Stimulus entrained dynamic effective connectivity analysis of fMRI

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Introduction

Granger causality (GC) has become a popular method to assess effective connectivity of brain networks from fMRI data [1]. However, hemodynamic variability [2] can affect the validity of GC-based inferences. In addition, it is difficult to obtain context-dependent and/or dynamic connectivity from traditional GC analysis (GCA) of short time series data. In order to alleviate these problems, we developed a stimulus-entrained, dynamic GC approach which not only models the time-varying connectivity but also determines whether the dynamics are entrained to external stimuli. We demonstrate the utility of this approach using a visual art paradigm.

Methods

T2*-weighted functional images were acquired using a single-shot gradient-recalled echoplanar imaging (EPI) sequence for BOLD contrast on a Siemens 3T scanner. 29 axial slices of 4 mm thickness were acquired using the following parameters: TR=2000 ms, TE=30 ms, FOV=220 mm, FA=90°, in-plane resolution 3.4×3.4 mm^2, and in-plane matrix 64×64. Each of the 8 participants completed 2 runs in a single scan session. Each run consisted of 50 trials of 2s duration, with a fixed interval of 8s between the end of one trial and the start of the next, in a 'slow' event-related design. In each trial, an image was presented for 1s, followed by a 1s response period; half the trials were art images and half were non-art images. Mean time series from regions significantly active on the art > non-art contrast as well as those exhibiting correlations between their activity and ratings of esthetic preference, were derived and used to obtain dynamic correlation-purged Granger causality (CPGC) for every run and every subject, using a first order model and wavelet transforms as described in previous reports [3,4]. The boxcar function corresponding to the experimental paradigm was smoothed by a standard HRF and entered into the design matrix along with subject factors. Using a general linear model, the CPGC paths which significantly ($p<0.05$, corrected) covaried with the experimental paradigm were determined. The advantage with this approach is that it does not suffer from the lack of sufficient TRs per event, which is often the case when applying traditional GC to event-related paradigms. Also, this approach formulates connectivity investigation within the methodological framework of "activity detection", which makes it easier to interpret the relationship between activity and connectivity. In order to demonstrate the effect of hemodynamic variability on this method, we simulated two time series by convolving the box car paradigm (Fig.1, green line) in one subject with two different hemodynamic response functions (Fig.1, red and blue lines), with an onset difference of 2.5 s between them, and obtained the corresponding dynamic CPGC and significance of its temporal variation using the Wald test [3].

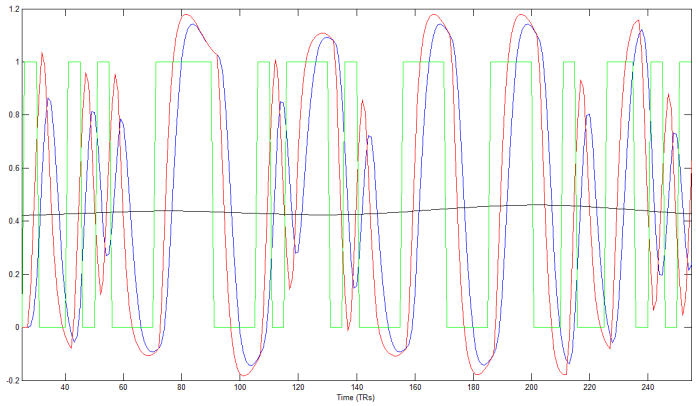

Fig.1 Green line: the stimulus paradigm in a subject, Red line: the product of the convolution of a hemodynamic response function (HRF1) with the stimulus paradigm, Blue line: the product of the convolution of a different hemodynamic response function (HRF2) and the stimulus paradigm with HRF2 lagging HRF1 by 2.5 s, Black line: dynamic CPGC between red and blue lines

