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SHORT COMMUNICATION

Structural changes in the temporal lobe and piriform cortex in frontal lobe epilepsy

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Summary
Background: Neuronal networks involved in seizure generation, maintenance and spread of epileptic activity comprise cortico-subcortical circuits. Although epileptic foci vary in location across focal epilepsy syndromes, there is evidence for common structures in the epileptogenic networks. We recently reported evidence from functional neuroimaging for a unique area in the piriform cortex, common to focal epilepsies in humans, which might play a role in modulating seizure activity.

In this study, we aimed to identify common areas of structural abnormalities in patients with frontal lobe epilepsy (FLE).
Methods: T1-weighted MRI scans of 43 FLE patients and 25 healthy controls were analysed using voxel based morphometry. Differences in regional grey matter volume were examined across the whole brain, and correlated with age at epilepsy onset, duration and frequency of seizures.
Results: We detected areas of increased grey matter volume in the piriform cortex, amygdala and parahippocampal gyrus bilaterally, as well as left mid temporal gyrus of patients relative to controls, which did not correlate with any of the clinical variables tested. No common areas of atrophy were detected across the FLE group.

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Conclusions: Structural abnormalities within the piriform cortex and adjacent structures of patients with FLE provide further evidence for the involvement of this area in the epileptogenic network of focal epilepsies. Lack of correlation with duration or age of onset of epilepsy suggests that this area of abnormality is not a consequence of seizure activity.

Introduction

Changes in grey matter volumes (GMV) have been reported in a number of epilepsy syndromes (Bernasconi et al., 2004; Keller et al., 2002; Lawson et al., 2002; Widjaja et al., 2011; Woermann et al., 1999). Regional increases and decreases of GMV have been identified within the epileptogenic region but also extending to brain areas distant from the seizure onset zone. Atrophy secondary to neuronal loss is the common pathological correlate of decreased GMV in the epileptogenic zone (Bernasconi et al., 2004; Keller et al., 2002). However, the biological significance of changes remote from the epileptic focus remains unclear.

In focal epilepsies, the network involved in the generation, modulation and spread of seizures may encompass not only the seizure onset zone but a number of areas believed to be involved in seizure modulation (Norden and Blumenfeld, 2002). Although seizure onset zones vary across different focal epilepsies, there is evidence for common cortico-subcortical circuits that underlie the maintenance and propagation of seizures. Animal and human studies have shown that areas comprising the nigro-striatial pathways, thalamus (Norden and Blumenfeld, 2002) are key parts of the epileptogenic network in both focal and generalised epilepsies. We recently reported evidence from functional neuroimaging for a unique area in the piriform cortex, common to focal epilepsies in humans, which might play a role in modulating seizure activity (Laufs et al., 2011).

Structural changes in patients with TLE have been widely studied using region and voxel-based morphometry (VBM) analysis (Bernasconi et al., 2004; Keller et al., 2002); however, these studies are usually dominated by areas of atrophy in the hippocampus and ipsilateral temporal lobe, which affects the accuracy of the normalisation process involved in this type of analysis. Only few studies have assessed structural abnormalities in patients with frontal lobe epilepsies (FLE) (Lawson et al., 2002; Widjaja et al., 2011). In this study we used whole brain VBM analysis of grey matter to explore common structural changes in a population with FLE.

Materials and methods

We recruited 43 patients with drug resistant FLE (26 left FLE and 17 right FLE). Diagnosis and lateralisation of seizure focus was performed by experienced neurologists based on video-EEG, seizure semiology, MRI imaging and FDG-PET/Ictal SPECT when available. The aetiology was cryptogenic in 32 patients. Small areas of focal cortical dysplasia in concordance with the suspected seizure onset zone were identified in 11 patients. Additionally, we scanned 25 healthy controls with no history of neurological or psychiatric disorders. Population characteristics are reported in Table 1.

The study was approved by the Research Ethics Committee of the UCL Institute of Neurology and UCL Hospitals.

Subjects were scanned with a 3 T General Electric Excite HD scanner. A 3-dimensional T1-weighted fast spoiled gradient echo (FSPGR) volumetric scan was obtained for each subject. Matrix size was $256 \times 256 \times 196$ voxels, with an isotropic voxel size of 1.1 mm (echo time/repetition time/inversion time 2.8/6.6/450 ms, flip angle 20°).

T1 images were processed and analysed using Statistical Parametric Mapping software (SPM8) (http://www.fil.ion.ucl.ac.uk/spm8).

Segmentation of the T1 images was performed using the ''New segmentation'' algorithm of SPM8. The grey matter, white matter and CSF tissue maps where normalised to MNI space using the *DARTEL* toolbox. The resulting tissue classification GM images were modulated by the Jacobian determinants derived from the registration step, in order to preserve subject's tissue volume after warping. Finally, images were smoothed by an 8-mm full width at half maximum isotropic Gaussian kernel.

Voxel-wise GMV differences between FLE patients and controls were examined using independent-sample *t*-tests. To account for differences in brain sizes, images were globally normalised using each subject's whole brain volume. Age and gender were used as regressors of no interest in the model.

Differences were considered significant at a threshold of $p < 0.05$ corrected for multiple comparisons (family wise error correction).

Correlation of structural changes with epilepsy duration, age of onset and monthly seizure frequency at the time of scan were explored by regressing the grey matter maps against these variables.

Results

FLE patients showed bilaterally, predominantly right-sided increases of grey matter volumes compared to controls in the piriform cortex, amygdala and parahippocampal gyrus as well as in the left mid temporal lobe gyrus (Fig. 1). Changes in medial temporal lobes were similarly distributed in patients with left and right FLE (Supplementary Fig. 1).

Supplementary Fig. 1 related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.eplepsyres.2014.03.001.

Regression analysis did not reveal any significant correlation of GMV changes with age at seizure onset, duration of epilepsy, or seizure frequency.