

# Evaluating Effective Connectivity in Auditory-Motor fMRI Using Dynamic Granger Causality Analysis

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**Target audience** - Physicist, Neuroscientist

## Abstract

Conditional Granger causality analysis (CGCA) has been employed to identify effective connectivity (EC) in the human brain [1]. However, the application of CGCA method using complete fMRI time series to calculate a single Granger causality (GC) pattern has faced many challenges. For example, the entire fMRI series are not necessarily covariance stationary (CS), which is one of the CGCA assumptions to be satisfied. In addition, previous studies have shown that brain activities are dynamic and could vary during fMRI sessions [2]. Here, we propose a windowing-based Granger causality analysis for analyzing effective connectivity in fMRI data called dynamic Granger causality analysis (DGCA). In DGCA, non-CS problem is avoided by analyzing a section of fMRI time series at a time. More important, the dynamic changes in causal relationships among brain regions can be revealed by DGCA. In this study, an auditory-motor fMRI experiment was used to test the proposed framework. Clustering was used in group analysis to find the principal EC patterns while performing auditory-motor task. Results show that DGCA provides more EC information that could potentially provide more knowledge of dynamic changes in the brain.

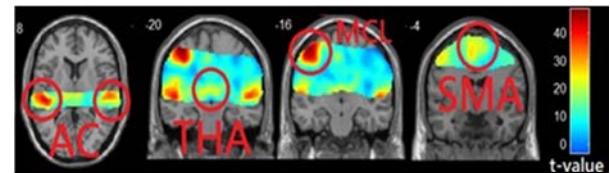
## Methods

Sixteen healthy subjects participated in this study. An auditory-motor task was used in fMRI scan (2D GRE EPI, TR/TE = 1000/30 ms, slice = 5 mm, 8 slices, 300 time points) with images acquired using a 3T scanner (Skyra, Siemens, Erlangen, Germany). During fMRI experiment, subjects were instructed to squeeze a ball with right hand when hearing the cue sound. The experiment was performed with alternating two blocks of tasks, a 5 sec of cue sound followed by the other 10 sec of rest. Due to the limited spatial coverage of the fMRI scan for the designed experiment, another pilot scan was performed with the same auditory-motor task to locate auditory and motor cortex of each subject. In fMRI data preprocessing, slice timing correction with four times of temporal upsampling was performed to increase detectability of effective connectivity [3]. General linear model (GLM) was then used to analyze fMRI data to look for task-related regions in SPM8. Four region of interest (ROIs) identified by GLM are auditory cortex (AC), left motor cortex (MCL), thalamus (THA) and supplementary motor area (SMA). The average time series from each of the four ROIs were calculated, giving four signals with 1156 time points after preprocessing, as input for DGCA. In DGCA, the window size was set to be 60 time points and sliding distance was 1 time point, resulting in a total of 1097 windows. Data from each window was analyzed by CGCA to compute Granger causality patterns. The entire 17552 (1097x16) GC patterns from all subjects were then transformed to vector form by the corresponding GC values among the ROIs. These GC vectors were subsequently classified by K-means clustering method. The cluster number was initially set to 25 and was gradually reduced whenever an empty cluster is found after applying statistical test ( $P < 0.05$ ).

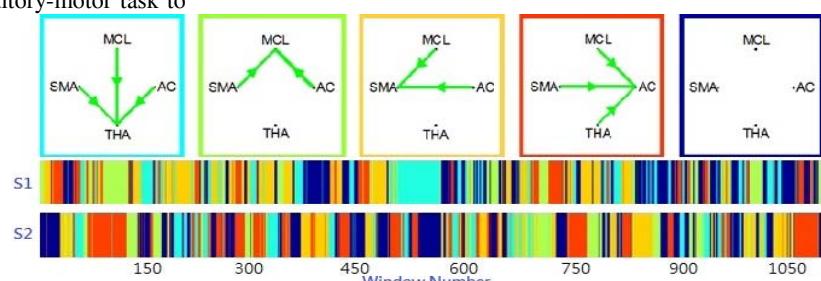
## Results and Discussion

Figure 1 shows four task-related ROIs identified by GLM including AC, MCL, THA and SMA from GLM, which are confirmed by previous auditory-motor fMRI studies [4,5]. In DGCA, K-means clustering converges to five GC patterns as shown at the top of Fig. 2. Each centroid is a principal GC pattern found from the auditory-motor fMRI experiment. The five colors (cyan, green, orange, red, and blue) represent each of five GC patterns respectively. DGCA results from two subjects (S1 and S2) are shown at the bottom of Fig. 2 demonstrating the dynamic switching among five GC patterns during the experiment. In addition, the five centroids are found evenly distributed in all subjects (data not shown), implying that the five GC patterns could be common brain states while processing auditory-motor task. The total number of brain states found in this study is similar to the circuits found in a resting-state fMRI study [6]. Note that among five centroids, green and orange patterns reveal the interactions among AC, MCL and SMA, which are directly related to the auditory-motor task. In addition, the blue pattern, which contains no link, represents windows with links that do not pass statistical test. The total occupancy rates of five centroids in all subjects are listed in Table 1. All centroids occupied almost equal number of windows within 16 subjects except for the empty GC pattern. To sum up, the proposed DGCA framework resolves dynamic changes in EC and has potential to find common brain states in subjects performing the same tasks. DGCA may also be employed to investigate how brain regions coordinate for specific tasks. However, further investigation is needed to gain insight of the temporal switching between brain states and different sequence of switching among subjects.

**References** [1] Friston, K. J. *Brain Connect*, 2011;1(1), 13-36. [2] Buckner, R. L. et al., *Nat Neurosci*, 2013;16(7), 832-837. [3] McFarlin, D.R. et al., *Brain Connect*, 2013;3(1): p. 61-71. [4] Abler, B. et al., *Magn Reson Imaging*, 2006;24(2): p. 181-185. [5] Zatorre R.J., *Nat Rev Neurosci*, 2007; 8(7): p. 547-558. [6] Jia, H. et al., *Proc Intl Soc Mag Reson Med*, 2013;p.21.



**Fig. 1** Four task-related ROIs identified by GLM: Auditory Cortex (AC), left Motor Cortex (MCL), Thalamus (THA) and Supplementary Motor Area (SMA) as marked with red circles.



**Fig. 2** Top: K-means clustering converges to five principal GC patterns that reflect common brain states among subjects in auditory-motor fMRI. Bottom: Dynamic switching among five GC patterns in two subjects during fMRI experiment. GC patterns are color coded as seen in color boxes at the top.

Centroid Color	Cyan	Green	Orange	Red	Blue
Occupancy Rate (%)	15.9	16.3	17.3	14.7	35.8

**Table 1** The occupancy rate of five GC patterns in 16 subjects. Each GC pattern appears at about the same frequency except for the empty pattern (blue).