Results and Discussion

Network analyses (Fig. 2) showed that, when viewing art images, the ventral striatum (VS) was driven by art-selective regions of visual cortex, particularly in the right hemisphere, but not by regions that were correlated with esthetic preference – these correlated regions did not show connectivity with the VS for either kind of image. When viewing non-art images, the VS was completely disengaged, with neither inputs nor outputs to any other region. Regions showing correlations between activation magnitude and esthetic preference ratings tended to drive visual cortical regions for both art and non-art images. These results show that art-selective activation of the VS is attributable to the status of images as art, rather than individual differences in esthetic preference [5]. The simulations showed that, given the temporally constant onset difference, the dynamic CPGC remains relatively constant around 0.4 (Fig.1, black line) and does not significantly vary across time ($p>0.05$). The simulation demonstrates that CPGC remains relatively constant over time even though its actual value is affected by the temporal onset time. Therefore, variation in CPGC should only reflect changes in causal influences from sources other than the hemodynamic response such as that due to the external stimulus. Therefore, stimulus dependent temporal variability of causality reported in this paper cannot be a spurious consequence of vascular-driven variability of the hemodynamic response.

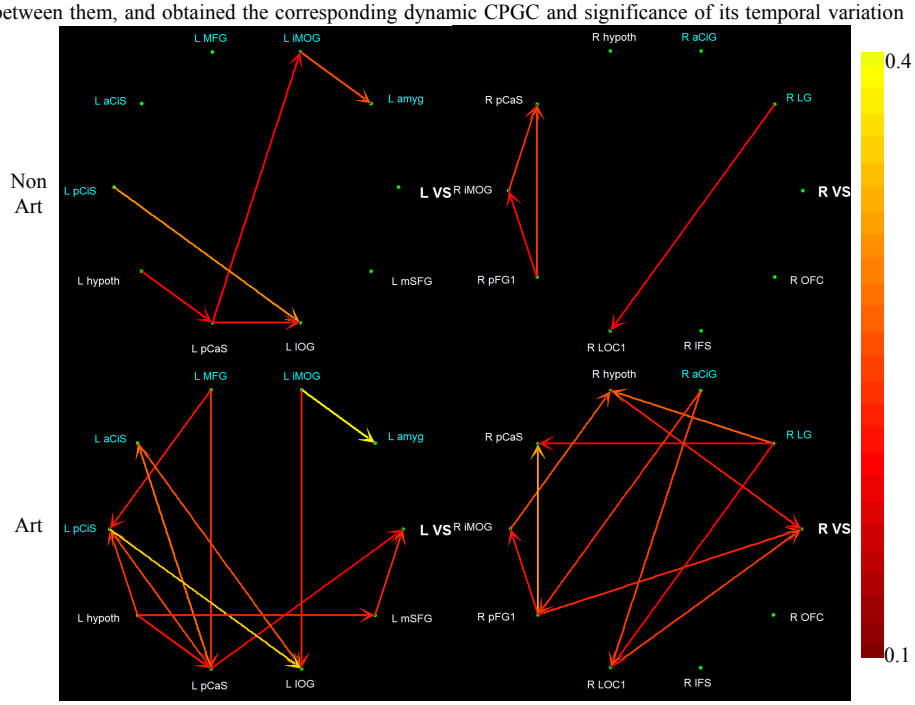

Fig.2 Paths between ventral striatum, art-selective regions (white) and regions correlated with esthetic preference ratings (blue) for non-art (top) and art (bottom) images, which significantly covaried with the stimulus paradigm. Left and right panels represent networks in the corresponding hemispheres. Abbreviations: amyg, amygdala; LG, lingual gyrus; CiG, cingulate gyrus; hypoth, hypothalamus; CaS, calcarine sulcus; MOG, middle occipital gyrus; FG, fusiform gyrus; LOC, lateral occipital complex; IFS, inferior frontal sulcus; OFC, orbitofrontal cortex; R, right; L, left; a, anterior; p, posterior

References

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Acknowledgement: Funding from University of Georgia (HH, VP, SR), National Institutes of Health (KS, GD, XH) and the Veterans Administration (KS).