ATYPICAL LANGUAGE LATERALIZATION IN ADULT TEMPORAL LOBE EPILEPSY PATIENTS: FMRI STUDY USING STATISTICAL THRESHOLD AND SPATIAL MASKING

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Target Audience

Radiologists and epileptologists using functional MRI (fMRI) to determine language lateralization in patients with temporal lobe epilepsy (TLE) as preoperative evaluation for anterior temporal lobectomy (ATL).

Purpose

Determining language lateralization using fMRI is important for TLE patients being considered for ATL, affecting extent of surgery planned to minimize potential language and verbal memory deficits. Localization of cortical language areas using fMRI closely correlates with intraoperative electrocortical stimulation. fMRI is also comparable to intracarotid amobarbital procedure (Wada test) in determining language hemispheric dominance. Laterality index (LI) calculated as relative difference of active fMRI voxels between left and right hemispheres has been used to measure degree of language dominance, which can be variable in patients with early brain injury, weak right hand dominance, and other genetic, developmental, and environmental factors. However, few studies have assessed LI as a function of varying statistical thresholds and spatial masks. We analyzed TLE patients with fMRI using language comprehension and word generation tasks and applied varying statistical thresholds and spatial masks to determine variability in language dominance and potential plasticity/reorganization of language function.

Methods

Nine patients (mean age 36.3 years, M:F = 4:5, handedness R:L = 7:2) with TLE (6 left-sided, 3 right-sided seizure focus by EEG and interictal FDG-PET localization) were studied. Six of the patients had Wada tests with language and memory related tasks, 5 of which were right-handed. Brain MRI was performed on a 3.0T clinical scanner. Functional images were obtained using T2* gradient-echo EPI (TE 30 ms, TR 3000 ms, slice thickness 3 mm, no gap, matrix 64x64, FOV 22 cm). Structural images were obtained using 3D T1 SPGR (TE 3-4 ms TR 9-10 ms, flip angle 200, slice thickness 1 mm, matrix 128x128, FOV 24 cm). Language comprehension and word generation tasks were visually presented. Both language tasks were presented as block design consisting of 17 periods of 30 s each with 9 control and 8 active conditions arranged in alternating sequence. fMRI data analysis was performed using AFNI with motion correction, interleaved slice timing correction, high-pass temporal filtering, and spatial smoothing using 5-mm full-width half-maximum Gaussian blur. Activation maps were co-registered to Talairach atlas. Whole-brain (WB), inferior frontal-temporal-inferior parietal (FTP) cortical region, and temporal lobe masks were applied, and LI was calculated as LI = $(L-R)/(L+R)$, where where L and R are number of active voxels in left and right hemispheres, respectively, based on correlation coefficient r threshold ranging 0 to 1.

Results

All patients who had Wada tests, including one left-handed patient, were left hemisphere dominant according to Wada language test. LI calculated using FTP mask consistently generated larger LI than that calculated using WB mask, presumably by removing confounding voxels near midline, including visual cortex. Only 2 patients demonstrated clear left lateralization with strongly positive LI > 0.2 that increased with r with all masks **(Fig. 1A,D)**. Remaining 7 patients have some atypical lateralization, including one patient (right-handed, no Wada) with biphasic LI pattern with all masks (weakly positive LI with $r < 0.5$ and negative LI with $r > 0.5$) **(Fig. 1B,E)**. Others had weak to intermediate positive LI with WB and FTP masks, and biphasic or negative LI with temporal lobe mask **(Fig. 1C,F)**.

Discussion

Majority (6/9) of TLE patients studied have left-sided seizure focus, which is a primary indication for language fMRI study. All 6 patients who had Wada tests were determined left hemisphere dominant by Wada language test; however, majority (7/9) of the patients had some atypical lateralization by language fMRI with biphasic or negative LI with temporal lobe mask, suggesting significant number of patients in this population have some reorganization of language function. This is supported by recent studies showing language plasticity in adult epileptic patients. Further work needs to be done with larger population and comparing similar age- and handedness-matched control group.

Conclusion

Graphing LI as a function of r with application of various spatial masks provides more confident interpretation of language lateralization, potentially identifying patterns of atypical lateralization, and is more objective than calculating LI with fixed statistical threshold. FTP mask emphasizes classical areas of language activation in the frontal and temporoparietal regions. Smaller regional masks localizing known cortical language areas may be helpful in determining reorganization of language function in patients with TLE.

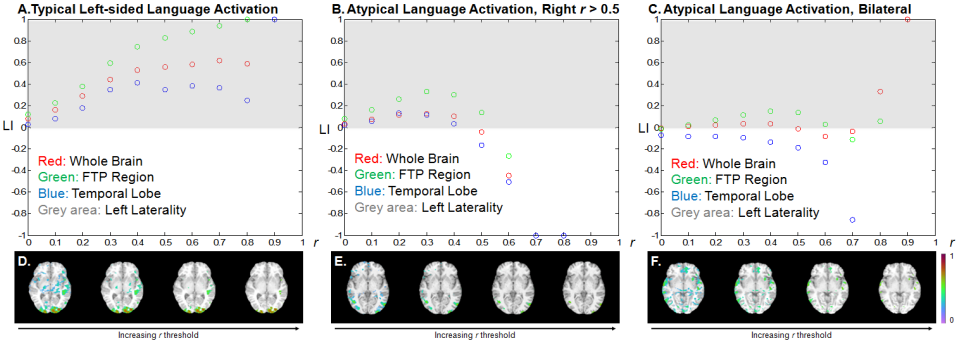

Fig 1. Effect of statistical threshold and spatial mask on LI calculation. **First column (A, D):** Patient with typical left hemisphere language dominance. **Second column (B, E):** Patient with right more than left hemisphere activation at thresholds $r > 0.5$. **Third column (C, F):** Patient with left more than right frontal activation but right more than left temporal activation. FTP region mask includes inferior frontal, temporal, and inferior parietal regions while excluding midline structures. Temporal lobe mask is similar to FTP region mask but excludes frontal and parietal lobes. **Top row (A, B, C):** Graphs of LI as function of r threshold. **Bottom row (D, E, F):** Axial maximum intensity projection (MIP) of language activation maps with variable r thresholds.

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