EPI tissue segmentation maps based on multiple-echo EPI with parallel imaging for the reduction of multicomparison issues in fMRI

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Target audience

The target audience for this abstract includes researchers concerned about false positives and negatives due to multiple comparison issues in their data analysis.

Purpose

This abstract reduces false positives and negitives in fMRI experiments by properly masking out the gray matter (GM) in the echo planar images (EPI) collected in functional studies. The reasoning behind masking GM is to reduce multiple comparison issues, which occur when studying functional activation maps. A single slice of the brain with a 96 × 96 resolution contains 9,216 voxels, and a slice-wise Bonferroni correction method would dictate dividing the p-value of 0.05 by 9216 to declare an activated voxel is significant[1]. This correction can many times be too stringent and result in losing many true positives. So a method for reduction in voxel number is needed to maintain the statistical power of the Bonferroni test without losing the truly active voxels. An accelerated multiple-echo sequence was performed for the first five repetitions of the functional study, from which relaxivity maps were produced[2]. The relaxivity maps were used to create tissues segmentation masks[3], which are directly aligned with the functional data and used as masks to reduce multiple comparison issues.

Methods

A healthy human subject was imaged after informed consent was obtained. An 8-channel head receiver was utilized on a 3.0 T General Electric Signa LX scanner. The GREASE-II scanning parameters were a TR = 2 s, effective echo time (ETE)1 = 31 ms, ETE2 = 32 ms, ETE3 = 32 ms, ETE4 = 0 ms and ETE5 = 64 ms. The first spin echo (SE)1 = 130 ms and the second at SE2 = 260 ms. The flip angle was at 90 degrees, acquisition matrix 96 x 96, field of view 19.2 cm, slice thickness 2 mm, and 135 repetitions. The generalized autocalibrating partially parallel acquisitions (GRAPPA) technique was used with an acceleration factor of 2 and 4 ACS lines. Tissue relaxivities were found through a nonlinear fit of the multiple-echo data, which utilized all 5 echo images in the first five repetitions. The relaxivity maps were then utilized to produce tissue segmentation masks. A functional task was paired with the 135-repetition run of the accelerated sequence. The subjects were asked to tap the fingers of both hands when prompted by a boxcar function task of tap or rest. The first echo, a standard gradient echo image, was then analyzed utilizing AFNI and correlated with a boxcar function. The p-value was chosen to be 0.05 and was then Bonferroni-corrected using either no mask, brain mask, or grey matter mask.

Results

Figure 1 displays the three tissue masks that are produced by setting a winner-take-all 50% threshold for tissue determination using the tissue percentage maps. The tissue masks are placed on the anatomical image that was collected during the scanning session. This is because the T_1-weighted anatomical image shows clear definition between the different tissues. Also, it is shown that even with different resolutions, the maps from the EPI images also display tissue segmentation. However, the registration is not perfect when compared to the anatomical image, which is partially due to the warping of EPI images. This warping illustrates the advantage of using EPI-based tissue maps to segment EPI-based functional images.

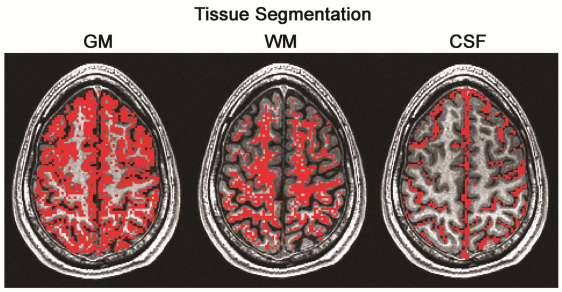

Figure 1: EPI tissue segmented maps overlaid on the

Figure 2 displays functional activation in echo 1 of the GRAPPA accelerated sequence. The functional activation maps are set at several different statistical thresholds, with multiple masks applied. Figure 2, no correction, has an uncorrected p-value of 0.05, and the correlation is calculated for every voxel in the slice. This image displays an overabundance of activation, and it can be assumed that many of the voxels are false positives. The slice Bonferroni correction image has no additional masking, but has a Bonferroni adjusted p-value threshold of 5.43×10^{-6} employed. The Bonferroni correction is a stringent statistical correction, which can lead to false negatives. This is why further masking is performed. The Bonferroni correction masks out the brain through the AFNI function 3dAutomask, which eliminates false positives outside of the brain. This masking cuts the number of voxels considered for activity down to 2,637 voxels and increases the Bonferroni corrected p-value to 1.896×10^{-5}. The reduction in voxel count and corresponding increase in p-value allowed for some newly activated voxels that were not seen in the Bonferroni slice correction. It can be assumed that these voxels were false negatives in the slice correction figure due to a stringent statistical threshold. The GM masked Bonferroni corrected image has 1,419-voxel. This increased the p-value by almost twofold to 3.5×10^{-5}. Masking just the GM not only allowed more activated voxels, which were not found in the brain masked Bonferroni, but also excluded delocalized positives found in the CSF voxels. It can be seen in the GM masked figure that the activation is typically one-voxel thick and runs along the cortical GM surface. This observation further demonstrates the quality and efficiency of the tissue mapping.

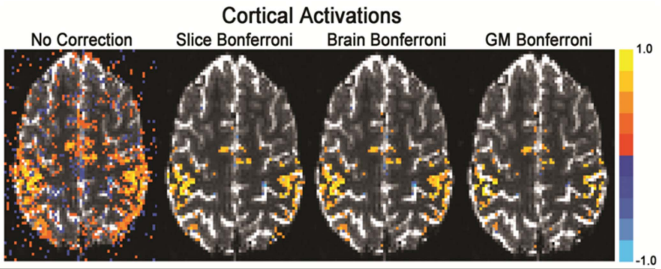

Fig. 2. Functional motor activation maps utilizing different masks and thresholds. From left to right: slice activation with p = 0.05, slice activation with Bonferroni correction, activated brain masked and Bonferroni correction, and activated GM masked with Bonferroni correction.

Conclusion

Ideally registered tissue segmentation reduces the multiple comparison issues that occur in correcting functional activation maps. By masking the activation maps with GM maps, false positives and negatives are reduced simultaneously. False negatives are lessened by the reduction in voxels of the image by the GM mask (which allows for a greater p-value threshold) when applying Bonferroni or other multiple comparison correction. False positives are reduced by masking the activation that occurs in the CSF and outside the brain. Furthermore, these relaxivity maps can be applied because they are in the same space as traditional fMRI and fcMRI experiments, allowing a one-to-one correspondence between data sets for aggressive data-masking for improved region-of-interest selection and reduced multiple-comparison statistical problems. The largest benefit is that this segmentation ability is theoretically free since it can be produced from the first five reps of a scan, which are typically not used in the analysis of functional studies.

References

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