

Effects of Temporal Resolution on Granger Causality Analysis in Auditory-Motor fMRI

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Target audience - Physicist, neuroscientist

Introduction

Functional MRI (fMRI) utilizing blood oxygenation level dependent (BOLD) contrast has been widely used to study neuronal activities in human brain [1]. However, the lower sampling rate of fMRI is one of its limitations compared with electroencephalography (EEG) [2]. In fMRI studies, repetition time (TR) of 2-3 seconds is typically used to detect neuronal activities. Nonetheless, for fMRI studies targeting effective connectivity (EC) [3], such long TR might be unfavorable for detecting causal relationship among brain regions. In this study, effect of TR on detectability of EC using conditional Granger causality analysis (CGCA) is investigated [4]. Results from auditory-motor fMRI experiments show that short TR (< 1 second) is preferred for analyzing effective connectivity among brain regions, which gives an important hint that current fMRI protocols might need to be adjusted to better study causal relationships in human brain.

Methods and Material

Fifteen healthy subjects (4 females, 11 males) participated in this study. All subjects underwent an auditory-motor fMRI session (TR/TE = 500/30ms, matrix 64x64, FOV 196mm, slice 5mm, 8 slices, 600 measurements) on a 3T MRI scanner (Skyra, Siemens, Erlangen, Germany). The auditory-motor paradigm used in this study is shown in Figure 1. Auditory stimulus was given for five seconds and then interleaved with ten seconds of rest. Subjects were instructed to press a sponge ball with their right hand whenever hearing auditory stimulus. Due to the limited spatial coverage of fMRI experiment, a pilot scan was performed first using same auditory-motor paradigm to precisely locate auditory and motor areas of each subject. FMRI data preprocessing was done in SPM8 [5]. General linear model (GLM) was then used to analyze data from all subjects with fixed-effect model. Subsequently, task-related ROIs were selected from common activation regions in all subjects. Four ROIs were found in auditory-motor fMRI including auditory cortex (AC), motor cortex (MC), supplementary cortex (SMA) and thalamus (THA) [6]. To simulate experimental conditions with different TRs, averaged temporal signal from each ROI was down-sampled for by factors of two and four, resulting in effective TR of one and two seconds, separately. Datasets of all subjects with TR of 0.5, 1, and 2 seconds were analyzed with CGCA to compare effective connectivity links among four ROIs.

Results

Figure 2 shows CGCA results from a subject with TR of 0.5, 1, and 2 seconds in (A), (B), and (C), separately. The GC values of statistical significant links among four ROIs (1: AC, 2: MC, 3: SMA, 4: THA) are represented as gray levels in matrix form ($P < 0.01$, with Bonferroni correction). Outflowing links from AC are observed in Figure 2, confirming the auditory-motor task. Note that the link MC → SMA (red box) disappears when TR increases from 0.5 to 1 second. In addition, the link AC → THA (yellow box) is detected when TR is 0.5 and 1 second but not in TR of 2 seconds. Table 1 calculates the detectability of three outflowing links from AC (AC → MC, AC → SMA, and AC → THA) in 15 subjects. It can be seen that when TR is 0.5 second, the detectability of these three links is very high (14 out of 15 subjects). However, the detectability drops substantially when TR increases to two seconds. Chi-squared test comparing TR of 0.5 and 2 seconds shows significant difference in all three links ($p < 0.05$). On the other hand, when comparing TR of 0.5 and 1 second, significant difference is found only in the link AC → SMA.

Discussion and conclusion

Effective connectivity is an important tool for studying information flow in human brain when processing tasks. The underlying assumption for EC analysis is that temporal delay of neuronal activation among brain regions is reflected in BOLD signal. Although using TR of 2-3 seconds gives satisfactory results in most fMRI experiments, such temporal resolution is not sufficient for resolving causal relationship and thus might lead to erroneous interpretation of brain networks. Results from this study demonstrate that for auditory-motor task, TR of 0.5 second (or at least < 1 second) is more appropriate for effectively detecting causal links between auditory and motor areas. Otherwise, CGCA would detect only part of causal links in the brain and complete evaluation of task-related information flow is not possible. In addition, to increase temporal resolution, a limited spatial coverage is used in this study for experimental simplicity. However, to achieve short TR, it is recommended to use accelerated imaging techniques such as parallel imaging and multi-slice excitation [7]. If TR of below 0.1 second is needed, inverse imaging (INI) can be used to further resolve small delay among fMRI signals [8].

References

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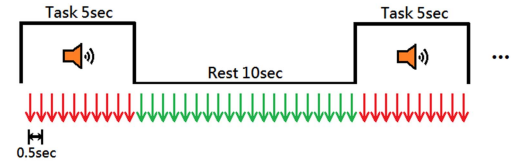


Figure 1 Auditory-motor fMRI paradigm. Subjects are given five seconds of auditory stimulus, interleaved with ten seconds of rest, as cues for motor task.

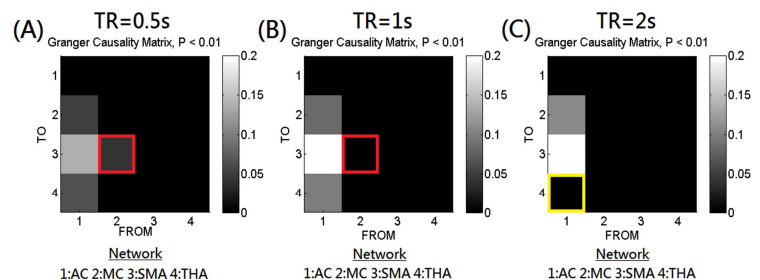


Figure 2 shows CGCA results from a subject with TR of 0.5, 1, and 2 seconds in (A), (B), and (C), separately. The GC values of statistical significant links among four ROIs (1: AC, 2: MC, 3: SMA, 4: THA) are represented as gray levels in matrix form ($P < 0.01$, with Bonferroni correction). Two links become undetectable (MC → SMA and AC → THA) as TR lengthens as marked in red and yellow boxes.

Causal Link	TR=0.5-sec (# of subjects)	TR=2-sec (# of subjects)	$\chi^2(1)$	p<	TR=0.5-sec (# of subjects)	TR=1-sec (# of subjects)	$\chi^2(1)$	p<
AC->MC	14	7	7.778	0.0053*	14	14	0	0
AC->SMA	14	7	7.778	0.0053*	14	9	4.658	0.0309*
AC->THA	14	7	7.778	0.0053*	14	13	0.370	0.5428

Table 1 calculates the detectability of three outflowing links from AC (AC → MC, AC → SMA, and AC → THA) in 15 subjects. With TR of 0.5 second, the detectability of three links is higher than that with longer TR. Chi-squared test also confirms the observation.