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Invited Review

Multivariate pattern analysis in functional brain imaging

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Abstract: The non-invasive recording of brain activity with functional brain imaging greatly advances our understanding of human cognition. At the meantime, more powerful multivariate analysis methods are being developed to compensate the limited capability of traditional univariate approaches. In this review, I will introduce the development of these multivariate methods for functional magnetic resonance imaging (fMRI), the dominant brain imaging technique used in cognitive neuroscience society. The physiological basis of this analysis approach and its future directions will be discussed as well.

Key words: fMRI; multivariate pattern analysis; brain imaging

功能性脑成像的多维模式分析方法

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摘　要：利用非侵入式的功能性脑成像记录大脑活动极大地提升了我们对人类认知功能的理解。与此同时，分析成像数据的手段也逐渐从传统的一元方式向更加有效的多元分析转变。在本综述中，特别针对在认知神经科学领域占主导地位的功能性磁共振成像技术，介绍其多元数据分析方法的发展以及这种分析方法的生理学基础和未来发展方向。

关键词：功能性磁共振成像；多维模式分析方法；脑成像
中图分类号：R338；Q64

1 Introduction

In recent decades, one of the most significant developments in human neuroscience is the application of functional brain imaging techniques. The majority of such techniques are non-invasive that they measure brain activity indirectly either by estimating the consumption of oxygen in cerebral blood flow, for example functional magnetic resonance imaging (fMRI), or by recording the scalp electric (electroencephalogram, EEG) or magnetic (magnetoencephalogram, MEG) field potentials produced by population neural activity inside the brain. These techniques have added tremendous values to various fields of neuroscience research ranging from sensory processing to social cognition. This is particularly true when human subjects are used in the experiments.

Among these techniques, fMRI emerged to be the most dominant measurement tool for investigating the human brain functions. fMRI measures the neural activity related hemodynamic response in the cerebral blood flow via blood-oxygen-level-dependent (BOLD) contrast[1]. The data collected from fMRI experiments are generally analysed with univariate statistical methods such as general linear model (GLM) in order to infer the cognitive functions underlying the recorded signals[2]. In this way, the recording units, i.e. the voxels (volumetric pixel), share the same experimental design

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but are analysed independently. Statistical hypotheses are tested separately for each voxel, and the resulting statistical parametric maps are corrected for multiple comparisons before further theoretical interpretation.

Despite the great success of GLM in fMRI research, the limitation of this univariate approach has also appeared. A major concern comes from the ignorance of spatial information of fMRI signal in the GLM framework. That is, a collection of spatially clustered voxels or different voxel clusters from spatially separated brain regions may contribute to specific sensory or cognitive functions, and such correlation is not included in the single voxel based GLM analysis. To overcome this limitation, in recent years, fMRI researchers started to introduce multivariate methods for fMRI experiments[3–12]. The following sections will provide a review on this emerging approach together with its physiological basis and the practical consideration that has to be taken into account by the experimenters.

2 Multi-voxel pattern analysis (MVPA)

The multivariate approach for fMRI data analysis has been specifically termed as MVPA and is widely applied within neuroscience society when human subjects are used for the purpose of the research[13–15]. In general, MVPA uses pattern classification algorithms that can extract diagnostic information from multi-dimensional space and separate data samples into different classes[16]. Thus, the idea behind MVPA is the belief that multiple voxels contain more information about the experimental manipulation whereas single voxels show only small response biases which can not be significantly detected with traditional GLM analysis. While a pattern classifier is chosen, the small biases from multiple voxels are pooled together, and the data samples from different experimental conditions are separated in a high-dimensional space by training the classifier with part of the whole data set. Leave one out cross-validation procedure is required when estimate the performance of the pattern classifier (i.e. the separability of the fMRI signal from different conditions). To achieve this, the data are divided into portions with equal size. At each cross-validation, one portion is left as validation set, and all the other portions together with the corresponding class labels are used as the training set to optimize the classifier. After being trained, the classifier is used to predict the class labels of the data samples from the validation set, and the accuracy of the prediction is calculated by comparing with validation set's original labels. The mean accuracy of all cross-validations is compared with chance level (e.g. 50% correct for binary classification), and the subsequent interpretation of the results is concluded in conjunction with anatomical constrains and experimental hypotheses.

