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TECHNICAL NOTE

Testing for Anatomically Specified Regional Effects

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Abstract: We present a simple method that allows statistical inferences to be made about the significance of regional effects in statistical parametric maps (SPMs) when the approximate location of the effect is specified in advance. The test can be thought of as analogous to assessing activations with uncorrected *P* values based on the height of SPMs but, in this instance, using the spatial extent or volume of the nearest activated region. The advantage of the current test is that it eschews a correction for multiple comparisons even though the exact location of the expected activation may not be known. *Hum. Brain Mapping 5:133–136, 1997.* © 1997 Wiley-Liss, Inc.

Key words: activations; clusters; SPM; Gaussian fields

INTRODUCTION

When making inferences about regional effects (e.g., activations) in statistical maps one often has some idea about where the activation should be. In this instance, a correction for multiple comparisons, implicit in searching the whole volume of the map, is inappropriate. However, there remains a problem in the sense that one would like to consider activations that are ''near'' the predicted location, even if they are not exactly coincident. Although it is now possible to correct *P* values when considering activations in small, well-defined, ''search regions'' [Worsley et al., 1996], we suggest a simpler solution to this problem that is based on the spatial extent of the nearest activation cluster.

In this technical note we draw attention to an application of the distributional approximations, pertaining to the spatial extent of suprathreshold regions in statistical parametric maps (SPMs), as presented in Friston et al. [1994]. That paper concentrated on statistical inference in the context of anatomically open hypotheses, where it is necessary to correct *P* values for the volume of brain analyzed. In this paper we focus on anatomically closed or specified hypotheses and use the same approximations to make inferences about predicted regional effects. Consider the problem of making an inference about an anatomically specified hypothesis, e.g., does the hand area in the primary motor cortex respond more to incongruent vs. congruent bimanual movements? Because this hypothesis is about a particular anatomical area we do not want to make any correction for multiple dependent comparisons. One approach would be to use the Z score at the

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prespecified stereotactic location to compute an uncorrected *P* value (e.g., a Z score of 1.64 corresponds to $P = 0.05$). However, the exact location of the hand area in the subject(s) analyzed may be very difficult to specify exactly and, for example, one may find that the activation is 8 mm away, rendering the Z score at the specified location insignificant. Because this activation is uniquely identified (by virtue of being the nearest to the prespecified location) one can, however, assign a *P* value to it on the basis of its spatial extent. This is the probability of finding a cluster of the volume observed or larger. If the cluster is significant, then one can infer a motor activation (assuming, of course, that the activation lies in the motor cortex). The probability of getting the observed number of voxels, or more, in a given cluster (conditional on that cluster existing) can be calculated using distributional approximations from the theory of Gaussian fields given below.

THEORY

The parameter of interest here is the volume (number of voxels) of a cluster above a reasonably high threshold in an SPM. Under the null hypothesis of no regional effects, the volume (n) of any cluster is distributed according to Equation 11 in Friston et al. [1994]. This approximation was derived by assuming a form for $P(n = k)$ which is asymptotically correct and by determining the parameters of the distribution by reference to its known moments, giving:

$$P(n \geq k) \approx \exp(-\beta k^{2/D}) \quad (1)$$

where β is given by

$$\beta = [\Gamma(D/2 + 1).E\{m\}/E\{N\}]^{2/D}.$$

$E\{m\}/E\{N\}$ is the ratio of the expected number of maxima and the expected number of voxels above a threshold u in an SPM of dimension D, where according to Hasofer [1978]:

$$E\{m\}/E\{N\} \approx (2\pi)^{(D+1)/2}.W^{D}.u^{D-1}.\exp(-u^2/2)/\Phi(-u)$$

where $\Phi(.)$ is the cumulative density function of the Gaussian distribution and W is the smoothness estimator $W = |\Lambda|^{-1/2D}$. Λ is the covariance matrix of the SPM's spatial derivatives. Note that these equations do not refer to the volume of the SPM analyzed because the inference is not corrected for this volume. Equation (1) can be used to assign a *P* value to any given cluster, selected in a way that is independent of its volume, on the basis of the probability of getting a cluster of the observed volume, or larger.

