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Depression recognition using functional connectivity based on dynamic causal model

Luo Guoping[1] Liu Gang[1] Zhao Jing[1] Yao Zhijian[2] Lu Qing[1]

([1] Research Center for Learning Science, Southeast University, Nanjing 210096, China)

([2] Nanjing Brain Hospital Affiliated to Nanjing Medical University, Nanjing 210029, China)

Abstract: Dynamic casual modeling of functional magnetic resonance imaging(fMRI) signals is employed to explore critical emotional neurocircuitry under sad stimuli. The intrinsic model of emotional loops is built on the basis of Papez's circuit and related prior knowledge, and then three modulatory connection models are established. In these models, stimuli are placed at different points, which represents they affect the neural activities between brain regions, and these activities are modulated in different ways. Then, the optimal model is selected by Bayesian model comparison. From group analysis, patients' intrinsic and modulatory connections from the anterior cingulate cortex (ACC) to the right inferior frontal gyrus (rIFG) are significantly higher than those of the control group. Then the functional connection parameters of the model are selected as classifier features. The classification accuracy rate from the support vector machine(SVM) classifier is 80.73%, which, to some extent, validates the effectiveness of the regional connectivity parameters for depression recognition and provides a new approach for the clinical diagnosis of depression.

Key words: depression recognition; fMRI; dynamic causal model; Bayesian model selection

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Depression constitutes a major mental health burden recently[1]. The diagnosis of depression is based on clinical symptoms and their rankings according to subjective diagnostic criteria. fMRI signals provide a possibility to recognize depression objectively. Nowadays, research interest has switched from mapping activation sites towards identifying the interconnectivities. Interesting patterns of abnormal interregional synchronization have now been described in various brain disorders and mapped for mental disorder diagnosis purposes.

Based on the observation data, the dynamic causal model (DCM) can infer the characteristics of functional connectivity between brain regions. Using the Bayesian model selection(BMS)[2-3], we can compare different models and select the optimal one, which may confirm our assumption. Functional connectivity between brain areas represents the synchronization level of the brain areas when responding to external stimuli, which can reflect the brain function status. Hence, the parameters from DCM analysis can be introduced for depression recognition purposes.

In this study, we select critical emotional related regions and build three information loops for DCM analysis. After the Bayesian model selection, the calculated functional connection parameters between brain regions are used as discriminative features for depression recognition. Then, the discriminative map is induced and analyzed.

1 Materials and Methods

1.1 Materials

Twelve patients are recruited from in-patient facilities. Eligibility screening procedures include a structured clinical interview for the DSM-IV (SCID), 24-item HDRS and common clinical laboratory tests. Patients with other psychiatric illnesses and a history of electroconvulsive therapy are excluded. Twelve healthy comparison subjects, matched by gender, age, education level and no history of any psychiatric disorder, are recruited. The study is approved by the Research Ethics Review Board. Imaging data are acquired using a GE Signa 1.5 T MRI scanner. Sad and neutral emotional faces are performed by young students from the Academy of Art of Southeast University. When scanned, the subjects are asked to identify whether the stimuli is sad or not.

1.2 Dynamic causal model

The dynamic causal model takes the brain as a stimulus-controlled input-output system, on which stimuli work either by acting directly on certain brain regions or regulating strength of function connections among these regions. The DCM is composed of a bilinear model[4] for the neurodynamics and a Balloon model[5-6] for the hemodynamics. The neurodynamics can be described by a multivariate differential equation as follows:

$$\dot{\boldsymbol{x}} = \left(\boldsymbol{A} + \sum_{j=1}^{m} u_j \boldsymbol{B}^j\right)\boldsymbol{x} + \boldsymbol{C}\boldsymbol{u} \tag{1}$$

where $\boldsymbol{x}$ is the vector of neuron states and the dot notation denotes a time derivative. Matrix $\boldsymbol{A}$ represents the strength of intrinsic connections between regions, matrices $\boldsymbol{B}^j$ represent the modulatory connections induced by the input $\boldsymbol{u}_j$, and matrix $\boldsymbol{C}$ specifies which inputs are connected to which regions.

