Voxel-Based Relaxometry for Cases of an Unresolved Epilepsy Diagnosis

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INTRODUCTION

T2 relaxometry is a sensitive tool for the detection of abnormalities associated with epilepsy, revealing lesions not visible on a standard structural MRI.[1] A patient may be diagnosed with epilepsy, but there may not be a firm understanding of the seizure focus, or in other cases the basic diagnosis of epilepsy may be uncertain. In any of these cases, additional information, such as that offered by T2 relaxometry may provide important information to corroborate, or refute indeterminate information from the other sources. The additional information may also provide a direction for more focused study using, for example, intracranial EEG electrodes.[2] Voxel-based relaxometry (VBR) is a recently developed T2 relaxometry technique, which allows for an unbiased statistical analysis of T2 values across the whole brain by running statistical tests on each voxel.[3] We and others have shown that single-subject VBR can be a valuable tool for detecting and localizing abnormalities in epilepsy patients.[2,4] Our objective was to assess the performance of single-subject VBR at 3 T as a diagnostic tool for patients whose diagnosis of epilepsy or seizure focus is uncertain.

METHODS

We scanned 149 eligible patients who provided written informed consent. A modified Carr-Purcell-Meiboom-Gill (CPMG) sequence was performed at 3 T (Signa VH/i; GE Healthcare, WI). The CPMG sequence parameters were: 8 echoes, TE 30 ms to 240 ms, TR = 2175 ms, 256 x 128 matrix, 24 cm FOV, 15 to 24 slices, 5 mm thick, 1 mm gap. The CPMG sequence was also performed on 25 healthy age-matched controls. The seizure focus of each patient was determined based on history, EEG, conventional structural MR, and neuropsychological testing. From the initial group, we obtained 51 patients with uncertain epilepsy diagnoses. These patients were first classified as having known epilepsy with a suspected, but unconfirmed focus (SF), known epilepsy with unknown focus (KE), or suspected but unconfirmed epilepsy (SE). The patients in the SF group were further classified as having a suspected lobe of origin, but the side of origin was unknown (SF-L) or as having a suspected lobe and side of origin (SF-LS). Cases of suspected primary generalized epilepsy were excluded. T2 maps were generated using a Levenberg-Marquardt non-linear fitting routine with a baseline to account for cerebrospinal fluid partial-volume. The T2 maps were spatially normalized (T2-weighted template) and smoothed (Gaussian filter, 6 mm full width half maximum) with SPM2 (FIL Methods Group, UK, 2004) using previously described methods.[2,4] A tissue mask was generated by defining CSF using a threshold on non-baseline corrected T2 maps and by performing brain extraction in FSL (FMRIB Software Library, www.fmrib.ox.ac.uk/fsl, 2004). Statistical analysis of the smoothed T2 maps was performed using a 2-sample *t*-test between the control patient group and individual patients using SPM2 ($\alpha = 0.05$). The number and location of significant T2 elevations on VBR maps were recorded. A VBR severity score was determined based on the presence of VBR significance in any of the following 13 regions for each hemisphere: *anterior temporal lobe, posterior temporal lobe, amygdala, hippocampus, frontal lobe, parietal lobe, occipital lobe, caudate, putamen, pallidum, thalamus, internal capsule and insular ribbon*. Patients were classified as having high (> 6 areas), medium (3-6 areas), low (1-2 areas) or no VBR severity (0 areas). Each of the control subjects underwent VBR analysis with the statistical analysis occurring between control and the remainder of the control group to provide a reference for false-positive detections.

RESULTS

Fifty-one patients were assessed for VBR abnormalities and twenty-five control subjects were used as a statistical control (mean age 26, range of 18-42). Seventeen of the 27 patients in the SF group (63%) exhibited a VBR abnormality in the suspected focus. In these patients, the VBR findings helped corroborate other findings. Fig 1 illustrates this corroboration in a patient classified as SF-L having a suspected temporal lobe focus but the side of origin was not known. In this case, clear T2 abnormality was present in the left temporal lobe white matter and mesially in the amygdala. Thus, VBR helped to identify the side of seizure origin in this subject. Compared to control data, all patient groups showed higher VBR severity, with the SF-L group showing the highest proportion of patients with high or moderate VBR severity (Fig 2). The average number of VBR abnormalities per patient were: SF; 1.96, SF-L; 5.55, SF-LS; 6.38, KE; 4.79 and SE; 4.6 Thus, all patient groupings exhibited more VBR abnormalities than controls with the SF groupings showing the highest.

DISCUSSION

A firm diagnosis of epilepsy can be difficult to establish, and may require multiple diagnostic tools. Our results show that single subject VBR can help identify or confirm a seizure foci in patients in whom conventional investigations have failed to yield a diagnosis. VBR abnormalities occurred more in patients with better-characterized epilepsy (i.e., with a suspected focus). In these patients, VBR can strengthen and hone the diagnosis to direct subsequent treatment and investigations.

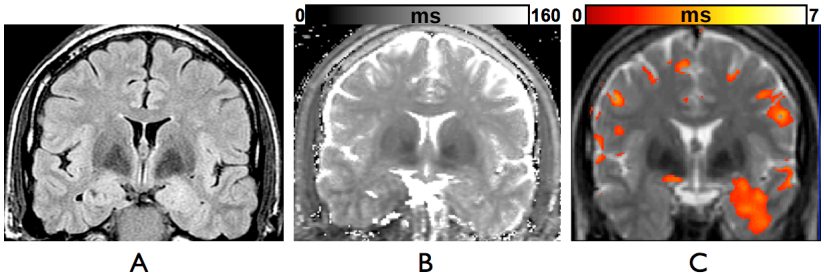

Fig 1. *VBR analysis performed on a 43 year old female with suspected temporal lobe epilepsy (side of origin unknown) and a normal EEG.* ***A:*** *FLAIR image shows questionable left amygdalar enlargement.* ***B:*** *T2 map (not registered or smoothed) shows relatively high T2 values in left temporal lobe, including amygdala.* ***C:*** *VBR map thresholded at $\alpha = 0.05$ (uncorrected) overlaid on the spatially normalized brain showing significance in left temporal lobe, including amygdala. Artifact appears in the outer cortex caused by CSF partial volume averaging.*

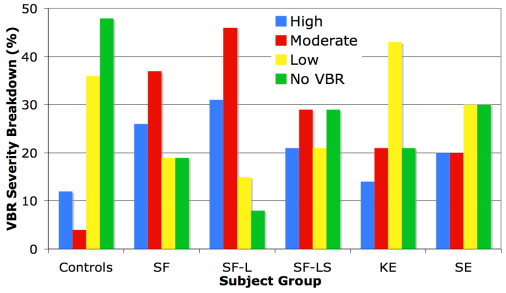

Fig 2. *Breakdown of VBR severity for patient groups.*

References

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