While the number of voxels from the whole brain scans can reach few hundreds of thousands, the number of experimental trials is rather limited. Even if region of interest (ROI) is defined, the number of voxels inside a single region can be up to a thousand. The large ratio of the number of voxels to the number of experimental trials poses serious problem for pattern classification algorithms so that the classifier can be easily over-fitted. The generalization capability of the classifier thus can be reduced by introducing uninformative voxels during the training stage. Therefore, voxel selection is commonly used in MVPA-based analysis as a preprocessing step to reduce the dimensionality of the input space. The choice of the voxels can be critical for the final performance of the classifier. In practice, ranking voxels can be achieved by comparing univariate signal between experimental conditions with baseline period and select certain number of most responsive voxels. The other option is to choose the voxels showing largest differential responses between the conditions to be classified. The latter approach is more sensitive, but the voxels can be selected only based on the training data set[17].

MVPA has been applied in experimental research on different cognitive levels. At the early sensory level, Haynes and Rees[5] provided the first evidence that fMRI signal in V1 contains reliable information about the orientation of the stimuli, and these orientations can be decoded with pattern classifier even if the stimuli were invisible due to the masking effect. Kamitani and Tong[12], on the other hand, showed that in addition to the orientation information, BOLD signal in early visual cortex can also tell us about participants' subjective perception. For higher perceptual functions, several studies investigated the neural representation of object categories (such as faces, houses, chairs) in the human brain with MVPA methods[3, 4, 9, 18, 19]. These studies have demonstrated that spatially distributed patterns in human higher visual cortex encode the category information[14]. In another study, Li *et al*.[8] developed a novel paradigm that dissociated two dimensions of features with a factorial classification analysis, and their results have demonstrated a network of cortical and subcortical regions that is involved in representing behaviorally relevant features to support the rule-based visual categorization. Furthermore, Chen *et al*.[20] developed a behavior-constrained classification algorithm for fMRI data analysis based on support vector machine (SVM) that can be adapted in the experiments involving behaviorally relevant perceptual tasks. In addition to the perceptual experiments, MVPA has also been used to decode the intention[6], fear[21], language[22], reward-based decision making[23], and other high level cognitive functions, making this technique a potential tool for investigating general human cognition.

3 The physiological basis of MVPA

The great capability of multi-voxel pattern classifier on detecting subtle response differences between neuronal populations was referred as 'hyperacuity'. It is generally believed that, at least in the level of primary visual cortex, the columnar architecture is the source of the high performance that the classifier has obtained with standard resolution of BOLD signal. Under such resolution (e.g. 3 mm × 3 mm × 3 mm), each voxel samples multiple orientation columns that differ in their preferred orientations. This will cause a voxel to be responsive to many orientations but the strength of the responses varies across orientations due to uneven sampling. Such aliasing effect is what the classifier pools to exploit the high spatial frequency information in the subvoxel resolution[24].

Recently, the hypothesis of 'hyperacuity' was challenged by other researchers who proposed that spatial smoothing does not hurt the performance of MVPA. According to the 'hyperacuity' hypothesis, the spatial smoothing will contaminate the fine scale information contained in the voxels population that is incorporated by the pattern classifier. Op de Beeck[25, 26] investigated the effect of spatial smoothing on MVPA and found that smoothing does not decrease the sensitivity of MVPA. He suggested the possibility that the biases in voxels' responses exist at multiple scales. While this proposal is still under debate[27], further investigation on the spatiotemporal properties of BOLD signal is required to address this controversy[28].

