ACCURATE LOCALIZATION OF FUNCTIONAL BRAIN ACTIVITY USING STRUCTURE ADAPTIVE SMOOTHING

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Introduction

The goal of neuro-oncologic brain surgery is to maximize tumor resection or to perform epilepsy surgery while preserving important brain functions. Presurgical fMRI can be used to localize motor, sensory, and language-control areas,[1] and has been used to study cerebral reorganization in tumor patients.[2] In presurgical planning of tumor resection,[3,4,5] it is of importance to have a high test power to avoid false positive (in particular in the lesion) and false negative (in particular outside the lesion) activations. False negative activations, i.e., there is no activation visible at locations where it should be, are of particular concern in brain tumor resection. Due to the low signal-to-noise ratio, fMRI signal detection requires using spatial information, or "smoothing." However, the commonly used smoothing by a Gaussian filter improves signal detection at the cost of loss of information on spatial extent and shape of the activation area. As an alternative we applied a novel structurally adaptive smoothing method, Adaptive Weights Smoothing (AWS),[6] to presurgical fMRI data of 26 epilepsy/tumor/vascular malformation patients. AWS achieves a similar variance reduction, but is able to adapt to different shapes of activation areas by generating a spatial structure corresponding to similarities and differences between time series in neighbored locations. Whereas due to the matched filter theorem, the bandwidth of a non-adaptive Gaussian filter is best chosen as the size of the usually not precisely known expected activation, AWS naturally adapts to different sizes of activated areas. In prior numerical simulations, AWS has been shown to be superior over Gaussian smoothing with respect to the accurate description of the shape of activation clusters and less false detections. In the present application we found that AWS and Gaussian smoothing occasionally give significantly different results, and we could identify examples which showed different aspects of the superiority of AWS in presurgical planning.

Methods

Subjects: We investigated pre-surgical functional MRI scans of 17 tumor patients, 4 patients with vascular malformations, and 5 epilepsy patients.

Data acquisition: Images were acquired on a GE 3T scanner using a 2D gradient echo EPI sequence with TE/TR = 40/2000 or 40/3000 ms. 24 to 34 axial slices of 4 or 5 mm thickness and a matrix size of 64 x 64 were acquired. Tasks were performed in three blocks during 3.7 min of scanning time. The tasks were: Motor (bilateral or right hand only tapping of thumb against all fingers of same hand); Language I (forming words beginning with given letter); Language II (rhyming with a given word), and Visual (naming of pictures).

Statistical evaluation: After reconstruction of the raw data and motion correction, the time series in each voxel was modeled by a linear model, with a design matrix specifying the explanatory variables including the task indicator function convolved with a hemodynamic response function template. Drift terms were modeled by polynomials. To account for temporal correlation, the data was whitened by using an AR(1) model together with a spatial smoothing of the correlation parameter in order to achieve a target number of degrees of freedom for the test statistic. After voxelwise estimation of the parameters, adaptive spatial smoothing (AWS) was applied to the array of parameters of interest to significantly reduce the variance of the parameter estimates. This also allowed weakening of the multiple test problem as well as defined thresholds for the test statistic. A map of t-statistics was obtained from the smoothed parameter map. Thresholds were then defined by random field theory. We used a conservative approach that accounts for the locally varying amount of correlation in the t-map obtained by adaptive smoothing. Therefore, the thresholds vary locally, with larger thresholds than in nonadaptive smoothing, especially in small activated regions. Due to the edge preserving properties of AWS, improved signal identification at the border of activated regions is obtained, which is particularly useful in applications where accurate description of the geometry of the activation areas is needed. Data was processed using afni[7], FORTRAN, C, and R (R Foundation for Statistical Computing).

Results

Of all activated voxels ($p<0.05$), 71% were detected by both AWS and Gaussian smoothing, 10% were detected only with AWS, and 19% only with Gaussian smoothing. We found significant differences between the two methods in 18 out of 26 patients, i.e., there were clusters of activation that could only be seen in one of the methods. Specifically, in one case Gaussian smoothing showed a significant additional cluster (false positive activation with Gaussian smoothing, if AWS is the correct method), and in six cases additional clusters were only seen with AWS (false negative activation with Gaussian smoothing if AWS is correct). Examples are shown in Fig. 1.

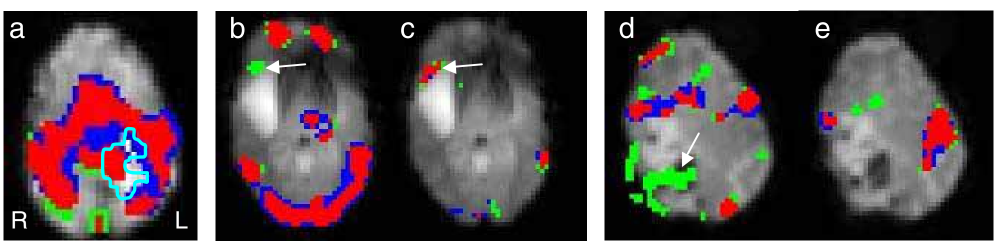

Figure 1 (color): Examples of activations seen only in Gaussian smoothing (**blue**), only in AWS (**green**), and in both (**red**). **(a)** In the bimanual motor task, AWS (red) and Gaussian smoothing alone (blue) yielded different results around a tumor, delineated by the bright blue line. **(b, c)** In the visual task, AWS detected activation next to a tumor (b, arrow) which was not seen with Gaussian smoothing. The potential neuronal activity of this region is known from a motor task, in which both methods detected this area (c, arrow); thus, Gaussian smoothing probably yielded false negative activations. **(d, e)** We observed frequently that AWS is more sensitive in regions with signal dropout in susceptibility artifact affected areas of the brain, such as next to a tumor in the language I task (d, arrow) as compared to the bilateral motor task (e).

Discussion

It is worth investigating if the problem of false negative activations next to tumors in the primary sensorimotor cortex,[8] which is probably caused by an altered hemodynamic response due to the tumor vascularity,[9] can be alleviated with AWS. We occasionally found a relatively improved detection in these areas due to the increased sensitivity of AWS in the presence of a poor signal-to-noise ratio. This finding correlates well with results from numerical simulations.

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