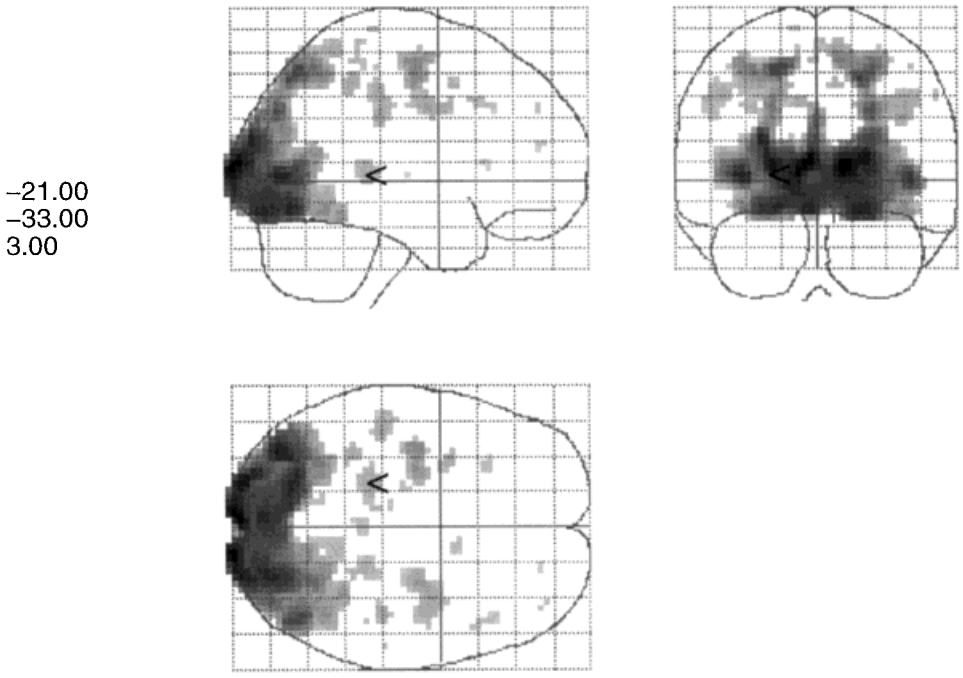
AN ILLUSTRATIVE APPLICATION

In this section we consider a few potential applications and demonstrate the use of this approach with an example. The applications of this sort of inference are restricted to regional effects that can be anatomically specified in advance, either in terms of known functional anatomy, or on the basis of other activations that can be considered homologous in some way, e.g., the motor activations repeatedly observed at different stages of learning [Karni et al., 1995].

For example, consider the fMRI experiment presented in Figure 1. The details of this experiment are irrelevant; suffice to say that this single subject experiment involved periodic photic stimulation with visual motion. If we wished to test the hypothesis that the lateral geniculate nuclei (LGN) responded significantly, one would take the two regions closest to the location of the LGN (i.e., ±24, −26, −1 mm). These two regions (at 18, − 36, 6 and −21, −33, 3 mm, i.e., 13.6 and 8 mm away) have 32 and 39 voxels, respectively, when thresholded at $u = 3.09$ (i.e., $P = 0.001$ uncorrected). The smoothness of the SPM's components was estimated to be 12.9, 12.0, and 10.7 mm (full width at half maximum in x, y, and z). At this smoothness and threshold, the expected volume of a cluster by chance would be 6.5 voxels. According to Equation (1) the probability of obtaining 32 and 39 voxels or more is $P = 0.030$ and 0.019, respectively. We can therefore infer significant and bilateral LGN activation. If we had made a correction for multiple comparison according to Friston et al. [1994], the *P* values, based on volume, would have been insignificant (0.166 and

Figure 1.

