Is dysplastic cortex functional?

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Introduction: Malformations of cortical development (MCD) are a frequent cause of epilepsy. Dysplastic tissue has intrinsic epileptogenic properties, and at least in some MCD's it can also support physiological function. Here we assess with functional MR the relationship between pathological function (activation associated with epileptiform EEG discharges) and physiological function (activation with language tasks) in patients with different types of MCD.

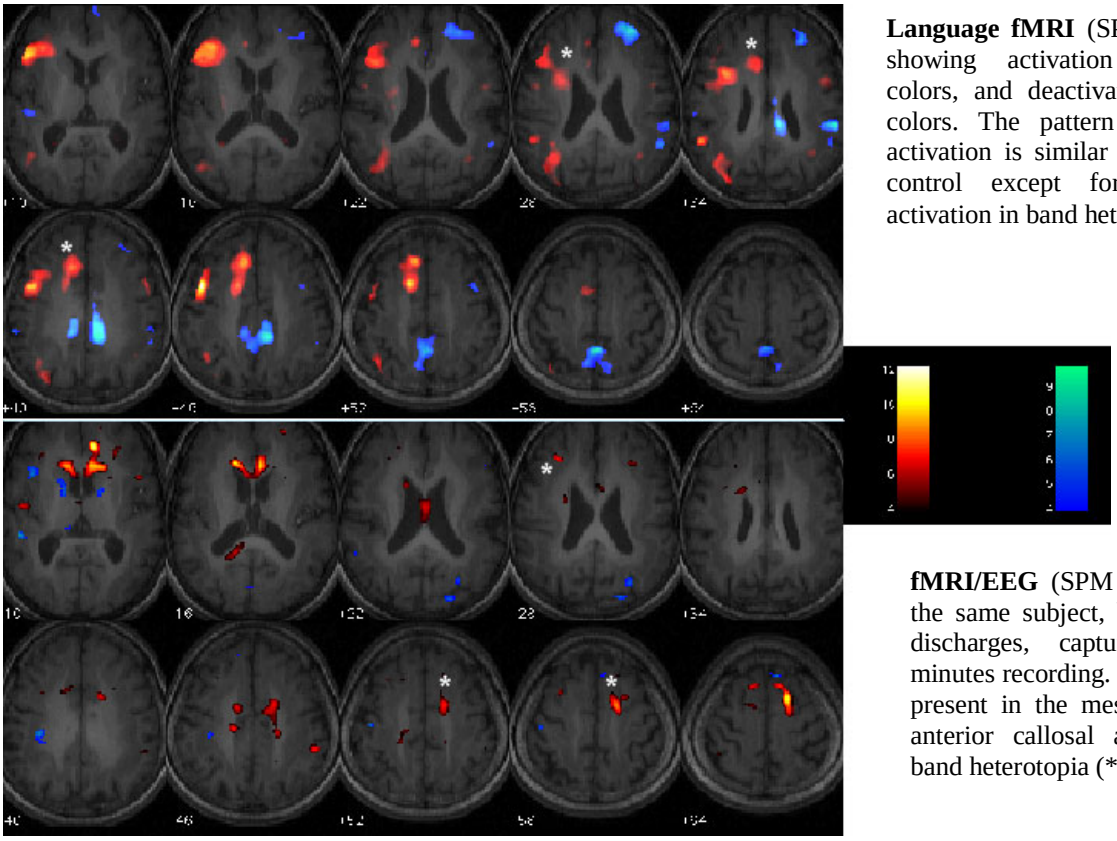
Subjects: 25 patients with MCD were assessed with fMRI of language tasks, seven of these had frequent interictal EEG discharges and had fMRI/EEG. Nine patients had focal cortical dysplasia (one with fMRI/EEG), eight had a dysembryoplastic neuroepithelial tumour (DNET, two with fMRI/EEG), five had polymicrogyria (two with fMRI/EEG), two had band heterotopia (both with fMRI/EEG) and one had tubero-sclerosis (TS).

MR methods*:* MR imaging was performed on a GE Signa 3T scanner. Functional sequences used Gradient-Echo Echo-Planar Imaging (EPI) with whole brain coverage (22 axial slices, 4mm thick, 1mm gap), 128 x 128 matrix, 24cm x 24cm FOV, 60º flip angle, TE 40ms, and TR 3000ms. Analysis of the imaging data was performed in SPM99 and iBrain®. For language activation, a verb generation (NVG) and a word fluency task (OLR) were used, both in a block design with visual stimulus presentation and covert response. Language lateralisation was determined by the number of activated pixels in language-related areas (laterality index, LI), and compared with 30 controls. For fMRI/EEG, EEG was recorded from eighteen non-metallic scalp electrodes with carbon fibre leads, using the conventional 10-20 EEG format. Event-related analysis was performed. Resultant statistical parametric maps are displayed at a threshold of $P<0.05$, corrected for multiple comparisons.

Results*:* Of the 25 subjects, only three showed right-lateralised language. Average LI was for NVG 0.53 ±0.3, and for OLR 0.48 ±0.3 (controls: 0.6 ±0.3 for both tasks). Five of the 6 patients with bilateral MCD had left lateralised language. Language lateralisation in left temporal lobe MCD (OLR, n=7, mean LI 0.49 ±0.3) was not different from patients with left-sided hippocampal sclerosis (n=10, mean LI 0.45 ±0.4). Only patients with proliferational abnormalities (DNET or TS) did not activate dysplastic tissue, whereas MCD's due to migrational or organisational abnormalities generally showed language activation in dysplastic tissue, if this was in eloquent areas (figure).

Four of the seven subjects with fMRI/EEG had discharges during scanning, of these two had band heterotopia (figure), one had polymicrogyria and one had focal cortical dysplasia. Discharge related BOLD signal change in all four studies was found in dysplastic cortex, but this did not overlap with language related activation.

Conclusion*:* Lateralisation of language function to the left hemisphere is a robust pattern that tends to be preserved even in presence of a MCD involving language eloquent cortex. The dysplastic tissue can be involved in complex physiological functions (language), probably depending on the timing of the onset of the developmental lesion. Confirming earlier studies, dysplastic tissue can also generate seizure discharges. Interestingly, the cortical areas involved in physiological and pathological function were in our cases spatially separated.



Language fMRI (SPM analysis) showing activation in warm colors, and deactivation in cold colors. The pattern of cortical activation is similar to a healthy control except for additional activation in band heterotopia (*).

fMRI/EEG (SPM analysis) of the same subject, based on 12 discharges, captured in 30 minutes recording. Activation is present in the mesial frontal / anterior callosal area and in band heterotopia (*).