Differential Resting-State Network Connectivity of Extrastriate Body Area and Lateral Occipital Complex

Kaundinya Gopinath[1,2], Aman Goyal[2], Richard Briggs[2], and K Sathian[3]

[1]*Department of Radiology & Imaging Sciences, Emory University, Atlanta, GA, United States,* [2]*Department of Radiology, UT Southwestern Medical Center, Dallas, TX, United States,* [3]*Department of Neurology, Emory University, Atlanta, GA, United States*

Introduction: A number of areas in the human occipitotemporal cortex (OTC) are specialized for processing particular types of sensory stimuli [1-4]. These include the lateral occipital complex (LOC), an object-selective area; the fusiform face area (FFA), a face-selective area; the parahippocampal place area (PPA), a scene-selective area; and the extrastriate body area (EBA), a body part-selective area. Examining resting state functional connectivity networks of these areas will yield insights into the processing of different types of stimuli. In this study, fcMRI networks of OTC sub-regions were delineated with seed and graph based approaches [5].

Methods: Nineteen right-handed normal subjects (16 male; 3 female; mean age = 30.9 yrs) were scanned in a Siemens 3T Tim Trio scanner using a 12-channel array receive-only head coil. Written informed consent was obtained from all participants in the protocol approved by the local Institutional Review Board. In the fcMRI paradigm, subjects underwent an 11-minute fcMRI scan during which they lay quietly in the scanner with their eyes open. FcMRI scans were acquired with an axial whole-brain gradient echo EPI (TR/TE = 2000/24 ms, FA = 80°, in-plane resolution = 3.4 mm x 3.4 mm; 40 slices with thickness 3.5 mm).The fcMRI time-series were, registered, spatially normalized to the MNI template and low-pass filtered (0-0.1 Hz), followed by spatial smoothing with a FWHM = 5 mm isotropic gaussian kernel. ROI-averaged time-series were obtained from 5mm spherical seeds placed at centers of activation in EBA, LOC, FFA and PPA seen in appropriate sensory processing studies [1-4], which served as reference vectors in cross-correlation analysis (CCA). Mixed-effects ANOVA (ROI X Subjects) was performed on z-transformed CC maps, to assess functional connectivity networks of EBA, LOC, FFA and PPA, as well as assess differences in functional connectivity between the 4 regions. The resultant statistical parametric maps were clustered and significance of cluster-level activation was assessed with Monte-Carlo modeling [6].Graph theory measures were employed to further probe the network structure of each OTC sub-regions' functional connectivity maps. Graphs for OTC ROIs were formed by considering areas significantly connected (average $CC_{ROI} > 0.3$; cluster $p < 0.0001$) to respective ROIs, resampled to 6 mm^3 voxels and restricted to gray matter. For each ROI, a binary distance matrix was constructed by averaging the individual correlation matrices for all subjects and setting all connections below the threshold average CC to 0. The threshold was adjusted so that the modularity, M [5, 7] of the graph was > 0.3 [7]. Modularities of equivalent random graphs [5], M_{random} were also obtained for comparison. Data analysis was performed with AFNI, FSL and Brain Connectivity toolboxes [5].

Results & Discussion: EBA exhibited strong functional connectivity (CC > 0.3, cluster-level $p < 0.0001$) with a number of different brain regions. When these regions were further examined with graph theory based modularity analysis they exhibited segregation into three modules (Figure 1; M > 0.3; $M_{random} = 0.02$): a module (blue) consisting of the default mode network (DMN) and limbic regions; a second module (red) more strongly connected with EBA, consisting of motor cortex, Brodmann area (BA) 6 and superior temporal gyrus (STG); and a third module (yellow) comprising occipital gyrus, OTC and medial posterior parietal cortex. When modularity analysis was applied to regions strongly connected to LOC (CC > 0.3, cluster-level $p < 0.0001$), three modules (M > 0.3; $M_{random} = 0.02$) were obtained (Table 1): an OTC and occipital module comprising lateral frontal and parietal attention networks and a third module consisting of somatosensory regions. In the EBA vs. LOC contrast (Figure 2; Table 2), EBA exhibited significantly (cluster-level $p < 0.05$) higher functional connectivity with DMN regions, motor and premotor cortex, and middle occipital gyrus. LOC exhibited significantly (cluster-level $p < 0.05$) higher functional connectivity with lateral frontal, parietal and somatosensory areas.

The stronger functional connectivity of EBA with DMN is consistent with studies that report a role for self-referential processing [8] in visual representation of bodies. The stronger functional connectivity of LOC with frontoparietal and somatosensory regions is consistent with a model of multisensory object representation, engaging both top-down and bottom-up connections [9]. FcMRI networks reveal different pathways for body and object representation in the brain. Graph theory based modularity analysis reveals sub-networks within the regions functionally connected to EBA and LOC, representing their involvement in different cognitive systems.

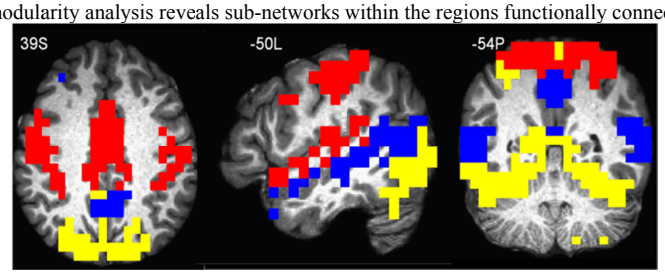

Figure 1: Brain regions functionally connected to EBA (CC > 0.3; $p < 0.0001$) segregated into 3 modules (2475 nodes). Slice locations in MNI co-ordinates.

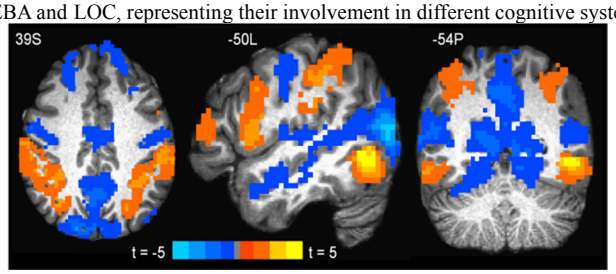

Figure 2: LOC – EBA t-contrast map ($p < 0.05$). Slice locations in MNI co-ordinates.

Table 1: Brain regions functionally connected to LOC (CC > 0.3; $p < 0.0001$; 2061-node graph) segregated into 3 modules

Module 1 $<CC_{LOC}> = 0.41$; 957 nodes	Occipital gyrus, OTC, cerebellum, cuneus
Module 2 $<CC_{LOC}> = 0.41$; 344 nodes	Frontal and parietal regions: inferior and superior parietal lobules (I/SPL), BA7, dorsolateral PFC, LOC, BA9, BA46
Module 3 $<CC_{LOC}> = 0.37$; 760 nodes	Sensory areas: primary (S1), and secondary (S2) somatosensory cortex, BA5, STG and insula

Table2: LOC vs EBA functional connectivity differences (ANOVA t-contrast cluster-level $p < 0.05$)

EBA > LOC	PCC, LPC, precuneus, medial PFC, ITR, MTG, amygdala, ventrolateral PFC, BA 38, cuneus, middle occipital gyrus, EBA, M1, premotor cortex, cingulate, SMA.
LOC > EBA	Dorsolateral PFC, inferior frontal gyrus, lateral BA6, IPL, SPL and BA 40, lateral BA7, LOC, S1, S2, insula

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