4 Practical consideration

There are several practical issues to be considered when analysing fMRI data with MVPA methods. First, if there is strong univariate signal, that is, a significant activation from GLM analysis, the multivariate methods become less necessary. Thus, testing the contrast with conventional GLM before conducting the MVPA is a good practice for all experiments.

Second, while most of the MVPA studies applied linear classifier to simplify the interpretation of the result, nonlinear classifiers also attracted increased attention[3, 11, 29, 30]. In machine learning, nonlinear classifiers are generally believed to provide better performance when compared with its linear counterpart. But this trend seems to be reverse when testing the fMRI signal with MVPA methods, although there are cases that nonlinear classifier can give higher accuracies[29]. Overfitting of the noisy BOLD signal might be the major driving factor for this unexpected phenomenon, but more evidence needs to be cumulated before making a conclusive claim.

Third, MVPA can be enhanced by introducing prior physiological knowledge. This is particularly true when the studied questions relate to the better understood sensory and perceptual processing. Kay *et al*.[31] developed an encoding method with quantitative receptive field models that characterize the tuning properties of voxels in early visual areas. The models were based on Gabor wavelet pyramid which is the standard model of primary visual cortex in neurophysiology research. By taking this prior knowledge into account, this biological inspired method gives decoders superior power on a natural image identification task. In another study, a combination of local image bases of multiple scales was used to reconstruct simple image patterns from fMRI activity of early visual area[32]. Further investigation along this line of research may lead us to better decoding capability of mental states from functional brain imaging signal.

5 Conclusion

The future of the MVPA methods points two directions for the cognitive neuroscience investigators. First, we need deeper understanding of the biological basis underlying the high performance of MVPA. This, in a broader sense, comes from the complete knowledge of the nature of the fMRI signal. Second, more advanced computational algorithms are to be developed to help the investigators to extract more useful information from fMRI signal in various kinds of experiments. These algorithms have to be specific for the design of fMRI experiments and the nature of the BOLD signal.

REFERENCES

1 Logothetis NK, Wandell BA. Interpreting the BOLD signal. Annu Rev Physiol 2004; 66: 735–769.

2 Friston KJ, Holmes AP, Worsley KJ, Poline J, Frith CD, Frackowiak RS. Statistical parametric maps in functional imaging: a general linear approach. Hum Brain Mapp 1995; 2: 189–210.

3 Cox DD, Savoy RL. Functional magnetic resonance imaging (fMRI) “brain reading”: detecting and classifying distributed patterns of fMRI activity in human visual cortex. Neuroimage 2003; 19(2 Pt 1): 261–270.

4 Haxby JV, Gobbini MI, Furey ML, Ishai A, Schouten JL, Pietrini P. Distributed and overlapping representations of faces and objects in ventral temporal cortex. Science 2001; 293(5539): 2425–2430.

5 Haynes JD, Rees G. Predicting the orientation of invisible stimuli from activity in human primary visual cortex. Nat Neurosci 2005; 8(5): 686–691.

6 Haynes JD, Sakai K, Rees G, Gilbert S, Frith C, Passingham RE. Reading hidden intentions in the human brain. Curr Biol 2007; 17(4): 323–328.

7 Kriegeskorte N, Goebel R, Bandettini P. Information-based functional brain mapping. Proc Natl Acad Sci U S A 2006; 103(10): 3863–3868.

8 Li S, Ostwald D, Giese M, Kourtzi Z. Flexible coding for categorical decisions in the human brain. J Neurosci 2007; 27(45): 12321–12330.

9 Carlson TA, Schrater P, He S. Patterns of activity in the categorical representations of objects. J Cogn Neurosci 2003; 15(5): 704–717.

10 Hanson SJ, Matsuka T, Haxby JV. Combinatorial codes in ventral temporal lobe for object recognition: Haxby (2001) revisited: is there a “face” area? Neuroimage 2004; 23(1): 156–166.

11 LaConte S, Strother S, Cherkassky V, Anderson J, Hu X. Support vector machines for temporal classification of block design fMRI data. Neuroimage 2005; 26(2): 317–329.