Given the parameters $\boldsymbol{\theta}$ and input $\boldsymbol{u}$, the measured BOLD response $\boldsymbol{y}$ is modeled as

$$\boldsymbol{y} = h(\boldsymbol{u}, \boldsymbol{\theta}) + \boldsymbol{X\beta} + \boldsymbol{e} \tag{2}$$

where $h(\boldsymbol{u}, \boldsymbol{\theta})$ is the predicted BOLD signal; $\boldsymbol{X}$ contains the effects of no interest such as signal drift; $\boldsymbol{\beta}$ is the param-

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Biographies: Luo Guoping (1987—), male, graduate; Yao Zhijian (corresponding author), male, doctor, associate professor, yaozhijian@yahoo.cn.

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eter vector; and $\boldsymbol{e}$ represents the Gaussian prediction errors with mean zero and covariance $\boldsymbol{C}_e$.

The parameters of the DCM are estimated by a Bayesian approach, the prior and likelihood distributions for a given model m are as follows:

$$\left.\begin{aligned} p(\boldsymbol{\theta} \mid m) &= N(\boldsymbol{\theta}_p, \boldsymbol{C}_p) \\ p(\boldsymbol{y} \mid \boldsymbol{\theta}, m) &= N(h(\boldsymbol{\theta}, \boldsymbol{u}) + \boldsymbol{X\beta}, \boldsymbol{C}_e) \end{aligned}\right\} \tag{3}$$

According to the Bayes rule, the posterior distribution is

$$p(\boldsymbol{\theta} \mid \boldsymbol{y}, m) = \frac{p(\boldsymbol{y} \mid \boldsymbol{\theta}, m) p(\boldsymbol{\theta} \mid m)}{p(\boldsymbol{y} \mid m)}$$

Taking the logarithm of both sides of the equation above,

$$\log p(\boldsymbol{\theta} \mid \boldsymbol{y}, m) = \log p(\boldsymbol{y} \mid \boldsymbol{\theta}, m) + \log p(\boldsymbol{\theta} \mid m) - \log p(\boldsymbol{y} \mid m) \tag{4}$$

The posterior distribution is estimated via the expectation-maximization (EM) algorithm, where the posterior mean $\hat{\boldsymbol{\theta}}$ and the posterior covariance $\hat{\boldsymbol{\Sigma}}$ are updated in E-step, and the hyperparameters of noise covariance $\boldsymbol{C}_e$ are updated in M-step. These steps are iterated until the posterior probability converges, and we obtain the posterior distribution,

$$p(\boldsymbol{\theta} \mid \boldsymbol{y}, m) = N(\boldsymbol{\theta}_{MP}, \boldsymbol{\Sigma}_{MP}) \tag{5}$$

Different models are compared by the model evidence,

$$p(\boldsymbol{y} \mid m) = \int p(\boldsymbol{y} \mid \boldsymbol{\theta}, m) p(\boldsymbol{\theta} \mid m) \mathrm{d}\boldsymbol{\theta} \tag{6}$$

Because this integral is analytically unsolvable, we use the Laplace approximation and obtain the log-evidence of the model.

$$\begin{aligned} \log p(\boldsymbol{y} \mid m) &= \text{accuracy}(m) - \text{complexity}(m) = \\ & -\frac{1}{2}\log|\boldsymbol{C}_e| - \frac{1}{2}(\boldsymbol{y} - h(\boldsymbol{u}, \boldsymbol{\theta}_{MP}))^{\mathrm{T}} \boldsymbol{C}_e^{-1} (\boldsymbol{y} - h(\boldsymbol{u}, \boldsymbol{\theta}_{MP})) - \\ & \frac{1}{2}\log|\boldsymbol{C}_p| - \frac{1}{2}\log|\boldsymbol{\Sigma}_{MP}| + \frac{1}{2}(\boldsymbol{\theta}_{MP} - \boldsymbol{\theta}_p)^{\mathrm{T}} \boldsymbol{C}_p^{-1} (\boldsymbol{\theta}_{MP} - \boldsymbol{\theta}_p) \end{aligned} \tag{7}$$

Based on the model evidence, the optimal model can be selected by the Bayes factors.

