation in the non-epileptic hemisphere. We also hypothesized that these changes would be more pronounced in individuals with factors associated with increased seizure burden (e.g., earlier epilepsy diagnosis, longer disease duration, higher seizure frequency, etc.). Determining the relationship between motor impairments, brain motor organization, and seizure burden factors may help better understand the underlying mechanisms of motor impairments experienced in FLE patients.

Materials and methods

Participants

This study was approved by the Conjoint Health Research Ethics Board of our institution. Written informed consent was obtained from all participants prior to participation. Patients with FLE were identified through the Alberta Health Services — Calgary Zone Epilepsy Clinic, the Seizure