Conditional Granger Causality analysis of fMRI data shows a direct connection from LGN to hMT+ bypassing V1

A. Gaglianese[1], M. Costagli[2], G. Bernardi[1], L. Sani[1], E. Ricciardi[1], and P. Pietrini[1]
[1]Laboratory of Clinical Biochemistry and Molecular Biology, Pisa, Italy, Italy, [2]Laboratory for Cognitive Brain Mapping, RIKEN - Brain Science Institute, Wako, Japan

Introduction

The human middle temporal complex (hMT+) is the main cortical area devoted to motion perception. Although major inputs to hMT +come from V1 and associative visual areas, findings from human and animal studies seem to suggest a direct anatomical link between the lateral geniculate nucleus (LGN) and hMT+ (1). This direct connection may be involved in the mechanisms for blindsight, that is, the persistent perception of motion in the absence of V1. The aim of this study was to verify the potential presence of a direct flow of information between LGN and hMT+ by measuring effective connectivity between thalamus, hMT+ and the primary visual cortex (V1) in healthy human subjects.

Material and Methods

Data were collected in two separate fMRI studies (GE Signa, 1.5 Tesla, TR = 1500 ms, 13 3mm-thick axial slices, FOV=24 cm, TE =40 ms, FA=90°, 128x128 pixels). In Experiment 1, four healthy volunteers (2F, 26±1 yr) were presented with block design visual stimuli alternating between moving (9s, radially outward, 100% coherence) and stationary (27s) white dot patterns. This moving/stationary pattern cycle was repeated seven times in each scan. In Experiment 2, events consisted of white dots moving radially at 100% coherence for 3 sec. The ISI consisted of stationary white dot patterns (6-12 sec).

Data analysis

The interaction among LGN and hMT+ was investigated using Granger Causality mapping (2). To discard the hypothesis that this connection could be simply an indirect effect mediated by the primary visual cortex, in addition to the traditional bivariate Granger Causality (BGC) measures, we used conditional Granger Causality (CGC) (3) analysis between LGN and hMT+ taking into account of V1 and Pulvinar (PUL) areas. After preprocessing (motion and slice scan time correction, spatial smoothing at 6-mm full-width at half- maximum (FWHM) 3D Gaussian filter and linear trend removal), two 5-mm spheres were located for each subject on the local maxima response in hMT+ and V1 as defined in multiple regression analysis and based on anatomical landmarks. LGN and PUL were defined in the Talairach space. Two control ROIs encompassed Broadmann Area 43 (BA43) and the white matter (WM).

Granger Causality & Conditional Granger Causality:

A process X is said to Granger cause a process Y, if knowledge of the past of X improves the prediction of Y compared to the knowledge of the past of Y alone. Thus, given two time series X(t) and Y(t), we can independently identify both influence from X to Y, and influence in the reverse direction. Yet, this approach does not take into account for indirect and spurious influences of third sources that play a role of common input to X and Y and that are not accounted for in the traditional BGC analysis. To prevent this ambiguity, our model is based on CGC measures in the frequency domain (Geweke,1982 Chen, 2006) applied on fMRI data. Therefore, a third model including additional processes Z(t) and W(t),was considered in the evaluation of the influence between X and Y. For example, to test the connectivity between LGN (X(t)) and hMT+ (Y(t)), V1 (Z(t)) and Pulvinar (W(t)) were included in the model. Algorithms were implemented in Matlab. Output functions were the spectra of the BGC and CGC coefficients for each pairwise combination of the ROIs averaged time series in the range (0-0.33Hz). To infer significance a bootstrapped null distribution of size 1000 was computed for each frequency, for each measure, by the shuffle of the estimated autoregressive coefficients from data. To evaluate CGC group map, the GC mean value for each connection was computed in the band 0.01~0.12 Hz, which encompassed the relevant frequencies of typical hemodynamic response functions (4). These values were compared with their corresponding mean null distributions to derive a P-value. A single group P-value for each connection was obtained using Fisher's method (p = 0.05, chi distribution) (5)

Results

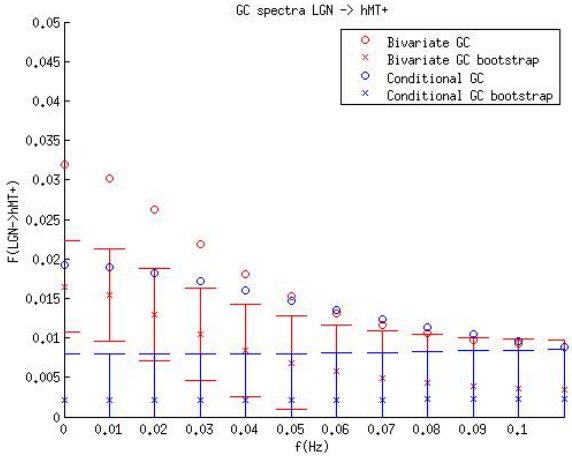

Fig.1

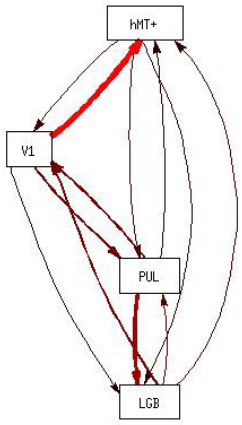

Fig.2

The BGC (blue dots) spectrum for one representative subject is presented in Fig.1, and shows significant causal influence from LGN to hMT+ in the range 0-0.12 Hz. The CGC spectrum for the same pair of regions (red dots), but with area V1 and PUL taken into account, is superimposed. The corresponding bootstrapped null distributions (blue and red stars respectively) are also presented. CGC spectrum was partially reduced respect to the bivariate analysis but was still statistically significant, meaning that the causal influence from LGN to hMT+ is not merely an indirect effect mediated by V1. Statistical significance in each frequency band was derived by comparing the GC coefficients to the 95% percentile of the bootstrap distribution. CGC group results on the pool of the 9 subjects from both experiments showed similar results (Fig. 2, thickness of arrows represents the CGC coefficients of each connection). In addition to the main, traditional pathway LGN→V1→hMT+, which was clearly detected by our analysis, the direct LGN→hMT+ pathway, though weaker, was statistically significant ($p<0.01$).

Conclusion

Results from effective connectivity, as measured by BGC and CGC, indicate the existence of a bilateral alternative pathway for visual motion processing that allows for a direct flow of information between LGN and hMT+. This direct flow may contribute to maintain residual perception of motion in individuals with lesions of primary visual cortex.

Reference

[1] Lanyon L.J. et al., 2009, 'Combined functional MRI and diffusion tensor imaging analysis of visual motion pathways', Journal of Neuro-Ophthalmology, vol. 29, pp. 96-103.
[2] Roebroeck A. et al., 2005, 'Mapping directed influence over the brain using Granger causality and fMRI', NeuroImage, vol. 25, pp. 230-242
[3] Chen Y. et al., 2006, 'Frequency decomposition of conditional Granger causality and application to multivariate neural field potential data', Journal of Neuroscience Methods, Vol. 150, pp. 228-237.
[4] Lauritzen T.Z. et al, 2009. 'Top–down flow of visual spatial attention signals from parietal to occipital cortex', Journal of Vision, Vol.10, no.2
[5] Deshpande G. et al, 2009. 'Multivariate Granger causality analysis of fMRI data', Human Brain Mapping, Vol.30, no.4, pp. 1361–1373