

Post-Surgical Failure after Temporal Lobectomy is Associated with Increased Medial Temporal Lobe Damage

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Synopsis
Using voxel-based morphometry (VBM) on MR images, we report that temporal lobe epilepsy (TLE) patients in whom seizures persisted after surgery had significantly reduced grey matter in ipsilateral temporal lobe regions, predominantly hippocampus, posterior parahippocampal gyrus, amygdala, and entorhinal cortex relative to patients with successful post-surgical outcome on pre-surgical MRI. Furthermore, we observed volume reduction of the contralateral hippocampus in failures relative to successes. We suggest that ipsilateral temporal lobe damage posterior to the margins of resection and contralateral medial temporal lobe sclerosis may contribute to persistent post-surgical seizures.

Introduction
Surgical intervention for the remediation of intractable temporal lobe seizures is associated with a favourable outcome in up to 80% of patients with lateralised ictal onset and MRI evidence of hippocampal sclerosis. The reasons for persistent seizures after temporal lobe resection in patients satisfying electrophysiological and MRI criteria for surgery are poorly understood. Reasons may include insufficient resection of epileptogenic hippocampal tissue, bilateral hippocampal sclerosis or extrahippocampal damage that contribute to epileptogenic activity. In the present study, we investigate whether patients with poor post-surgical outcome show evidence of 1) temporal lobe damage ipsilateral to seizure onset outside the margins of resection or 2) contralateral medial temporal lobe damage relative to surgical successes on pre-surgical MRI using VBM. Such abnormalities could potentially contribute to persistent post-surgical seizures.

Methods
We studied 22 patients with intractable left TLE with histopathological evidence of left hippocampal sclerosis. The epileptogenic focus was determined using routine pre-surgical methods, including surface electroencephalograph (EEG) recordings, invasive foramen ovale recordings in combination with video telemetry when EEG was non-lateralising, neuropsychological evaluation, and Wada testing. Of the 22 patients, 10 were defined as post-surgical successes (Engel's scale I) and 12 were defined as failures (Engel's scale II, III and IV). Optimized VBM analyses were performed using SPM99 as described in Good *et al* [1]. Comparisons of grey matter volume (GMV) were performed between surgical failures, successes and a group of healthy controls (n=77). All significance thresholds were set at $p < 0.05$ (corrected for multiple comparisons).

Results
Relative to controls, surgical failures had reduced GMV in ipsilateral hippocampal head, body and tail, amygdala, entorhinal cortex, temporal pole and lateral temporal neocortex. Conversely, surgical successes had reduced GMV in ipsilateral hippocampal body. In addition, both patient groups had GMV reduction of ipsilateral thalamus. When patient groups were compared directly, GMV reduction of ipsilateral hippocampal head, body and tail, posterior parahippocampal gyrus, amygdala, and entorhinal cortex was observed in surgical failures relative to successes (Figure). Furthermore, GMV reduction of the contralateral hippocampal body was observed in surgical failures relative to successes (Figure). There was no reduced GMV in successes relative to failures.

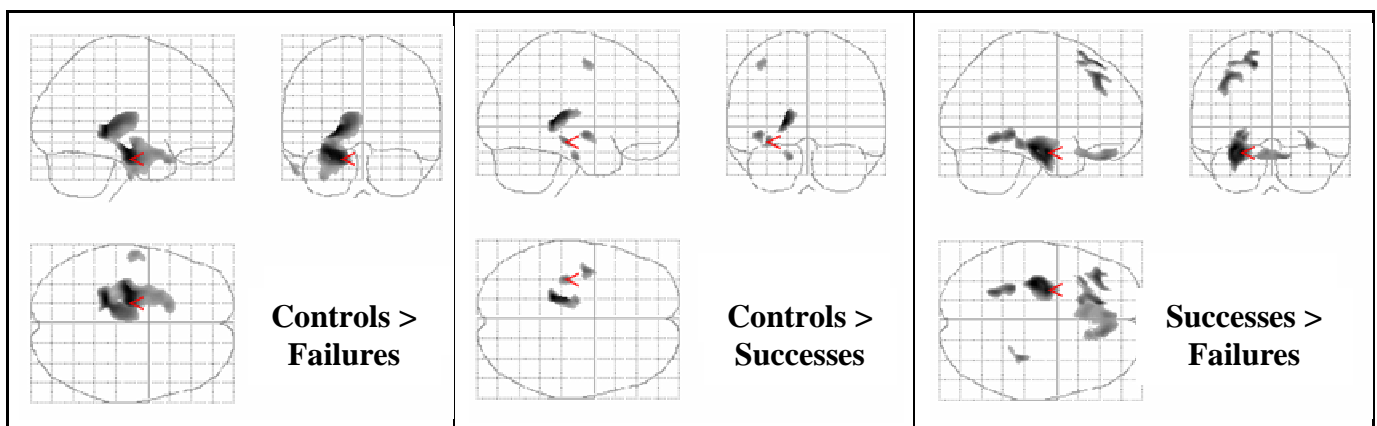


Figure. Statistical parametric maps of regional GMV differences between controls, failures and successes. Arrows indicate peak voxel of medial temporal lobe GMV reduction.

Conclusion
We have found evidence indicating that patients failing surgery for temporal lobectomy have reduced GMV in ipsilateral temporal lobe regions posterior to the margins of resection, such as posterior hippocampus and parahippocampal gyrus, which may contribute to persistent post-surgical seizures. Furthermore, the possibility remains that persistent post-surgical seizures may be due to contralateral epileptogenic activity, which may be reflected by the finding of atrophy of the contralateral hippocampus in surgical failures.