2 Connection Models

The visual stimuli from visual sensory area are received by the anterior cingulate cortex[7-8], which integrates emotional and cognitive signals. When the integrated signals conflict with the original emotions and cognitions, the ACC asks for adjustment by sending signals to other regions, such as the prefrontal lobe, which in turn sends signals to adjudicate response conflicts and refresh active representations. Based on the prior knowledge above, we extract fMRI signals from these areas for the connection model study and build the intrinsic connection model as shown in Fig. 1, where V1 is the primary visual cortex, the ACC is the anterior cingulate cortex, rIFG is the right inferior frontal gyrus and Hipp is the hippocampus. In order to test how the executive task modulates connectivity within the proposed network, stimuli are placed in different positions of the intrinsic model, which constructs the three modulatory models in Fig. 1.

In each region, the ROI is defined by the sphere centered at the strongest activated voxel, and with a radius of 3 mm. The convolved BOLD response under sad stimuli inside each ROI is analyzed via the PCA. And the first principle component is selected as the signal of the dynamic causal model to calculate connection parameters between brain regions. Finally, these parameters are taken as characteristics for classification and identification.

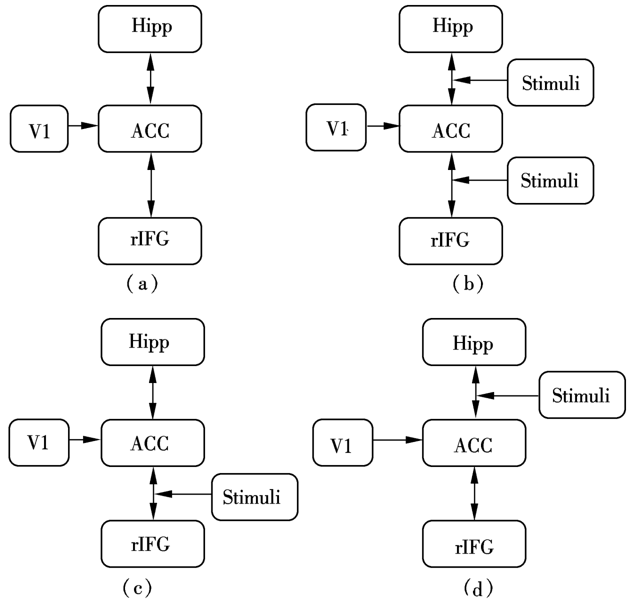

Fig. 1 Connection models with different task-related modulatory inputs. (a) Intrinsic model; (b) Modulatory model 1; (c) Modulatory model 2; (d) Modulatory model 3

3 Results

3.1 Model selection

After comparisons between the connection models using the Bayesian model selection, we find that model 2 is the most suitable for the observed data. The Bayes factors for the three models are summarized in Tab. 1. The average Bayes factor for the comparison between model 2 and model 1 is greater than 7.83, and that between model 2 and model 3 is greater than 2.71. It is evident that the stimuli input mainly modulates the bidirectional connection from the ACC to the right inferior frontal gyrus.

Tab. 1 The Bayes factors for the three models

Model	1	2	3
1	1		
2	7.83	1	2.71
3	2.89		1

3.2 Results of classification

Based on the results from Bayesian model comparison, the intrinsic connectivities from the visual sensory cortex (BA17, 18) to the ACC, from the ACC to the right inferior frontal gyrus, from the ACC to the hippocampus, and the modulatory connectivities from the ACC to the hippocampus, from the ACC to the right frontal gyrus are selected as classifier characteristics. Using the leave-one-out cross-validation approach, the accuracy of the support vector machine classifier is 80.73%. The SVM weights of connection parameters are displayed in Fig. 2.

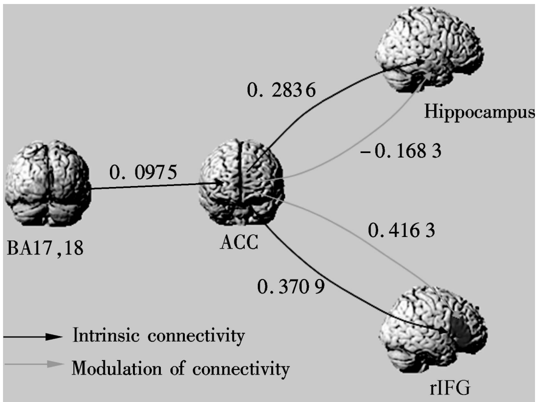

Fig. 2 SVM weights of connection parameters between brain regions for depression recognition