12 Kamitani Y, Tong F. Decoding the visual and subjective contents of the human brain. Nat Neurosci 2005; 8(5): 679–685.

13 Haynes JD, Rees G. Decoding mental states from brain activity in humans. Nat Rev Neurosci 2006; 7(7): 523–534.

14 Norman KA, Polyn SM, Detre GJ, Haxby JV. Beyond mind-reading: multi-voxel pattern analysis of fMRI data. Trends Cogn Sci 2006; 10(9): 424–430.

15 O’Toole AJ, Jiang F, Abdi H, Penard N, Dunlop JP, Parent MA. Theoretical, statistical, and practical perspectives on pattern-based classification approaches to the analysis of functional neuroimaging data. J Cogn Neurosci 2007; 19(11): 1735–1752.

16 Duda RO, Hart PE, Stork DG. Pattern Classification. New York: John Wiley & Sons, 2000.

17 Kriegeskorte N, Simmons WK, Bellgowan PS, Baker CI. Circular analysis in systems neuroscience: the dangers of double dipping. Nat Neurosci 2009; 12(5): 535–540.

18 Polyn SM, Natu VS, Cohen JD, Norman KA. Category-specific cortical activity precedes retrieval during memory search. Science 2005; 310(5756): 1963–1966.

19 Spiridon M, Kanwisher N. How distributed is visual category information in human occipito-temporal cortex? An fMRI study. Neuron 2002; 35(6): 1157–1165.

20 Chen D, Li S, Kourtzi Z, Wu S. Behavior-constrained support vector machines for fMRI data analysis. IEEE Trans Neural Netw 2010; 21(10): 1680–1685.

21 Pessoa L, Padmala S. Decoding near-threshold perception of fear from distributed single-trial brain activation. Cereb Cortex 2007; 17(3): 691–701.

22 Mitchell TM, Shinkareva SV, Carlson A, Chang KM, Malave VL, Mason RA, Just MA. Predicting human brain activity associated with the meanings of nouns. Science 2008; 320(5880): 1191–1195.

23 Hampton AN, O’Doherty J P. Decoding the neural substrates of reward-related decision making with functional MRI. Proc Natl Acad Sci U S A 2007; 104(4): 1377–1382.

24 Boynton GM. Imaging orientation selectivity: decoding conscious perception in V1. Nat Neurosci 2005; 8(5): 541–542.

25 Op de Beeck HP. Against hyperacuity in brain reading: spatial smoothing does not hurt multivariate fMRI analyses? Neuroimage 2010; 49(3): 1943–1948.

26 Op de Beeck HP. Probing the mysterious underpinnings of multi-voxel fMRI analyses. Neuroimage 2010; 50(2): 567–571.

27 Kamitani Y, Sawahata Y. Spatial smoothing hurts localization but not information: pitfalls for brain mappers. Neuroimage 2010; 49(3): 1949–1952.

28 Kriegeskorte N, Cusack R, Bandettini P. How does an fMRI voxel sample the neuronal activity pattern: compact-kernel or complex spatiotemporal filter? Neuroimage 2010; 49(3): 1965–1976.

29 Hanson SJ, Schmidt A. High-resolution imaging of the fusiform face area (FFA) using multivariate non-linear classifiers shows diagnosticity for non-face categories. Neuroimage 2010; 54(2): 1715–1734.

30 Misaki M, Kim Y, Bandettini PA, Kriegeskorte N. Comparison of multivariate classifiers and response normalizations for pattern-information fMRI. Neuroimage 2010; 53(1): 103–118.

31 Kay KN, Naselaris T, Prenger RJ, Gallant JL. Identifying natural images from human brain activity. Nature 2008;

452(7185): 352–355.
32 Miyawaki Y, Uchida H, Yamashita O, Sato MA, Morito Y, Tanabe HC, Sadato N, Kamitani Y. Visual image reconstruction from human brain activity using a combination of multiscale local image decoders. Neuron 2008; 60(5): 915–929.

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