Epilepsia
Official Journal of the International League Against Epilepsy

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Journal:	*Epilepsia*
Manuscript ID	Draft
Manuscript Type:	Letter
Date Submitted by the Author:	n/a
Complete List of Authors:	Keller, Simon; University of Liverpool, Molecular and Clinical Pharmacology; King's College London, Department of Clinical Neuroscience
Key Words:	Prognosis, Imaging, Outcome, Atrophy

Brain atrophy in seizure-free temporal lobe epilepsy: implications for predicting pharmacoresistance

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To the Editors:

I read with interest the recent manuscript by Alvim et al.[1] entitled "Progression of gray matter atrophy in seizure-free patients with temporal lobe epilepsy". Using voxel-based morphometry (VBM) applied to conventional 3D T1-weighted images, the authors report widespread extrahippocampal atrophy in patients with well-controlled temporal lobe seizures, and that progressive atrophy occurs over time in the absence of recurrent seizures. As the authors point out, this suggests that "extrahippocampal atrophy has multifactorial causes and cannot be defined as the origin of the pharmacoresistance. Although seizures might be responsible to some extent for this atrophy, this probably does not influence the AED response" (pg 8). This work could be interpreted to indicate that more widespread brain atrophy is not necessarily a reflection of a seizure disorder that is less amenable to pharmacological or surgical therapy. This idea is not entirely consistent with the authors' previous interesting papers, which indicate – using the same VBM techniques – that pharmacological[2] and surgical[3] control of temporal lobe seizures is less likely in patients with more widespread atrophy.

TLE is a network disorder. Diffusion tensor imaging (DTI) studies are increasingly reporting that seizure freedom after temporal lobe surgery is less likely when deficits are observed in temporal lobe pathways.[4, 5] Given the current paucity of data, it is currently unknown whether pharmacoresistance can be predicted using similar approaches in patients with a new diagnosis of TLE. Magnetic resonance spectroscopy may offer important insights.[6]

A crucial point is that the development of robust, individualized, imaging prognostic markers of treatment outcome in TLE is more likely to be achieved using imaging approaches that provide biological information that exceeds what is afforded by conventional structural MRI scans, which are typically acquired in context of the clinical evaluation of patients. The volumetric, thickness and surface area information afforded by conventional scans constrain inferences to macroscopic brain morphology. There is no doubt that these approaches have furthered our understanding of pathological brain changes in focal epilepsy. However, the ability to develop highly sensitive and robust prognostic imaging measures of treatment outcome – and a detailed understanding of the mechanisms underlying pharmacoresistance and postoperative outcome - are more likely to be achieved using imaging techniques that probe neurobiology on a microscopic scale. Diffusion approaches are not without limitation, but do represent an important development. Techniques that probe neuroinflammation may represent an important pathway,[7] but there is of yet no evidence indicating that MRI can be used to directly, accurately and validly determine neuroinflammation in epilepsy. In large scale imaging studies (i.e. >100 patients), imaging modalities are invariably restricted to what is collected for clinical purposes. New advanced imaging approaches that may have the sensitivity to discriminate between individual patients who will or will not achieve seizure remission are likely to be administered in context of research projects in smaller groups of patients, which limits the generalizability of findings. It may therefore be important to consider a coordinated effort across institutions to

harmonize advanced imaging protocols to identify non-invasive markers of seizure control.

Acknowledgement

SSK is funded by a UK Medical Research Council grant (Grant Number MR/K023152/1).

Disclosure

The author has no conflicts of interest to disclose. I confirm that I have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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