Kernel Smoothing GEE for Longitudinal fMRI Studies

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Longitudinal fMRI studies are beginning to play an important role in understanding the development of the human brain. In this setting random effects models have convergence issues and, typically, generalized estimating equations (GEE) are employed. However, due to the large number of multiple comparisons, GEE methods suffer from a lack of statistical power. To increase power, we propose a kernel smoothing generalized estimating equation (KernGEE) method with a locally adaptive bandwidth to study the temporal trend of fMRI measurements for each brain voxel. In order to address the spatial correlation among voxels and to increase power, we use a kernel function that borrows information across neighboring voxels—spatially smoothing parameter estimates. The kernel bandwidth at each voxel is determined by leave-one-out cross validation. Therefore, our method can provide a set of spatially smoothed estimators for each voxel with increased efficiency. Meanwhile, correction for multiple comparisons is obtained using Efron's empirical null distribution method. We apply our KernGEE method to a longitudinal dataset studying brain mechanisms of risk for alcoholism and other substance abuse. We will also investigate the relationships between activated brain regions and several covariates including IQ, age, gender, behavioral and personality variables.

Keywords: fMRI; longitudinal data; GEE; kernel smoothing.