4 Conclusion

In this paper, we build three different DCMs according to different modulatory influences of sad facial expression stimuli. The intrinsic connections of the models are specified with prior knowledge, Papez circuit[9] and the conflict monitoring model[7,10]. By the BMS, the best model is selected, which indicates that the sad facial expression stimuli mainly modulate the connection from the ACC to the right inferior gyrus. From the group analysis, we find that the patients' intrinsic and modulatory connections from the ACC to the rIFG are significantly higher than those of the control group. The ACC, as an important area of integrating emotional and cognitive signals, is hypothesized to monitor the response conflicts. The frontal cortex is thought to guide response selection under conditions of response conflicts. One explanation for the connectivity abnormality in depression patients can be that the frontal cortex fails to restrain the interference brought on by the negative stimulus, which gives rise to a reduced regulation of the ACC and a bias of negative cognitive processing.

For classification purposes, the intrinsic connectivity and the modulation of connectivity are selected as the features, which obtain an accuracy rate of 80.73% with the SVM. From the feature weights shown in Fig. 2, the intrinsic connectivity and the modulatory connectivity from the ACC to the rIFG contribute mostly to classification. It demonstrates that these connectivity parameters are discriminative enough for clinical diagnosis.

References

[1] Ebmeier K P, Donaghey C, Steele J D. Recent developments and current controversies in depression [J]. *Lancet*, 2006, **367**(9505): 153-167.

[2] Penny W D, Stephan K E, Mechelli A, et al. Comparing dynamic causal models [J]. *Neuroimage*, 2004, **22**(3): 1157-1172.

[3] Stephan K E, Weiskopf N, Drysdale P M, et al. Comparing hemodynamic models with DCM [J]. *Neuroimage*, 2007, **38**(3): 387-401.

[4] Friston K J, Harrison L, Penny W. Dynamic causal modelling [J]. *Neuroimage*, 2003, **19**(4): 1273-1302.

[5] Buxton R B, Wong E C, Frank L R. Dynamics of blood flow and oxygenation changes during brain activation: the balloon model [J]. *Magnetic Resonance in Medicine*, 1998, **39**(6): 855-864.

[6] Friston K J, Mechelli A, Turner R, et al. Nonlinear Responses in fMRI: the Balloon model, volterra kernels, and other hemodynamics [J]. *Neuroimage*, 2000, **12**(4): 466-477.

[7] Badre D, Wagner A D. Selection, integration, and conflict monitoring: assessing the nature and generality of prefrontal cognitive control mechanisms [J]. *Neuron*, 2004, **41**(3): 473-487.

[8] Mega M, Cummings J, Salloway S, et al. The limbic system: an anatomic, phylogenetic, and clinical perspective [J]. *J Neuropsychiatry Clin Neurosci*, 1997, **9**(3): 315-330.

[9] Papez J W. A proposed mechanism of emotion [J]. *Arch Neurol Psychiatry*, 1937, **38**(4): 725-743.

[10] Schlösser R G M, Wagner G, Koch K, et al. Fronto-cingulate effective connectivity in major depression: a study with fMRI and dynamic causal modeling [J]. *Neuroimage*, 2008, **43**(3): 645-655.

基于动态因果模型中功能连接的抑郁症识别

罗国平[1]　刘　刚[1]　赵　竞[1]　姚志剑[2]　卢　青[1]

([1] 东南大学学习科学研究中心，南京 210096)
([2] 南京医科大学附属脑科医院，南京 210029)

摘要：为了探索悲伤刺激下的关键情感神经回路，利用功能核磁共振信号进行了动态因果建模. 在 Papez 环路和相关先验知识的基础上建立情感环路的固有连接模型，并相应建立了 3 个调节连接模型. 在这些模型中，实验刺激作用于不同的连接点，它们对脑区间的神经活动影响及对神经活动的调节方式都各自不同. 然后通过贝叶斯模型比较，选出了最优模型. 从群组分析中发现抑郁症患者前扣带回至右额下回的固有连接和调节连接均显著强于健康被试. 随后将这些功能连接参数作为特征用于抑郁症分类，其中 SVM 分类器的准确率为 80.73%. 这也在一定程度上验证了功能连接用于抑郁症识别的有效性，并为抑郁症临床诊断提供了新的思路.

关键词：抑郁症识别；功能核磁共振；动态因果模型；贝叶斯模型选择

中图分类号：Q64；TP310.4