Top: SPM{Z}. This is a maximum intensity projection of a SPM{Z} based on a fMRI photic-stimulation study, of a single subject, at 2 Tesla analyzed using SPM96 (http://www.fil.ion.ucl.ac.uk/spm). The display format is standard and provides three views of the brain from the front, below, and left-hand side. Data are presented only for clusters that survive the height threshold (u = 3.09). The grey scale is arbitrary, and the space conforms to that described in the atlas of Talairach and Tournoux [1988]. **Bottom:** Suprathreshold regions (white) superimposed on a structural MRI conforming to the same standard space. The bilateral activations in the LGN can be seen with the optic radiations emanating from them. The cross hairs pass though the maximum of the left LGN at −21, −33, 3 mm.



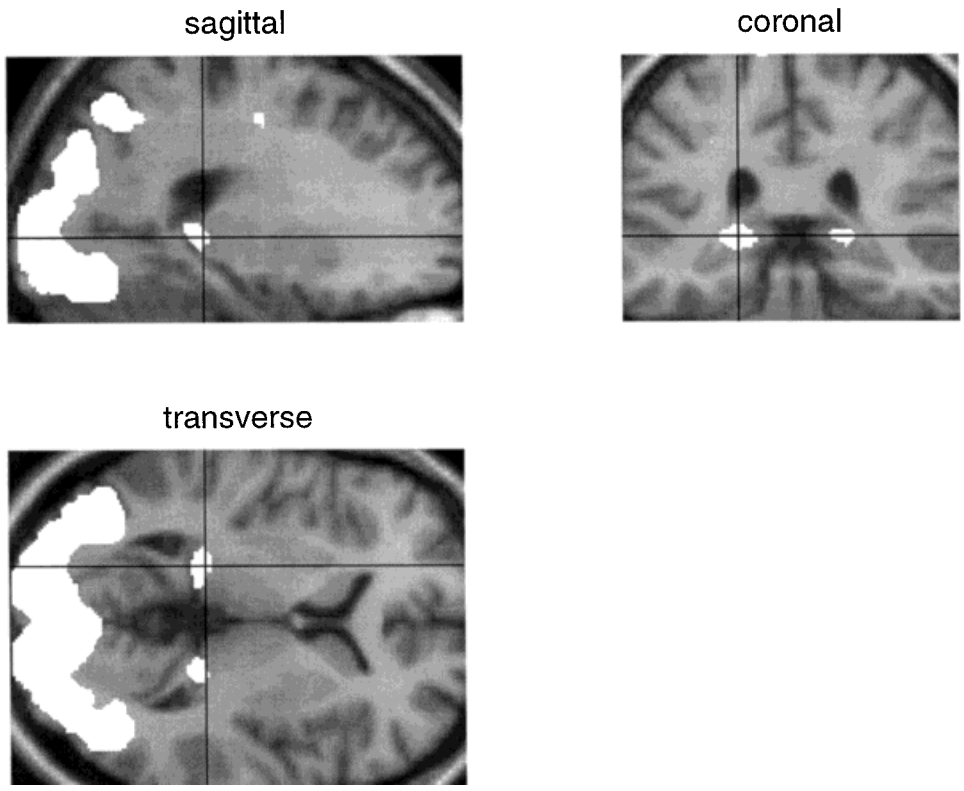


Figure 1.

0.105, respectively). This illustrates the potential power of using an anatomical constraint when specifying the hypothesis to be tested.

CONCLUSIONS

We have presented a short technical description of one approach to making inferences about predicted regional effects using functional neuroimaging and statistical parametric mapping. This approach is based on the volume of the region most proximate to a specified location. Distributional approximations from the theory of Gaussian fields allow one to assess the probability of obtaining the given volume, or larger, under the null hypothesis of no regional effects. The approach is analogous to using the uncorrected *P* value associated with an observed Z score at a prespecified point in the brain. In other words, it is the spatial extent equivalent of an anatomically specified inference based on the height of the SPM. Both these inferences eschew the need for a correction for multiple dependent comparisons associated with anatomically open hypotheses.

The test can be applied to any cluster that is identified in a way that does not bias its spatial extent, e.g., a homologous activation nearest the coordinate of an activation in the contralateral hemisphere. It should be noted that one way to bias the expected volume is to threshold clusters on the basis of spatial extent itself. Therefore, the inference described above should not be used, without modification, in conjunction with a spatial extent threshold.

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