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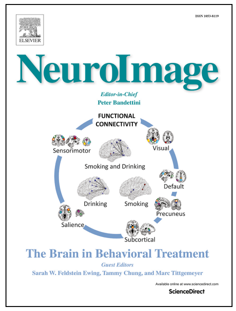

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ACCEPTED MANUSCRIPT

MIDAS: regionally linear multivariate discriminative statistical mapping

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Abstract

Statistical parametric maps formed via voxel-wise mass-univariate tests, such as the general linear model, are commonly used to test hypotheses about regionally specific effects in neuroimaging cross-sectional studies where each subject is represented by a single image. Despite being informative, these techniques remain limited as they ignore multivariate relationships in the data. Most importantly, the commonly employed local Gaussian smoothing, which is important for accounting for registration errors and making the data follow Gaussian distributions, is usually chosen in an ad hoc fashion. Thus, it is often suboptimal for the task of detecting group differences and correlations with non-imaging variables. Information mapping techniques, such as searchlight, which use pattern classifiers to exploit multivariate information and obtain more powerful statistical maps, have become increasingly popular in recent years. However, existing methods may lead to important interpretation errors in practice (*i.e.*, misidentifying a cluster as informative, or failing to detect truly informative voxels), while often being computationally expensive. To address these issues, we introduce a novel efficient multivariate statistical framework for cross-sectional studies, termed MIDAS, seeking highly sensitive and specific voxel-wise brain maps, while leveraging the power of regional discriminant analysis. In MIDAS, locally linear discriminative learning is applied to estimate the pattern that best discriminates between two groups, or predicts a variable of interest. This pattern is equivalent to local filtering by an optimal kernel whose coefficients are the weights of the linear discriminant. By composing information from all neighborhoods that contain a given voxel, MIDAS produces a statistic that collectively reflects the contribution of the voxel to the regional classifiers as well as the discriminative power of the classifiers. Critically, MIDAS efficiently assesses the statistical significance of the derived statistic by analytically approximating its null distribution without the need for computationally expensive permutation tests. The proposed framework was extensively validated using simulated atrophy in structural magnetic resonance imaging (MRI) and further tested using data from a task-based functional MRI study as well as a structural MRI study of cognitive performance. The performance of the proposed framework was evaluated against standard voxel-wise general linear models and other information mapping methods. The experimental results showed that MIDAS achieves relatively higher sensitivity and specificity in detecting group differences. Together, our results demonstrate the potential of the proposed approach to efficiently map effects of interest in both structural and functional data.

Keywords: statistical mapping, permutation testing, brain mapping, multivariate statistics

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